

Screen it! Treat it! Beat it!

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Treatment of Colorectal Cancer



A diagnosis of colorectal cancer can be an overwhelming event. The emotional impact is intense. And, at the same time, you feel under pressure to act quickly, knowing the importance of getting treatment as soon as possible.

This guide was developed to help you through this immediate situation – and throughout your cancer journey. With so many things going on, you need practical, useful information about therapeutic options in order to ask the right questions of your physician and to share in decisions about your treatment.

Each person is different and a personalized approach to treatment takes into account factors related to your tumour, your body, your overall health and your preferences. Advances in research over recent years have meant that more treatment options than ever are available to meet the needs of individual patients.

Colorectal Cancer Resource & Action Network (CCRAN) has prepared descriptions of treatments according to each stage of disease: surgery, radiation therapy, chemotherapy and targeted anti-cancer drugs.

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Treatment of Colorectal Cancer

PART I: INTRODUCTION

Receiving a diagnosis of colorectal cancer is an overwhelming event. Not only are you on an emotional rollercoaster, but at the same time you feel under pressure to make decisions about your treatment. It's hard to think things through logically when your feelings are blocking out your rational thought processes.

This booklet is intended as a practical guide to help you through this 'tsunami' of events and emotions. It provides a basic outline of treatment options available at each stage of the disease. It also contains links to more in-depth information from reputable sources if you want to know more about certain topics.

Focusing on your own situation and needs is the starting point in considering treatment options. Each person is different. These are some of the factors that make your situation unique:

Your cancer

- The stage (0, I, II, III and IV) and grade (G1 to G4) of the cancer
- Biological and molecular profile
- Location of the tumour within the colon or rectum

Your body & medical history

- Other medical conditions
- Age and sex

Your preferences

- Do you want to try all possible options, regardless of their potential downsides, or are there circumstances where you would not want treatment?
- If there is a choice, would you prefer one mode of therapy over another?

Practical considerations

- Will you have to travel to receive treatment?
- Will there be long-term side effects of treatment?
- Will you need personal support during your recovery?

Remember that treatment decisions are a shared responsibility between you and your treating physician. Knowing the basics about your disease and possible treatments will allow you to fully take part in discussions and decisions. Understanding the roles of each member of your oncology care team will ensure that you get the information and attention that you need.

PART II: OVERVIEW OF TREATMENT OPTIONS

There are three types of therapy for colorectal cancer: surgery, radiation therapy and systemic therapy (chemotherapy, biologic therapy, and immunotherapy).

Surgery is the most common treatment for colon and rectal cancer. In stage 0/I, a local excision (removal of a tumour or polyp) using a colonoscope may be all that is needed. For most patients, however, a bowel resection is required in which part of the intestine and nearby lymph nodes are removed.



Radiation therapy is also used in colorectal cancer treatment, especially for rectal tumours that need to be reduced in size before surgery or chemotherapy. Radiation therapy may also be used in the treatment of colorectal cancer that has spread to other organs such as the liver.

Systemic therapy uses medicines that travel through the bloodstream, reaching and affecting cells all over the body. Examples of systemic therapies include chemotherapy, biologic therapies or targeted therapies and immunotherapies. Chemotherapy is sometimes recommended for stage II colorectal cancer, and usually recommended for stage III and stage IV colorectal cancer. For stage IV colorectal cancer, chemotherapy may be given in combination with targeted therapies, or on its own.

PART III: CONSIDERATIONS WHEN DECIDING ON A TREATMENT PLAN

Treatment protocols for colorectal cancer are based on proven therapies. These are personalized according to the following factors:

- Stage and grade of disease
- Tumour profile (biological and molecular markers, as well as location within the gastrointestinal tract)
- Patient's age, sex and health status
- Patient preferences and practical considerations

This information needs to be known before having a discussion with your doctor about which treatment options are best for you.

Here is what all of this means in practical terms.

i. Stage of Colorectal Cancer

Staging is a system of classification which describes how advanced the cancer is in your body, and whether or not it has penetrated the wall of the colon or rectum or spread to other systems or organs in the body. (More information is available in the Staging section of this website.)

There are five stages of colorectal cancer – the higher the stage (represented by the roman numeral), the more advanced the cancer.

Stage 0 (also called carcinoma in situ)- The cancer is confined to the innermost layer of the colon or rectum. It has not yet invaded the colorectal wall.

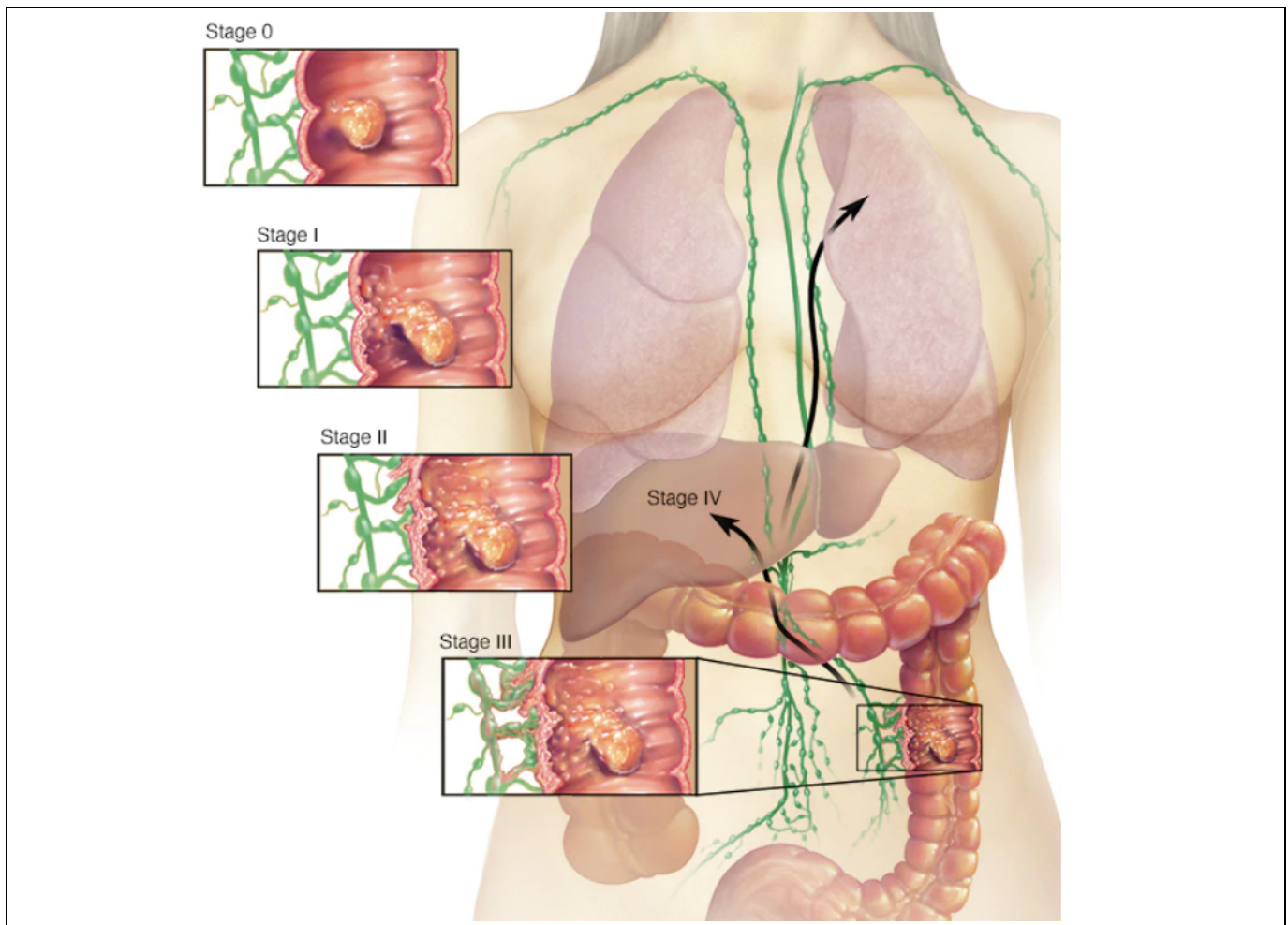
Stage I - The cancer has penetrated some or several layers of the colon or rectum wall.

Stage II - The cancer has penetrated the entire wall of the colon or rectum and may extend into nearby tissue(s).

Stage III - The cancer has penetrated the entire wall of the colon or rectum and has spread to the regional lymph nodes. Lymph nodes are small pea sized glands that we have all over our body. Cancer can spread from the primary site to these small glands. If cancer is found in these glands, when checking under the microscope, it is an indication that this cancer has the ability to spread to distant organs in the body.

Stage IV - The cancer has penetrated the entire wall of the colon or rectum, spread to the regional lymph nodes and has spread to distant organs, often to the liver or lungs.

STAGES OF COLORECTAL CANCER



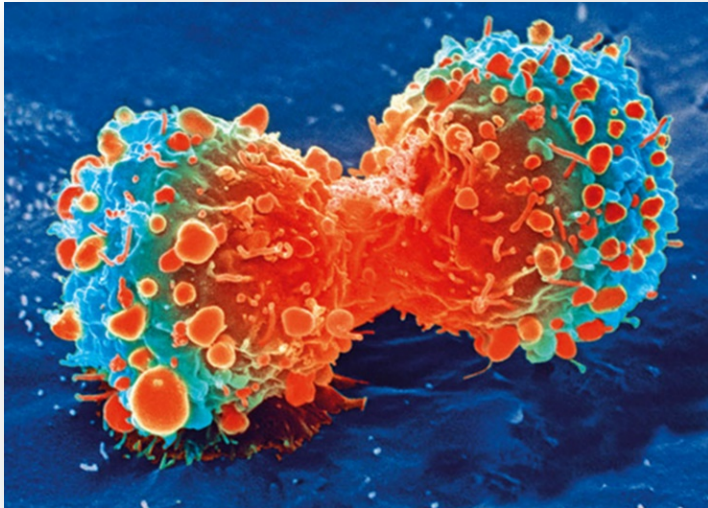
Source; <https://www.mayoclinic.org/diseases-conditions/colon-cancer/multimedia/colon-cancer-stages/img-20007084>

Early stage colorectal cancers (Stages 0, I and II) can be detected by routine testing of healthy individuals, using techniques such as the Fecal Occult Blood Test (FOBT), Fecal Immunochemical Test (FIT) or colonoscopy. With treatment, the prognosis of early stage colorectal cancer is very good.

Because symptoms generally do not appear until the colorectal cancer is more advanced, most patients are diagnosed at Stage III or IV. These cancers require more aggressive forms of treatment.

ii. Grade of Colorectal Cancer

Colorectal cancer can also be classified by its grade, which describes how closely the cancer looks like normal tissue when viewed under a microscope. Cancer cells are less differentiated, or mature, than normal cells. The more undifferentiated the cells are, the more likely the tumour is to be aggressive.



There are 4 grades of cancer (G1 to G4), however this is often simplified as either Low Grade (G1 or G2) or High Grade (G3 or G4). Low-grade cancers tend to grow and spread more slowly than high-grade cancers.

courtesy of the National Cancer Institute)

Cancer cell during division :(Photo

iii. Anatomical Location and Biological Profile

You should know the location of your tumour within the colorectum and whether or not your tumour has biological or molecular markers that could affect its response to certain anti-cancer drugs. (See the Biomarkers section for more details.)

Here are some examples.

Biomarker	Impact on treatment
Tumour originating on the right side of the body	Respond to drug regimens such as bevacizumab (Avastin [®] , Mvasi [®]) plus ‘triple chemotherapy’ (combinations of three anti-cancer drugs).
Tumour originating on the left side of the body	Respond to drug therapies such as bevacizumab (Avastin [®] , Mvasi [®]) or anti-EGFR antibodies (such as cetuximab or panitumumab, provided no RAS mutation is harbored) combined with conventional chemotherapy.
KRAS or NRAS gene mutations BRAF mutations	Patient will not respond to standard therapies that inhibit epidermal growth factor receptors (EGFR), such as Erbitux [®] or Vectibix [®]
PIK3CA gene mutations	Patients with this mutation may benefit from aspirin therapy after surgical resection to help decrease the risk of recurrent cancer
HER2 receptor	Anti-HER2 agents are being explored, such as trastuzumab (Herceptin [®]) and lapatinib (Tykerb [®]) for HER2 positive colon cancers.
TRK gene fusions	May respond to Larotrectinib (Vitrakvi [®]) if an NTRK Gene Fusion is identified.
MSI-H/dMMR testing	Immunotherapies show promise in treating MSI-H tumours: <ul style="list-style-type: none"> • Pembrolizumab (Keytruda[®])

iv. Your Sex, Age and Medical History

Your sex may affect your tumour profile and influence the choice of treatment. For example, tumours originating on the right side of the body (cecum and ascending colon) are more prevalent in women and tend to have a worse prognosis. The opposite is true for men, who tend to develop tumours on the left side of the body, which have a better prognosis.

The risk of developing colorectal cancer increases significantly with age, therefore, many patients will be older. At the same time, the risk of developing other medical conditions, such as diabetes, vascular disease and impaired renal function, also rises with age. These conditions may increase the risk of side effects from chemotherapy.

Cancer found in its early stages is usually curable by surgery and adjunctive therapy, regardless of the patient's age. The efficacy of drug treatments and radiotherapy also is likely to be the same regardless of age.

Elderly patients (over age 75) may be at greater risk for harm from treatments for more advanced colorectal cancers, including surgery, chemotherapy and radiotherapy, and may be less able to tolerate aggressive surgery.

v. Your Preferences and Practical Considerations

It is important that you discuss your preferences with your oncology care team throughout your cancer treatment journey.

For example: Is it important for you to try all possible treatment options, regardless of their potential downsides? Are there circumstances where you would not want treatment? If there is a choice, would you prefer one mode of therapy over another?

Starting a conversation with your doctor based on questions like these will help to define a range of options that best suits your needs.

There are also practical considerations related to treatment that you will need to think about and discuss with your oncology care team.

For example:

- Will you have to travel to receive treatment?
 - Is travel feasible for you?
 - Are there financial or other practical supports available if you need to spend a prolonged period of time in accommodations near the hospital?
 - Is someone available to care for your dependants at home while you're away?

- What could be the side effects of treatment and how can they be managed?
- Will you need personal support during your treatment and recovery?

It is important that your questions are properly addressed with your doctor before commencing treatment. Below are some general treatment-related questions that may be helpful for you to review prior to discussing therapy options with your surgical oncologist, medical oncologist or radiation oncologist. A more extensive list of questions related to each of the three types (modalities) of treatment is provided later on in this section.

We recommend that a family member or friend be present for meetings with your oncologist as a “second set of ears” to ensure you capture everything that is said during those appointments.

Questions to ask your doctor about treatment options

Deciding on an overall approach to treatment

Is there a cure for my condition? What is my prognosis, as you see it?

Do I have an inherited form of colorectal cancer? If so, do I need to inform my family?

How does my past medical history affect which treatments are options for me?

Based on the stage of my disease, what is your recommended treatment option?

What is the goal of treatment?

What other types of colorectal cancer treatments are available?

What are the benefits, disadvantages, and possible complications of the proposed treatment plan for colorectal cancer? (this may include: chemotherapy, radiation therapy, targeted therapy, immunotherapy)

What do these colorectal cancer treatments involve?

How long will I have to undergo the treatment?

For each possible treatment option, what are the chances that my cancer might come back?

Does my hereditary colorectal cancer diagnosis mean I am at higher risk for any other type of cancer?

Tailoring treatment to my situation

Is combination chemotherapy a treatment option that is appropriate for me?

Are there any “high-risk” features of my tumour that make it more important for me to consider combination chemotherapy?

For Stages I, II, and III:

What would the benefit be from additional treatment after the cancer is removed by surgery?

For each possible treatment option, what are the chances that my cancer might come back?

Stage IV/Recurrent/Relapsed:

Will the results of the treatment be worth the side effects I may suffer?

Can I choose a less aggressive treatment so as to keep me comfortable?

Does my cancer have targetable mutations to treat?

Am I a candidate for immunotherapy?

What possible long-term effects might occur as a result of the treatment?

For younger patients: Will the treatments affect my ability to have children? Is there a way to protect my fertility?

Details about the treatment plan

What are the names of the drugs I require and what are they for?

How long does each type of the treatment take?

What are the potential benefits and drawbacks of this treatment?

What are the common side effects of the recommended treatment?

What should I do if I experience severe side effects? Telephone # to call: _____

What can I do to safeguard against the onset of side effects?

How will you know that my treatment is working?

How can I expect to feel during treatment?

What happens if I miss a treatment?

Are there any alternative or complementary therapies that I should consider?

Is a clinical trial appropriate for my situation? Why or why not? Would I receive better medications?

Practical considerations

What will the treatment schedule look like in terms of how many days I will need to come into the clinic, how long I will have to stay each day, and how many days after a treatment I might need to take off work or limit other plans?

Which centre would be able to provide the best treatment for my cancer?

When should I start treatment?

Is it okay to wait to start treatment as a result of?

Will I need to spend time in the hospital? If so, for how long?

Is the recommended therapy covered? If not, will my insurance plan cover the therapy?

If I do not have third party coverage, what are my options?

During treatment

How will my condition be monitored after my cancer treatment?

Can I work during treatment if I wish to do so?

If other specialists take part in my care, who will coordinate my entire treatment program?

If I don't feel ill, does this mean the treatment is not working?

Are there any steps I should take during or after treatment to help myself stay healthy?

Follow-up

How often should I be seen for follow-up appointments?

Why do I need blood tests and how often will I need them?

Once I finish treatment, how will I be monitored for recurrent cancer?

What follow-up tests will be done and at what intervals?

Do you regularly measure CEA (carcinoembryonic antigen) levels? If so, how often? What will you do if this level increases?

Can you recommend a local or online support group for people who have colorectal cancer and for their families to me?

Deciding against treatment

If I decide to receive treatment, what is my chance of remaining disease-free?

If I decide not to receive treatment, what is my chance of remaining disease-free?

What will happen if I refuse further treatment?

What happens if I react badly to treatment and need to stop? Will we try something else instead?

Thinking it over

How do I contact you if I have further questions?

vi. Getting a Second Opinion Through Tumour Board Rounds

Deciding on a treatment plan for your colorectal cancer can be quite complex. It is an important decision and you may feel swept up in the process without having time to think through the implications. Many cancer centres have tumour board rounds where cases are discussed with other cancer specialists including medical, radiation and surgical oncologists. If you live near a smaller cancer centre, your case may be discussed with a larger cancer centre. This may provide a different perspective on your case. Your doctor might mention that your case was or will be discussed at tumour board rounds. As a patient, you can also ask for your case to be discussed at tumour board rounds to obtain a different perspective on your case and on the management of your disease.

Many patients seek the security of having their case presented to tumour board rounds who can look at their test results in an objective manner and provide an opinion on their case.



If you do not have a therapeutic relationship with your doctor, you can ask for a transfer of care. The following questions may help you to raise the subject with your doctor:

- I would like to get a second opinion and would therefore like to be transferred. Will you assist me with that?
- If you had my type of cancer, who would you see?
- I think I would like to speak to another doctor to be sure I have all my bases covered.
- I'm thinking of seeking out another opinion. Can you recommend someone? If so, who would you recommend and why?

Your doctor may refer you to another specialist, or you may wish to seek out a second opinion/transfer of care on your own. If so, your family doctor may forward a referral, or your treating physician can forward the referral. Most centres in Canada will supply the referral but the patient will typically not be permitted to go back to the original oncologist.

Please note: some locations in Canada may not accommodate a second opinion. Hence, the Tumour Board Rounds are the best way to secure another opinion on your case.

PART IV: TREATMENT OPTIONS ACCORDING TO DISEASE STAGE

A. Stages 0 and I

This is the earliest stage of the disease, where the cancer is either confined to the innermost layer of the colon or rectum or has penetrated some or several layers of the colon or rectum wall. With treatment, the prognosis at this stage is very good.

Polyps, which may become cancerous if untreated, are detected by colonoscopy and can be removed through the colonoscope (polypectomy).

Less-Invasive Surgical Techniques to Treat Early Stage Rectal Cancer

Unlike traditional surgery where a major portion of the large intestine is removed, newer less-invasive techniques precisely remove the diseased tissue from the rectum and lower part of the colon, leaving the rest of the bowel intact to function normally.

Every rectal cancer is different and, therefore, every treatment strategy requires thoughtful consideration as to the best surgical approach for each individual patient. For some very early stage rectal cancers and rectal polyps, natural orifice surgery or **transanal minimally invasive surgery (TAMIS)** allows the surgeon to precisely remove the tumour from within the rectum. This is done with special instruments to magnify and project the area onto a monitor and with long thin instruments the tumour is removed, and the area is sutured. Patients can walk out of hospital the very same day; they require no incisions at all to treat their rectal lesions.



Image Source: <https://sunnybrook.ca/content/?page=minimally-invasive-surgery-colon-rectal-cancer>

For larger rectal cancers, local removal with TAMIS is not appropriate and these patients historically require large open abdominal incisions in order to remove the rectum itself. Instead, at regional cancer centres such as Sunnybrook, surgical procedures such as **TaTME (transanal total mesorectal excision)**, have been implemented, which means they complete the same removal of the rectum, wherein the cancer dwells, through natural orifice surgery with laparoscopic instrumentation. Once the cancer is removed the two ends are joined together (anastomosis) to make a new connection. This is all done through laparoscopic natural orifice surgery in order to avoid incisions and offer more magnified accuracy during the surgery.

“This novel approach
is changing rectal
cancer management
worldwide.”
– Dr. Shady Ashamalla

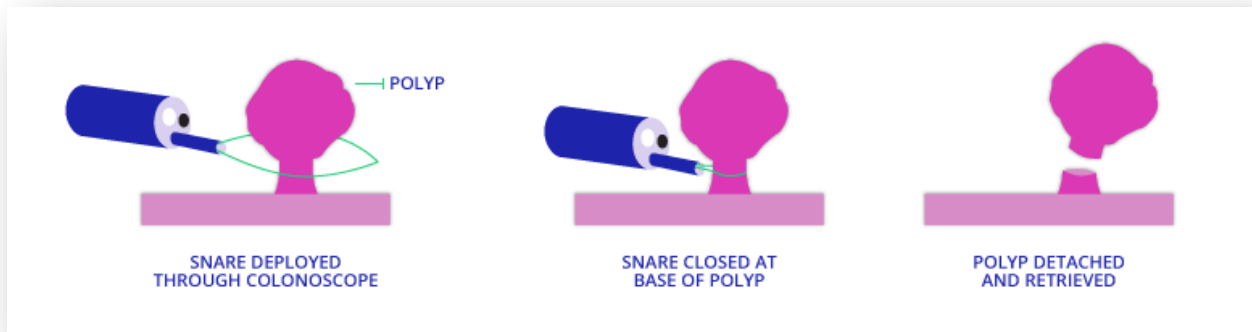
This novel approach is changing rectal cancer management worldwide and provides new hope for patients with very low rectal cancers to avoid permanent pouches.

Transanal Endoscopic Microsurgery (TEMs) involves specially designed microscope and instruments that are inserted through the anus, allowing surgery to be performed inside the rectum. This can be done in very early cancers or considered where the TEMs operation is safer than major surgery.

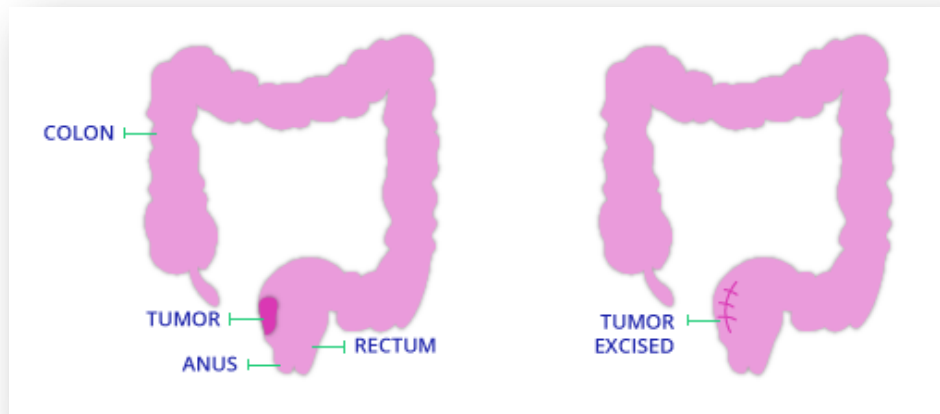
Transanal Minimally Invasive Surgery (TAMIS) is a further development of the TEMs technique which requires less expensive equipment and specialized training of surgeons.

The illustrations below show how three types of early-stage colorectal cancer are removed using two less-invasive approaches as well as a low anterior resection procedure.

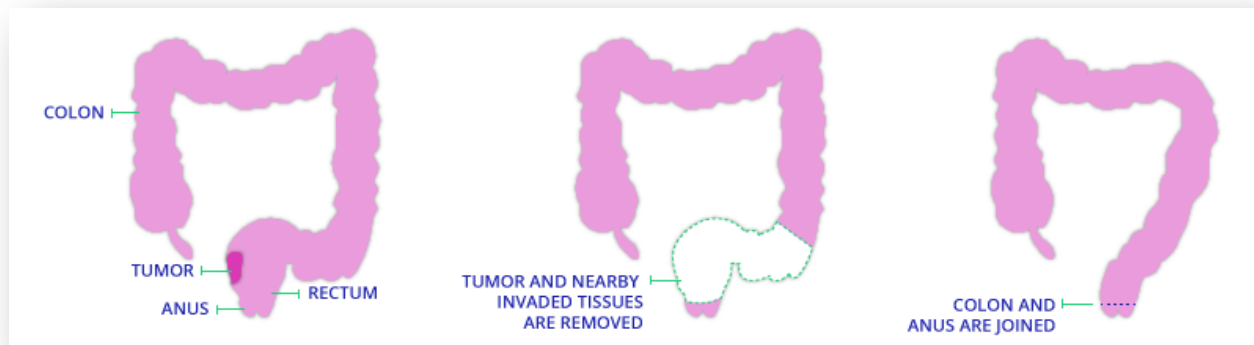
a) Polyp Removal



b) Local Excision of Early Cancers



c) Lower Anterior Resection (LAR)



Source: <http://www.tamisurgery.com/options>

Follow Up After Surgery

No further treatments are recommended for stage 0/I colorectal cancer following surgery or polypectomy. However, because your risk of developing colorectal cancer is elevated, a follow-up plan should be put in place. FOBT or FIT testing should be done annually (as is recommended for all adults over age 55). Follow-up colonoscopies should be performed every 3 to 5 years. Any new polyps can be removed at that time.

B. Stages II and III

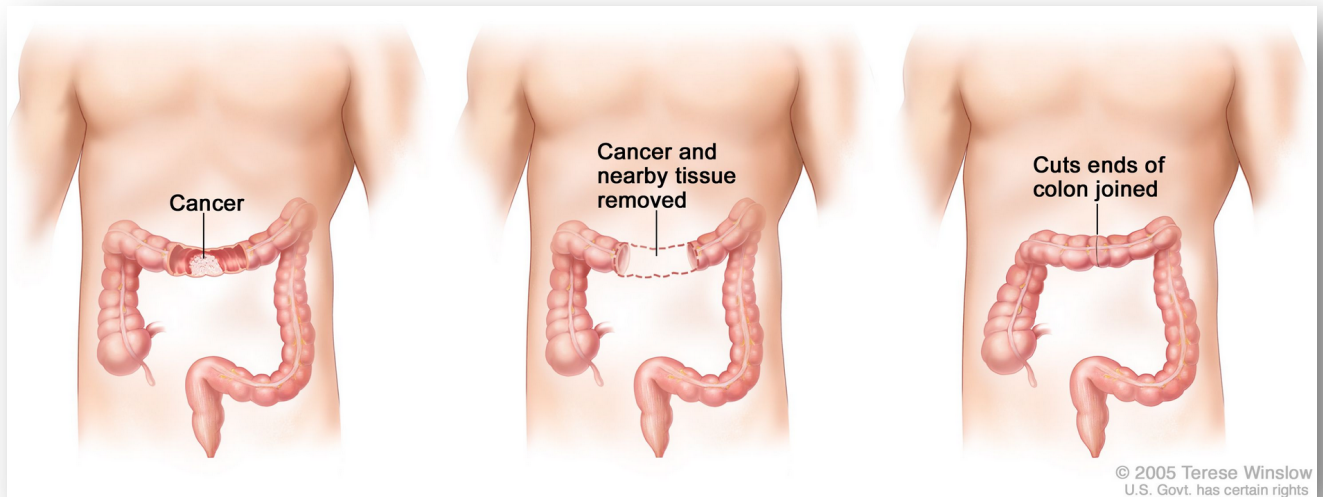
i. Surgical Therapies for Stage II/III Colorectal Cancer

Surgery is the mainstay of treatment for stages II and III colorectal cancer where the tumour has penetrated the entire wall of the colon or rectum and may have spread to the regional lymph nodes.

Colon cancer

The tumour, lymph nodes and some of the healthy surrounding tissue is removed (resected) in a procedure known as a partial colectomy. If a portion of the colon is removed, the two ends are then joined together (anastomosis) so that healthy bowel function can resume.

Illustration of resection of the colon with anastomosis



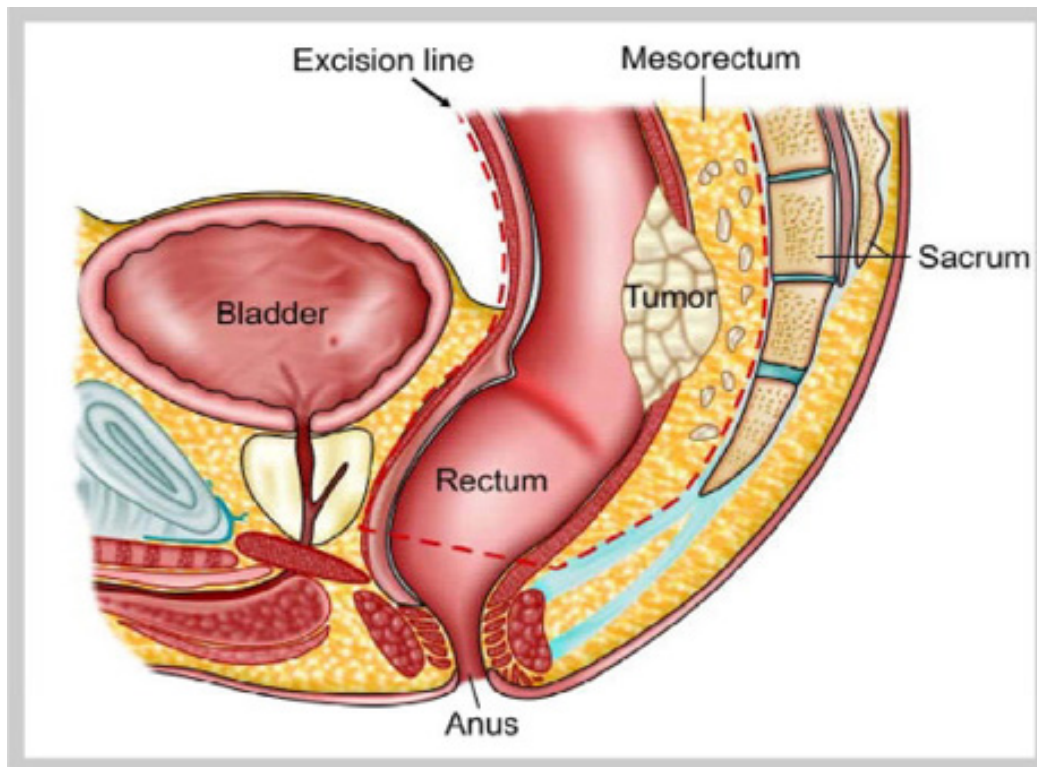
During a colectomy, surgery for colon cancer, the cancer and nearby tissue is removed and the remaining sections of colon are rejoined.

Source: National Cancer Institute. https://www.cancer.gov/types/colorectal/patient/colon-treatment-pdq#_162

Rectal cancer

Because of its anatomical location, the surgical procedure to remove a rectal cancer is somewhat different. The rectum is tightly enclosed with several other organs within the pelvic area, making it more difficult to isolate the tumour. A surgical technique, called **Total Mesorectal Excision (TME)**, which removes the sheet of fatty tissue (mesentery) around the rectum, thus ensuring that all of the cancerous cells are taken out.

Illustration of Total Mesorectal Excision for Rectal Cancer



Area inside red dotted lines removed during surgery

In TME, the rectum and the mesorectum are removed. The mesorectum is the area of fatty tissue below the rectum that contains lymph nodes, which are the most common area for the cancer to spread.

Source: <https://www.iaypeedigital.com/book/9789350250518/chapter/ch28>

The surgeon removes the part of the rectum that contains cancer, as well as some healthy tissue on either side. They also remove the fatty tissue (mesorectum) around the rectum, which contains blood vessels and lymph nodes. Removing the mesorectum reduces the risk of any cancer being left behind.

In the diagram above, the black dotted line shows an example of the tissue that may be removed during a TME operation.

Types of Surgical Procedures

The type of procedure your surgeon will perform depends primarily on the location of your tumour. There are two main types of surgery for colorectal cancer: Abdominal Perineal Resection (APR) and Lower Anterior Resection (LAR).

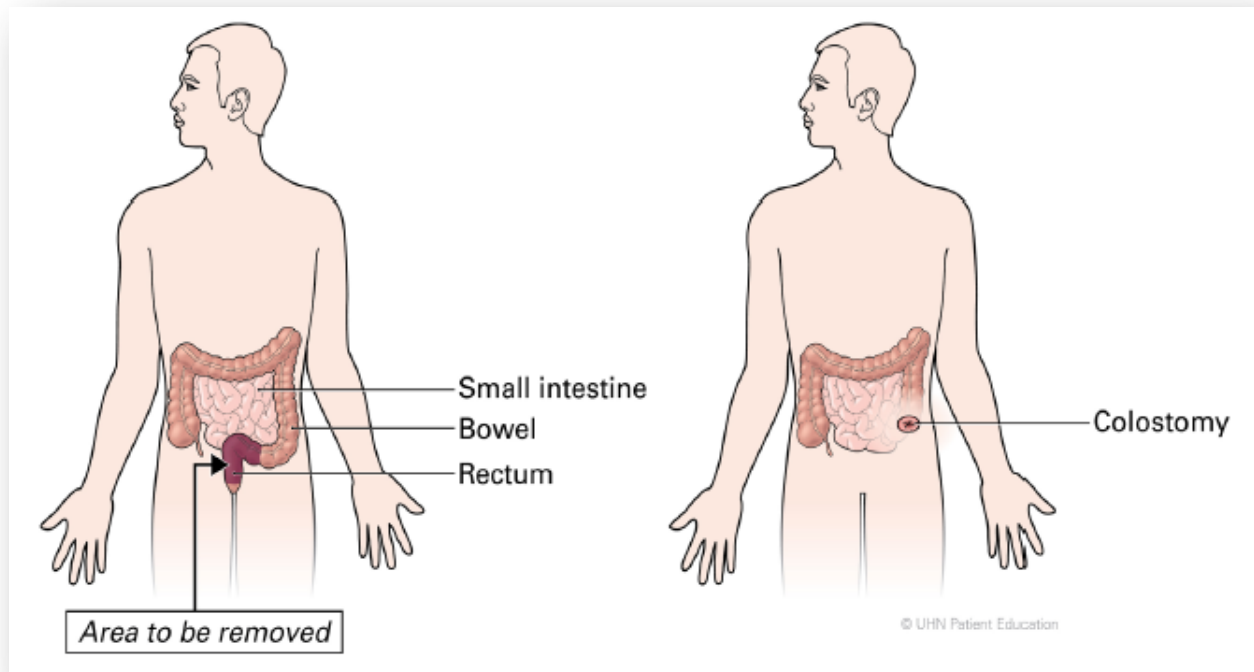
Abdominal Perineal Resection (APR)

APR is a surgery that's done to treat anal or rectal cancer. To remove the cancer, your surgeon will remove all of the following:

- The lower part of your colon (sigmoid colon)
- Your rectum
- Your anus

An APR can be done using different techniques. Open surgery involves making one long incision on your abdomen and another incision in your perineal area (between your vagina and anus or scrotum and anus). When several small incisions are made on your abdomen, this is called minimally invasive, or laparoscopic, surgery. Small surgical tools and a video camera are inserted into the incisions to remove the cancer. Please note that an APR will have a permanent colostomy.

Illustration of Abdominal Perineal Resection (APR) with Colostomy



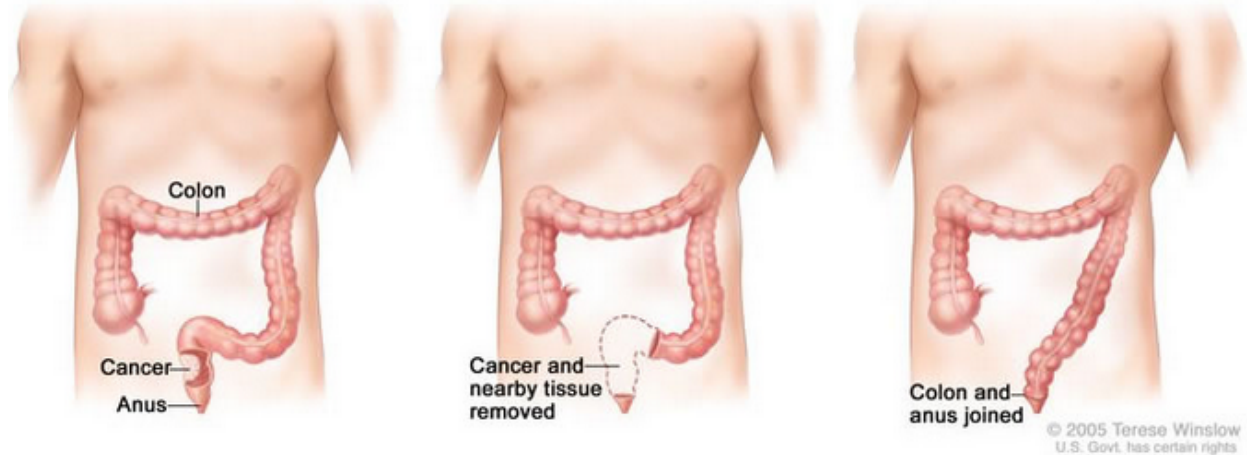
Source: University Health Network Patient Information

Lower Anterior Resection

A low anterior resection (LAR) is a common surgery for rectal cancer. This procedure involves the removal of the rectum. The colon is then attached to the remaining section of the rectum to allow for regular bowel movement. Some stage I rectal cancers and most stage II or III cancers in the upper part of the rectum (close to where it connects with the colon) can be removed by low anterior resection (LAR). In this operation, the part of the

rectum containing the tumour is removed. The colon is then attached to the remaining part of the rectum (either right away or sometime later) so that the patient moves their bowels in the usual way. The colon is then reattached to the remaining rectum so that a permanent colostomy is not needed.

Illustration of Lower Anterior Resection Procedure



Source: National Cancer Institute.

https://www.ncbi.nlm.nih.gov/books/NBK65940/figure/CDR0000062959__195/

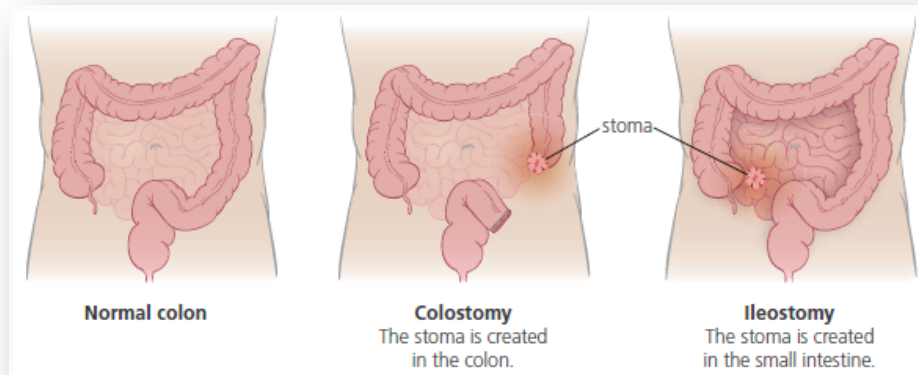
Colostomy and ileostomy

In cases where it is not possible to join the two ends of the colon or rectum after removing the tumour, a colostomy or ileostomy is required.

In a colostomy, the new end of the colon or rectum is routed to an opening, or stoma, through the abdominal wall. The opening allows feces and gas to pass through the opening and into a bag or pouch attached to the skin.

An ileostomy routes the ileum (lowest part of the small intestine) outside the abdominal wall to create a stoma through which digested food passes into an external pouching system.

Illustration of Colostomy and Ileostomy



Source: <https://intermountainhealthcare.org/services/wound-care/wound-care/conditions/ostomy/>

In most cases the colostomy or ileostomy may be temporary while the colon heals sufficiently so that a second surgery can be performed to join the two ends of the colon and close the ostomy. In some cases a second surgery is not possible and the colostomy or ileostomy will be permanent. Although having a temporary or permanent stoma means an adjustment in lifestyle, people can enjoy normal lives. Specialized stomal therapy nurses are available to give you information on living with the stoma and discuss any questions or concerns you may have.

For more information, visit the website of the Ostomy Canada Society at: <https://www.ostomycanada.ca/>

Side effects of surgery

Side effects can develop during, immediately after or a few days or weeks after surgery. Most side effects are temporary or can be treated, while some may be long-lasting or permanent.

The type of side effects you experience (if any) will depend on the type of surgical procedure performed, how much healthy tissue was removed, the effects of other treatments, and your general state of health.

As with any other surgery, you can expect to feel some pain and tenderness in the days following the procedure. Until your bowel resumes its normal function, you may experience some gastrointestinal effects such as constipation, diarrhea or gas pains. Some patients may experience bleeding or develop blood clots. Infection is always a risk when the bowel is cut.

If you have a colostomy or ileostomy you may find that the skin around the stoma becomes irritated. A qualified nurse can teach you how to care for the stoma at home.

There are many options available to help manage these side effects. Tell your oncology care team as soon as possible if you have symptoms that you think might be from surgery.

Pathology Report

During surgery, biopsies will be taken of your tumour, lymph nodes and other tissues. These samples will be sent to a specialist (pathologist) who will analyze them to determine the characteristics of the tumour. Based on the final pathology report, and the success of surgery in removing all of the visible cancer, your doctor may be able to estimate the future progression of your disease (prognosis) based on these figures.

Questions to Ask your Surgeon

The following questions are meant as a guide to topics you should discuss with your surgeon and medical team before and after undergoing surgical treatment for colorectal cancer.

Questions to ask before surgery

Do you have a specialty in surgical oncology? Do have any fellowship level/extra training in the management of colorectal cancer?

Is surgery the standard therapy for my stage of disease?

Why do you recommend surgery for my colon/rectal cancer?

What type of surgery do you recommend (conventional vs. laparoscopic)?

Can you describe the surgery that you recommend?

What is the goal of surgery?

What are you planning to remove during surgery (the colon, nearby colon tissue, rectum, mesorectum, lymph nodes)?

How many times have you performed the recommended surgery?

Will you personally be performing the surgery?

What is your success rate and how do you define success?

What is your experience with complications? What should I do if I develop complications after surgery? Tel. # to call: _____

Is a biopsy part of the surgery?

How soon after surgery will I have all test results and a firm diagnosis?

Will I need blood transfusions and can my family donate blood?

Why is bowel preparation necessary for abdominal surgery?

Will you perform a pelvic lymph node dissection?

I have read that at least 12 lymph nodes need to be examined to accurately stage colon and rectal cancers, do you routinely accomplish this? Can more than 12 lymph nodes be tested? If so, how many are you willing to test in excess of 12?

What happens if one or more of the lymph nodes is found to be positive?

How long will I be unable to eat?

What are my options for pain control after surgery?

Do you think I will require a temporary or permanent colostomy? If so, what will this involve? (If yes, proceed to List of Questions in Respect of Colostomy Found Below.)

If you find that the disease is more extensive than originally believed, what will you do?

Considering my age and general health, am I at a higher or lower risk for complications?

What might my recovery involve? Restrictions: _____ Date to resume normal activities: _____

What are my options besides surgery?
Are there clinical trials for my stage of disease?
Will I require adjuvant (post surgical) therapy after my surgery?
Are there any protocols for neoadjuvant (before surgery) therapy for my stage of disease?
What are the pros and cons of each type of colon/rectal surgery for the treatment of my particular cancer?
What diagnostic tests are needed prior to surgery and how will these assist in surgical planning?
Do you feel it is appropriate to perform surgery even if there are metastases present in more than one place?
If yes, under which conditions?
Who will give me information about how I should get ready for surgery and a hospital stay? How long will I be in the hospital?
Might I require special assistance at home after the procedure? If so, how can I arrange for the help I need?

For rectal cancer:

Should I have radiation therapy and chemotherapy before my rectal cancer surgery?

Questions to ask after surgery

Can you explain my pathology report (laboratory test results) to me?
What is my prognosis?
What additional treatment do you recommend? Why?
What is the goal of this treatment?
Is it a standard treatment or part of a clinical trial?
What are the risks and possible side effects of treatment, both in the short term and the long term?
How will the treatment affect my daily life? Will I be able to work, exercise, engage in sexual activity and perform my usual daily activities?
How long will it be before I can go back to work after surgery? Can I work during chemotherapy?
What follow-up tests will I need, and how often will I need them? When will I be seen for a follow-up examination?
What support services are available to me? To my family?

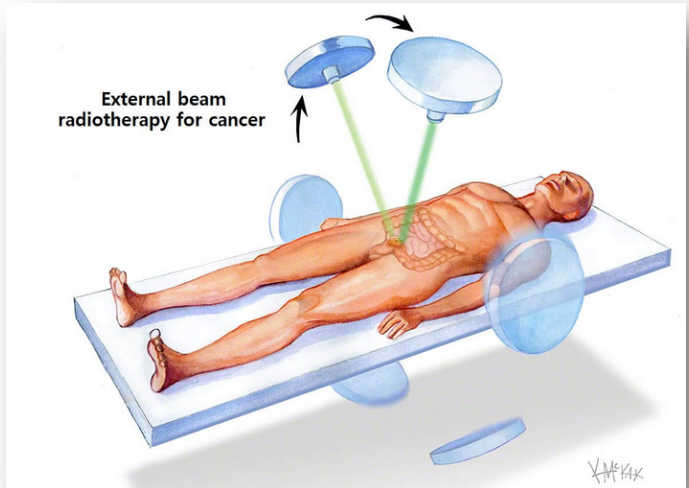
Colostomy-related questions

Will I require a colostomy?
If I have a colostomy, will it be temporary or permanent?
If I have a temporary colostomy, when will I have additional surgery to have the stoma removed?
Will I be assigned a colostomy nurse to provide detailed information, answer questions and help me learn to manage it after the surgery?
What type of ostomy will I have? (colostomy or ileostomy)
Will I be required to change my diet?
How will the colostomy be placed to minimize discomfort and inconvenience?

ii. Radiation Therapy for Stage II/III Colorectal Cancer

Radiation therapy, also called radiotherapy, is often used with surgery and chemotherapy to treat cancers of the rectum. Radiation oncologists use radiation therapy to try to cure cancer, control cancer growth or relieve symptoms, such as pain. Other times, radiation is given at surgery to keep the cancer from returning.

External Beam Radiation Therapy is the most common technique used to treat colorectal cancer. It involves focusing a beam of high-energy x-rays to the bowel and pelvis to kill cancer cells in the area and stop them from dividing. The radiation beam usually comes from a machine called linear accelerator. A series of daily outpatient visits is required to accurately deliver radiation to the area requiring treatment. Surrounding healthy tissue can be affected, but normal cells are often better able to heal from radiation injury than are cancer cells.



Source: Colorectal Surgeons Sydney

In rectal cancer, radiation therapy is commonly used before surgery (neoadjuvant) to shrink large tumours and make it easier for the surgeon to remove the entire growth. Radiation therapy may also be given after surgery (adjuvant), either alone or in combination with chemotherapy, to reduce the chance of recurrence. It is administered during several short sessions over a 5-week period, usually at a local cancer centre. Short course radiation therapy may also be delivered.

Side effects of radiation therapy, although temporary, may include:

- Nausea and diarrhea
- Fatigue
- Mild skin irritations at the site of irradiation
- Sexual dysfunction
- Changes in bowel function and burning sensation

If you experience any of these side effects, speak with your oncology care team. They can recommend treatments to help manage these symptoms and often times avoid some of these altogether.

Questions to ask your radiation oncologist

This list of questions has been provided for you to ask your radiation oncologist if radiotherapy is part of your treatment plan.

Questions to ask before radiation therapy

What is the purpose of radiation treatment for my type of colorectal cancer?

What areas of my body will be treated with radiation?

How will the radiation therapy be given? Will it be external beam or brachytherapy? What do the treatments feel like?

For how many weeks will I receive radiation? How many treatments will I receive per week?

What are the chances that radiation therapy will work?

Can I participate in a clinical trial? If so, what is the trial testing? What are my benefits and risks?

What is the chance that the cancer will spread or come back if I do not have radiation therapy?

How will I feel after the treatments?

Will I be able to work? Will I be able to take care of my family?

What are the side effects of radiation?

Is there anything I can do to lessen the side effects?

Can I eat or drink anything I want during the weeks I have radiation?

Can I drink alcohol?

Will I need chemotherapy, surgery, or any other treatments in conjunction with radiotherapy? If so, in what order will I receive these treatments?

How soon after radiation therapy can I start receiving other treatments? Can I receive several treatments at the same time?

What are some of the support groups I can turn to during treatment?

If I have questions after I leave here, who can I call? Tel. # _____

Will radiation therapy affect my ability to have children?

Questions to ask during radiation therapy

How can I expect to feel during treatment and in the weeks following radiation therapy?

Can I drive myself to and from the treatment facility?

Will I be able to continue my normal activities?

What side effects may occur from the radiation and how are they managed?

Do I need a special diet during or after my treatment?

Can I exercise?

Can I engage in sexual activity?

Can I smoke or drink alcohol?

Will side effects change my appearance? If so, will the changes be permanent or temporary? If temporary, how long will they last?

Is it safe to take vitamins during treatment?

What are the reasons that I should call you at night or on a weekend?

Questions to ask after radiation therapy is completed

How and when will you know if I am cured of cancer?

What are the reasons that I should call you after my treatment ends?

What are the chances that the cancer will come back?

How soon can I go back to my regular activities? Work? Sexual activity? Aerobic exercise?

How often do I need to return for checkups?

Are there any additional side effects I should look for? How should I manage them?

iii. Chemotherapy for Stage II/III Colorectal Cancer

Most patients with stage II and III colorectal cancer will have had surgery to remove the tumour. In some patients there is a risk that cancer cells that are undetectable at the time of surgery break loose and are taken up by the surrounding lymphatic system. Once lodged in the lymph nodes, they may begin to grow into secondary tumours. Chemotherapy can be used to prevent the growth and spread of these cancer cells.

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. The way the chemotherapy is given depends on the type and stage of the cancer being treated.

Patients with stage III or high-risk stage II colon cancer are given adjuvant (meaning “after surgery”) chemotherapy to minimize the risk of developing secondary tumours after surgery. (As noted above, people with rectal cancer are sometimes given neoadjuvant or adjuvant chemotherapy in conjunction with surgery or radiation therapy.)

Some patients with colorectal cancer will already have small amounts of cancer that have spread outside the colon or rectum (micrometastases) and cannot therefore be removed by surgery. These tiny metastases cannot be detected with any of the currently available tests but, if they are not treated with chemotherapy or radiation therapy, they can cause recurrences. Surgery is often followed by adjuvant chemotherapy (chemotherapy administered after surgery) to cleanse the body of micrometastases.

High risk Stage II and Stage III patients will usually be prescribed adjuvant chemotherapy such as FOLFOX post surgery. FOLFOX is an acronym that stands for the names of 3 drug therapies. It is a combination chemotherapy consisting of Folinic Acid plus 5Flourouracil plus **Oxaliplatin**. **Folinic Acid** (Leucovorin) is a synthetic vitamin designed to increase the efficacy of the chemotherapy **5 Fluorouracil** or better known as 5FU. Oxaliplatin is the other chemotherapy that will try to reduce the chances of a recurrence. The combination chemotherapy is administered to help reduce the risk of a recurrence after surgery.

Details about chemotherapy and targeted therapies are found in the following section on stage IV colorectal cancer.

Watch-and-Wait Approach for Rectal Cancer

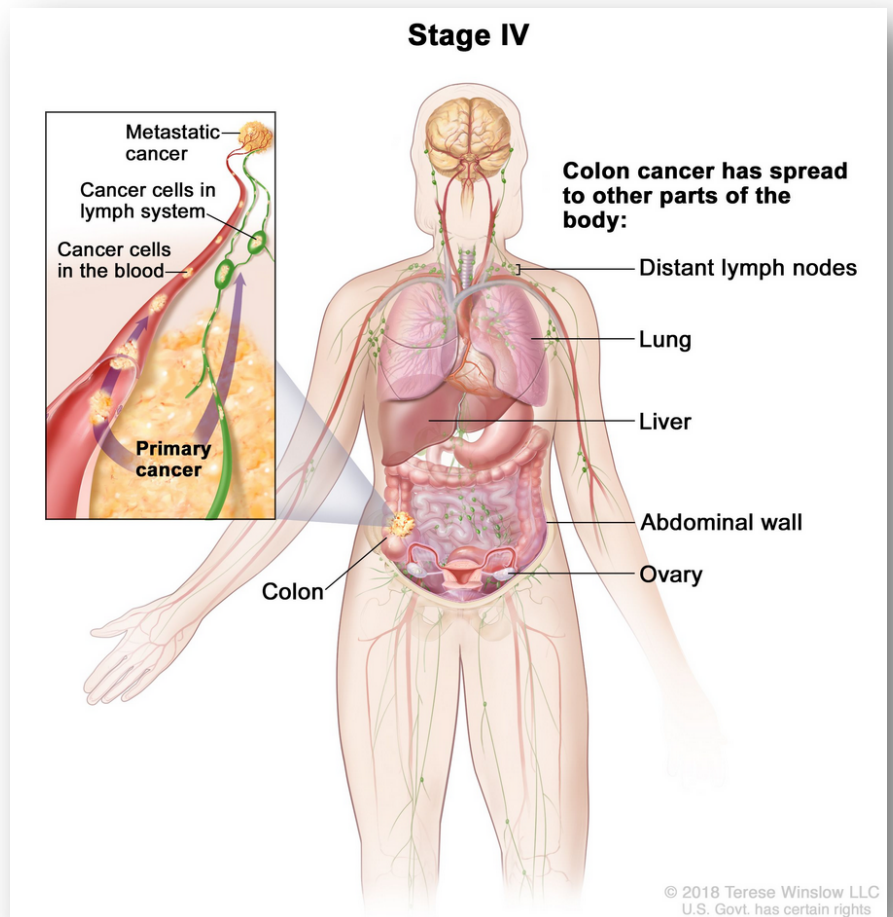
When chemotherapy and radiation therapy have been successful in shrinking a rectal tumour, some patients may be candidates for a 'Watch-and-Wait' approach. When complete response to treatment has been achieved, close monitoring of the patient through regular examinations may be as effective as radical surgery and patients may be able to avoid its attendant complications. Further research is needed to confirm the early promise of this approach; however, evidence is showing that regular monitoring may be an effective alternative to surgery in highly selected cases. If the patient chooses to undergo a watch and wait approach after successful shrinking of their rectal tumour and disease is detected while under close monitoring, surgical resection can always be discussed with the patient's surgeon to address the identified disease.

C. Stage IV and Recurrent Colorectal Cancer

In stage IV (also called metastatic colorectal cancer), the cancer has travelled (metastasized) to distant organs, often the liver or lungs. Other organs may include the peritoneum (the lining that covers the abdominal organs and abdominal cavity), ovaries, adrenal glands, distant lymph nodes etc. Treatment is aimed at reducing or eliminating cancers at the original site and those that have spread to other organs and tissues.

Recurrent colorectal tumours are treated in much the same way as stage IV cancer, since they have stopped responding to previous therapy and require more aggressive treatments.

Most patients are offered more than one form of treatment, or modality, to treat stage IV and recurrent colorectal cancer: surgery, radiation therapy, chemotherapy and/or targeted therapy. With the introduction of precision medicine or personalized medicine, the patient's genomic profile now guides treatment selection to optimize treatment response which may improve patient outcomes. Tumour profiling is providing the necessary information on genetic mutations to guide selection of therapeutic options to enhance the patient journey.



Source: National Cancer Institute

i. Surgery for Stage IV and Recurrent Colorectal Cancer

Removal of primary tumours

For patients newly diagnosed with stage IV colorectal cancer, surgery is the most highly sought-after treatment. (Patients with recurrent cancer are likely to have had surgery already.) The surgical procedure to remove the tumour from the colon or rectum is the same as described for stage II and III patients. The procedure may be accompanied by radiation therapy or chemotherapy either before (neoadjuvant) or after surgery (adjuvant).

Removal of secondary tumours

In addition, because the cancer has spread to other organs, these secondary tumours may also be surgically removed. Cancers originating in the colorectum tend to spread to the peritoneum (the membrane lining the organs in the abdomen), and to the liver and lungs.

Secondary cancers may, in turn, spread to other organ systems. Sometimes the secondary tumours are too small and scattered throughout the body to be removed by surgery. In these cases, other treatment modalities such as radiation therapy and chemotherapy may be alternative treatment options.

ii. Treating Liver Metastases

Stage IV colorectal cancer commonly spreads to the liver. Surgery, if possible, is the preferred way of treating cancer that has metastasized to the liver. Chemotherapy can also be used to shrink the tumours in cases where surgery is not an option. It also can be used before surgery, to shrink the tumours, or after surgery, to prevent recurrence.

Surgical Treatment of Liver Metastases

Liver metastases occur in more than 50% of the colorectal cancer population and liver resection can provide the best chance for long term survival. If colorectal metastases are confined to the liver and the metastases are not involving critical structures such as the portal vein or hepatic artery, you may wish to have a thoughtful discussion with your treating oncologist about surgical treatment for the management of your disease.

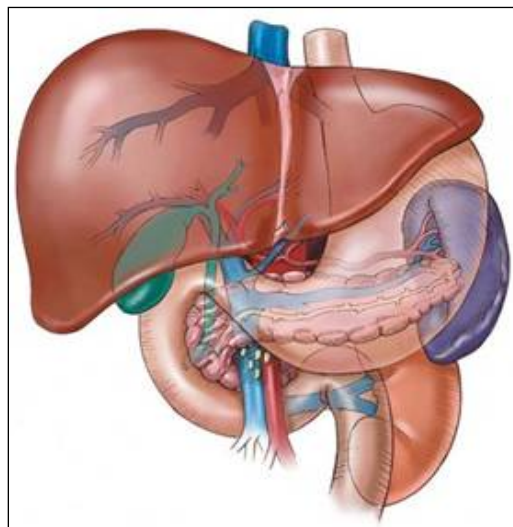


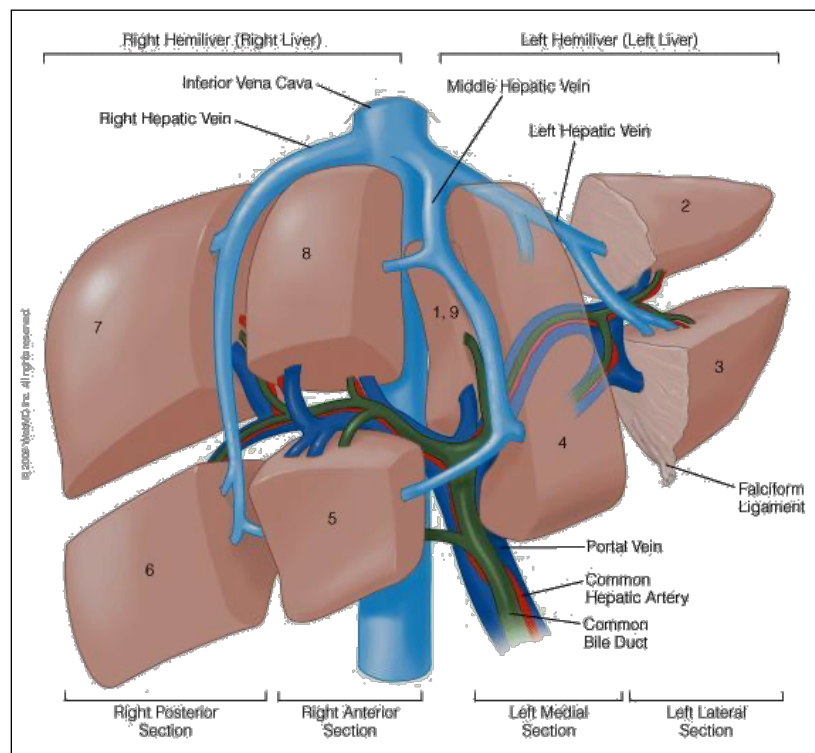
Diagram Illustrating the Liver & Adjacent Organs

Patients whose colorectal cancer has travelled to their liver will seek out consults for surgical treatments because they are aware that surgery may provide the best chance for a cure. There are however important considerations in the selection process for surgical candidacy. In order to identify which subset of patients will benefit most from resection, various prognostic factors have been identified. The variables most commonly associated with a recurrence after the surgery are:

- A positive resection margin and extrahepatic disease. Thus, inability to completely remove all tumors or the presence of extrahepatic disease (disease located outside of the liver) is considered a contraindication for surgery.
- More than 1 lesion in the liver
- Extent of liver involvement greater than 50%,
- A margin of resection less than 1 cm,
- CEA level > 200 ng/ml, and
- Intraoperative blood transfusions.

However, none of these prognostic variables are an absolute contraindication to surgery. They were mainly formulated to assist in patient selection.

The liver can be divided into 8 segments: segment 1 is the caudate lobe, segments 2 through 4 form the anatomic left lobe and segments 5–8 form the anatomic right lobe. Please see diagram below.

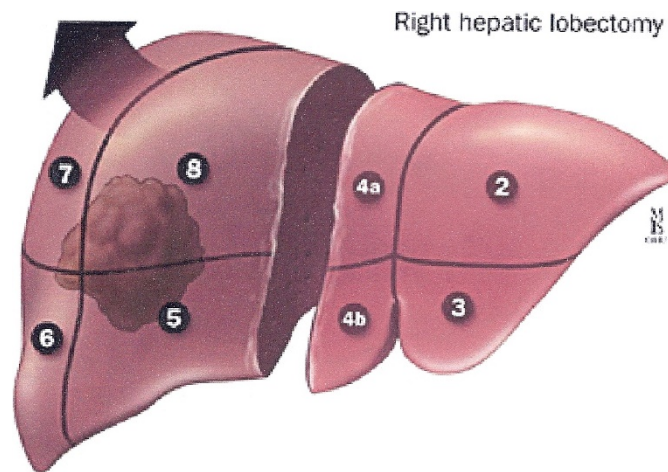


- Lesions confined to the **right lobe** are amenable to an **en bloc removal** (removal in one piece) with a right hepatectomy (liver resection) surgery.
- Smaller lesions of the **central or left liver lobe** may sometimes be resected in anatomic “segments”.
- Large lesions of the **left hepatic lobe** are resected by a procedure called hepatic trisegmentectomy (see diagram and explanation below).

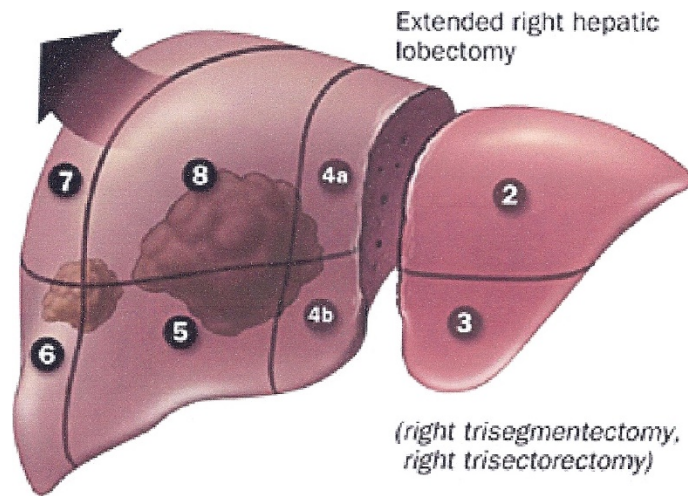
- When lesions are located **peripherally (on the edges of the liver)**, hepatic wedge resection or anatomic segmentectomy are performed.
- If a tumor is adjacent to or **involving major intrahepatic vessels**, resection of the entire segment or lobe is necessary.
- Lobectomy (removal of the entire lobe of the liver) is indicated when **multiple lesions** are located in different areas of one lobe.
- Wedge resection is universally accepted for **small superficial lesions**.

Appearing below are the common surgical procedures performed for the removal of colorectal liver tumours:

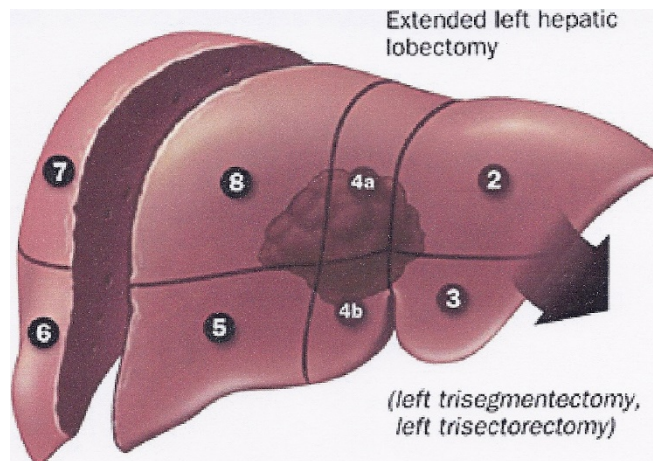
1. Right lobe which consists of two segments – **Right Lobectomy**



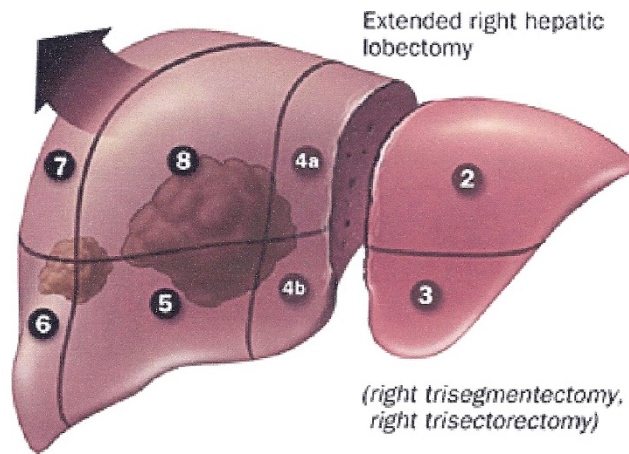
2. Left lobe which consists of two segments – **Left Lobectomy**



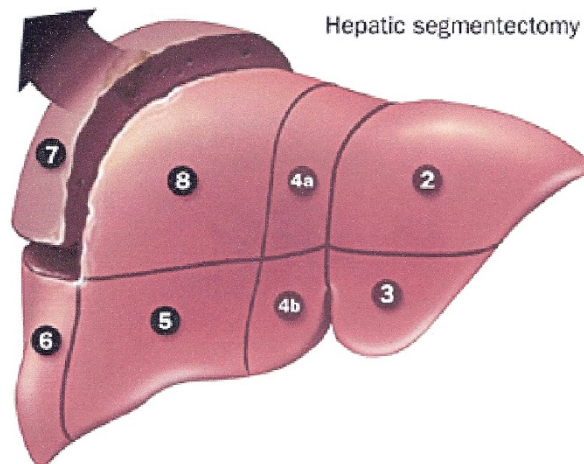
3. Removal of the complete left lobe plus the medial segment of the right lobe – **Left Trisegmentectomy** (also known as extended left hepatic lobectomy)



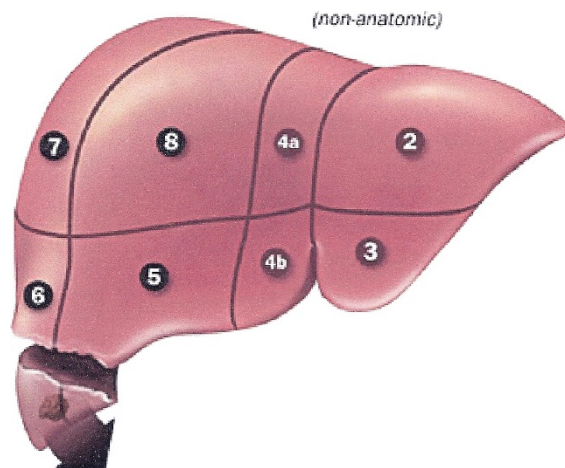
4. Removal of the complete right lobe plus the medial segment of the left lobe – **Right Trisegmentectomy** (also known as extended right hepatic lobectomy)



5. Liver to the left of the falciform ligament (a ligament that attaches part of the liver to the diaphragm and the abdominal wall) in a single segment - **Lateral Segmentectomy**



6. Small triangular-shaped portion of the liver whose tumour is situated on the surface and located peripherally (on the edges of the liver), so that it can be safely removed without injury to the blood vessels of the liver. The tumour with a small amount of normal tissue around it are removed – **Wedge Resection**.



Patients with colorectal cancer and metastatic disease to the liver may be treated in either a single surgery or in staged surgeries (with the colon tumor traditionally removed first) depending upon the fitness of the patient for prolonged surgery, the difficulty expected with the procedure with either the colon or liver resection, and the comfort of the surgery performing potentially complex hepatic surgery.

Additional Treatment Options

For liver metastases, there are several treatment options beyond surgery and chemotherapy. Some of these treatment options are still considered fairly experimental and are rare, while others are not widely available throughout Canada. CCRAN is nevertheless providing the information to help inform patients and caregivers of these evolving therapies in the management of colorectal liver metastases.

- ALPPS Procedure (Associating Liver Partition & Portal Vein Ligation for Staged Hepatectomy)
- Living Donor Liver Transplant
- Hepatic Arterial Infusion Pump Chemotherapy
- Stereotactic Body Radiation Therapy (SBRT)
- Selective Internal Radiation Therapy (SIRT)
- Radiofrequency Ablation (RFA)
- Embolization Procedures
 - Chemoembolization
 - DEBIRI
 - Portal Vein Embolization

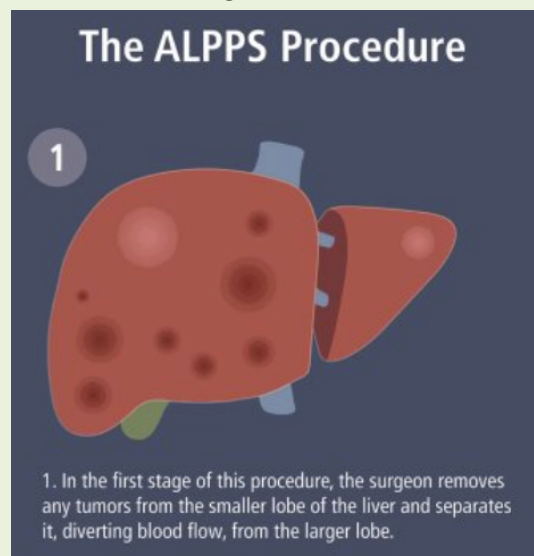
ALPPS – Associating Liver Partition & Portal Vein Ligation for Staged Hepatectomy

The ALPPS procedure is one of today's most advanced treatments for liver cancer and metastasis to the liver from cancers originating in other organs (e.g., colon or rectal cancer). Because the liver is capable of regenerating itself, it may be possible for a surgeon to remove part of the organ when treating liver tumours, provided that enough liver tissue can be left in place. However, when liver tumours have spread extensively throughout the organ or when there are multiple tumours, it can be difficult for a surgeon to preserve adequate amounts of the patient's original liver tissue. In these instances, a surgeon may recommend the ALPPS technique, which promotes rapid regrowth of the liver, in turn increasing the surgeon's ability to remove all cancerous tissues from the organ.

An ALPPS procedure is actually performed as two separate surgeries:

1. The surgeon blocks off a branch of the portal vein (the main vein that delivers blood to the liver). This makes the liver behave as though part of the organ has been removed, triggering the process of tissue regeneration on the other side. Small surface tumours may be removed during this part of the operation as well. Additionally, a cut on the liver is performed which delineates what the future resection line will be and induces faster and more significant growth of the portion of the liver that will remain.
2. After performing tests to ensure the liver has regenerated enough, roughly one to two weeks after the first operation, the surgeon performs a liver resection, removing the diseased portion of the liver. The remaining part of the liver, which by this point has grown significantly, will be able to compensate and provide all the necessary functions of the liver.

This technique is especially valuable for patients who are not appropriate candidates for traditional liver resection due to multicentric disease and an inadequately small future liver remnant. The ALPPS procedure allows surgeons to treat patients who have a substantial amount of tumour, with both lobes affected by tumour. Some centers in Canada are now performing this type of surgery. Because the two-stage procedure is very taxing on patients, they must be in otherwise good health to be considered as candidates.



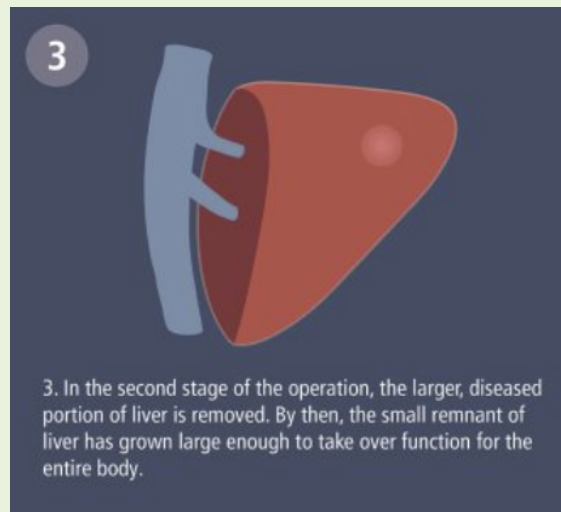
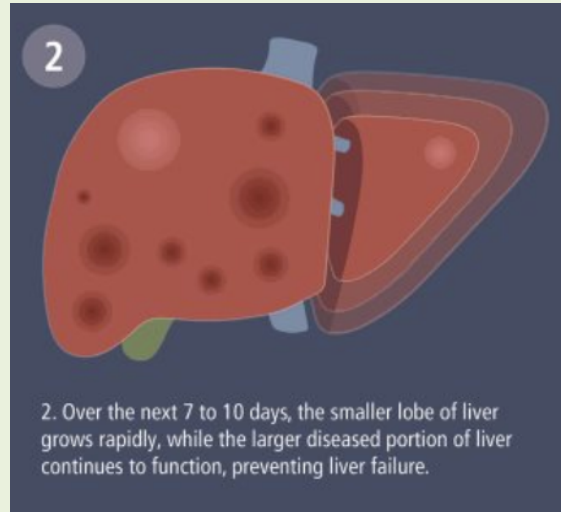
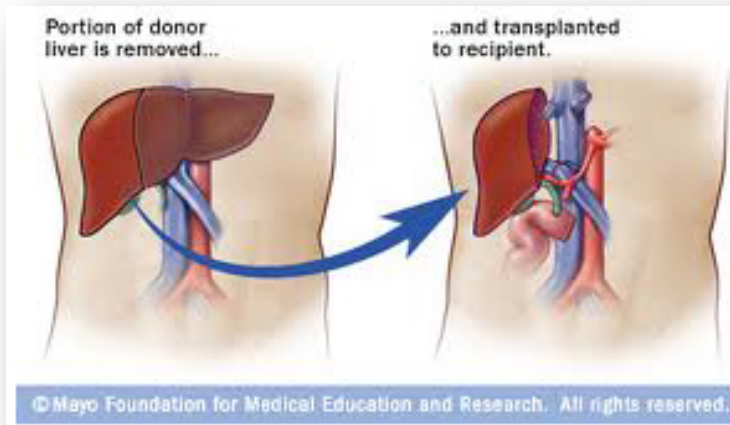


Image Source: <https://www.urmc.rochester.edu/cancer-institute/newsroom/dialogue-blog/june-2017/finding-hope-and-time.aspx>

- **Living Donor Liver Transplant (An experimental therapy available at the University Health Network, Toronto, Ontario)**

In a living donor liver transplant, someone who is living gives part of their liver to a recipient. This approach generally shortens the wait for a liver to become available from a deceased donor, which can significantly improve the outcome for the colorectal cancer patient who receives the organ.

Illustration of Living Donor Liver Transplant



A detailed screening process ensures that the tissues are a biological good match, so that the chances of rejection by the recipient's immune system are minimized, and that both the donor and recipient are aware of the possible outcomes and accept the risks associated with the procedure.

At present, living donor liver transplant is available in Canada only at the University Health Network, including Princess Margaret Hospital, in Toronto.

- **Hepatic Arterial Infusion Pump Chemotherapy (A Ongoing Study Available at Sunnybrook Health Sciences Centre)**

Hepatic Arterial Infusion Pump Chemotherapy (HAIP-C) is used where colorectal cancer that has spread to the liver cannot be removed with surgery. The Hepatic Artery Infusion Pump (HAIP) is a small, disc-shaped device that is surgically implanted just below the skin of the patient and is connected via a catheter to the hepatic (main) artery of the liver. About 95 percent of the chemotherapy that is directed through this pump stays in the liver, sparing the rest of the body from side effects. The therapy is intended for select patients whose metastatic disease is confined to the liver that cannot be surgically resectable. For additional information, please visit:

<https://sunnybrook.ca/content/?page=colorectal-colon-bowel-haip-chemotherapy>

Surgical Insertion of Hepatic Arterial Infusion Pump



Source: <https://sunnybrook.ca/content/?page=colorectal-colon-bowel-haip-chemotherapy>

Patients receive HAIP-directed chemotherapy in addition to regular intravenous (IV) chemotherapy (systemic chemotherapy), to reduce the number and size of tumours.

At present, Sunnybrook Hospital in Toronto is the only Canadian centre offering HAIP chemotherapy.

- **Stereotactic Body Radiation Therapy (SBRT)**

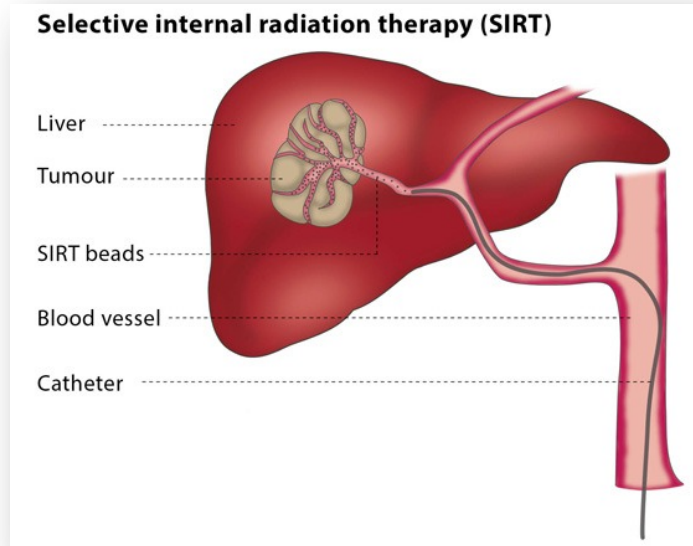
Stereotactic Body Radiation Therapy (SBRT) is a specialized external beam radiation treatment which can accurately target some liver tumours that cannot be removed surgically.

It delivers extremely precise, very intense doses of radiation to cancer cells while minimizing damage to healthy tissue. SBRT involves the use of sophisticated image guidance that pinpoints the exact three-dimensional location of a tumour so that the radiation can be more precisely delivered to cancer cells.

Conventional radiation is typically delivered in relatively small doses each day over several weeks. This can delay or interfere with other cancer treatments, such as chemotherapy. By contrast, SBRT can usually be given in five or fewer daily sessions and requires no anaesthesia. SBRT also can lead to better outcomes and fewer side effects than conventional radiation therapy.

- **Selective Internal Radiation Therapy (SIRT)**

SIRT (sometimes called radioembolization) is a type of internal radiotherapy used to control cancers in the liver that can't be removed with surgery. Tiny radioactive beads (microspheres) are placed into an artery that takes blood into the liver. The beads get stuck in the small blood vessels in and around the cancer, and the radiation destroys the cancer cells. Since the radiation only travels a few millimetres from where the beads are trapped, it should cause little damage to the surrounding healthy tissue.

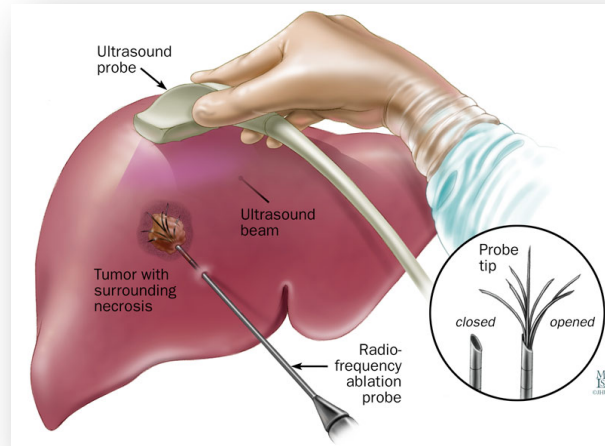


Source: *Cardiovascular and Interventional Radiological Society of Europe.*
<https://www.cirse.org/patients/ir-procedures/selective-internal-radiation-therapy-sirt/>

- **Radiofrequency Ablation (RFA) or Microwave Ablation**

Ablation can be used in patients with a few small tumours and when surgery is not a good option (often because of poor health or reduced liver function). RFA uses electromagnetic energy to kill the tumour by heating it to greater than 50°C for more than 5 minutes. The energy waves are delivered to the tip of a small needle that penetrates the skin and is guided to the tumour under CT (computerized tomography) imaging or ultrasound (US) imaging. Ablation may also be combined with surgery in the operating room to treat multiple liver tumours. Radiofrequency Ablation may be performed percutaneously (through the skin) or intraoperatively (on the operating table, in combination with surgical resection of the liver).

Illustration of Radiofrequency Ablation of a Liver Tumour (Intraoperative)



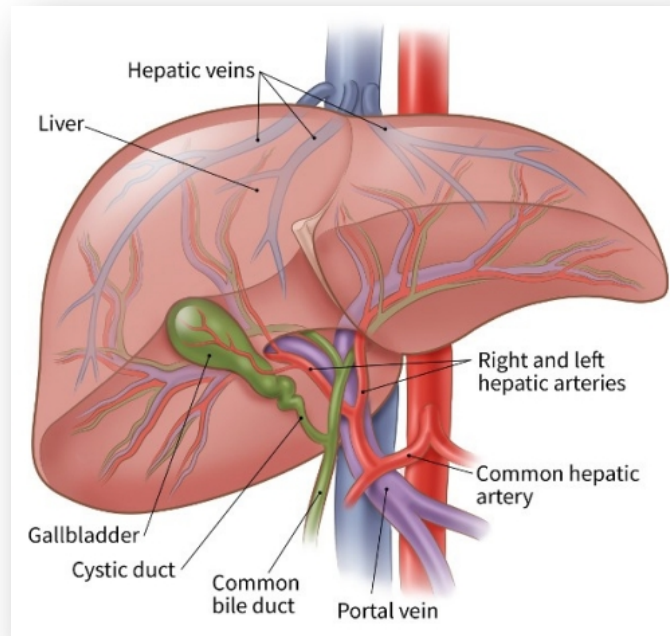
Source: Johns Hopkins University

- **Embolization Procedures**

Embolization is a procedure that injects substances directly into an artery in the liver to block or reduce the blood flow to a tumour in the liver.

The liver is special in that it has two blood supplies. Most normal liver cells are fed by the portal vein, whereas a cancer in the liver is mainly fed by the hepatic artery.

Illustration of Blood Supply to the Liver



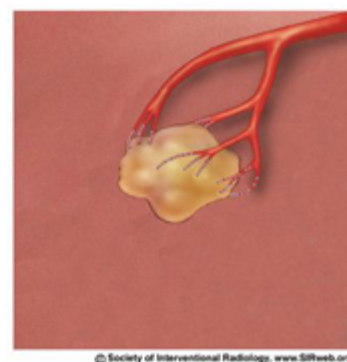
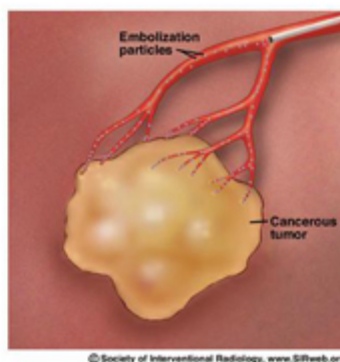
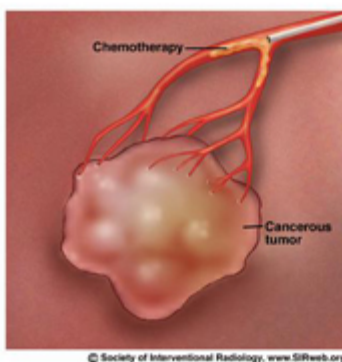
Source: American Cancer Society.

<https://www.cancer.org/cancer/liver-cancer/treating/embolization-therapy.html>

Chemoembolization

Chemoembolization, also known as transcatheter arterial chemoembolization (TACE), is a treatment for tumors in which large doses of chemotherapy are directly administered at the site. This procedure spares patients from unpleasantness caused by traditional chemotherapy administered throughout to the whole body.

The procedure is performed by placing a small catheter (tube) into the artery and navigating with real-time imaging for guidance to the artery feeding the tumor. A high dose of cancer-killing drug is then delivered directly in the tumor while depriving the tumor of its blood supply by blocking, or “embolizing,” the arteries feeding the tumor.



DEBIRI

DEBIRI consists of intra-arterial infusion of irinotecan-loaded drug-eluting beads. With DEBIRI, (also known as liver chemoembolization), beads are threaded through a small catheter line from the blood vessel into the artery, located in the groin, that supplies blood to the liver. These tiny beads contain a very highly concentrated dose of the chemotherapy drug irinotecan. With this treatment, the blood vessels are partly blocked with the beads, starving the tumor of its blood supply, while concentrating chemotherapy in high doses to the tumours. This devastating “one-two punch” slows, and in some cases, may even halt tumor growth.



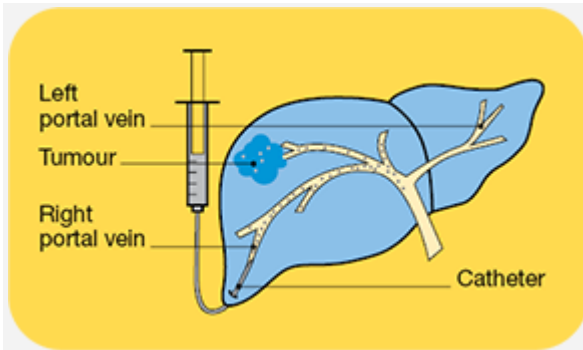
The therapy is available at select centres including Sunnybrook Health Sciences Centre.

Portal Vein Embolization (PVE)

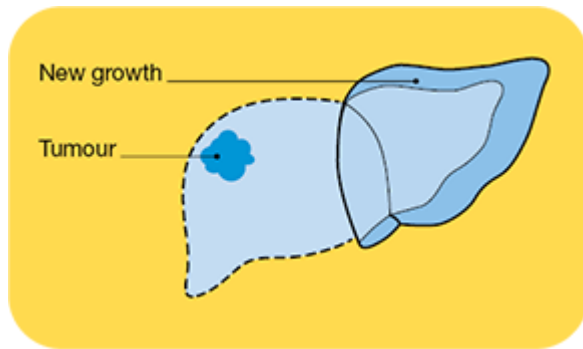
PVE blocks blood flow to the section of the liver where the tumour is located, causing it to get smaller. At the same time, the other section of the liver gets bigger as more blood is flowing to the unblocked side. Liver resection surgery is performed several weeks after the portal vein embolization to remove the part of the liver that has cancer.

How a portal vein embolization (PVE) is done:

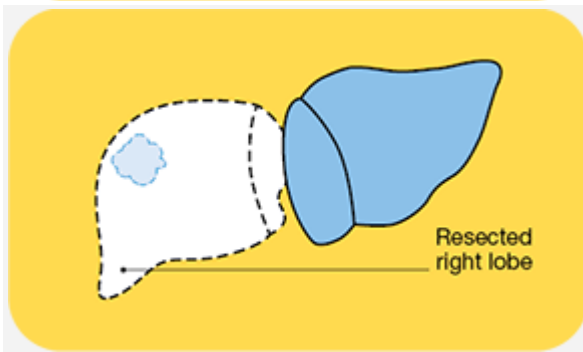
The portal vein divides into left and right branches as it enters the liver. A PVE blocks the branch of the portal vein that carries blood to the part of the liver that is going to be surgically removed. This means the other part of the liver will get bigger.



1. The interventional radiologist inserts a tube (catheter) through the skin into the portal vein under ultrasound guidance. A dye is injected to identify the portal vein, and then the targeted branch will be blocked with tiny plastic beads, soft gelatine sponges or metal coils.



2. Blood is redirected to the part of the liver that will be kept to help it grow.



3. After 4–8 weeks, you will have a CT scan to measure the size of your liver. If the liver has grown enough to safely do a liver resection, the surgeon will remove the part of the liver with the tumour.

Image Source: <https://www.cancercouncil.com.au/liver-cancer-2/treatment/portal-vein-embolisation-pve/>

iii. Treating lung metastases

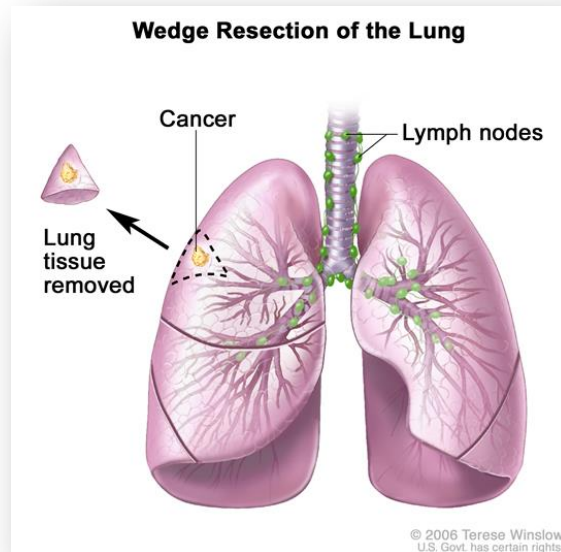
The best treatment for colorectal cancer that has spread to the lungs is surgery, however this is not an option for most patients. If surgery is not possible, chemotherapy is recommended. The same medications are utilized as those used to treat primary colorectal tumours, and the same considerations apply with respect to the tumour's biomarker profile. In some cases, the chemotherapy may shrink the tumours enough that surgery is now possible. Chemotherapy may also be given after surgery, to prevent recurrence. Beyond surgery and chemotherapy, lung tumours can be treated by specialized radiation therapy techniques.

Surgery

The surgical approach balances the need to remove as much as possible of the cancer with the need to preserve the function of the lungs. Depending on the number, size and location of the tumours, the surgeon may remove a small portion of the lung (wedge resection), a lobe (lobectomy) or the entire affected lung (pneumonectomy).

a) Wedge Resection

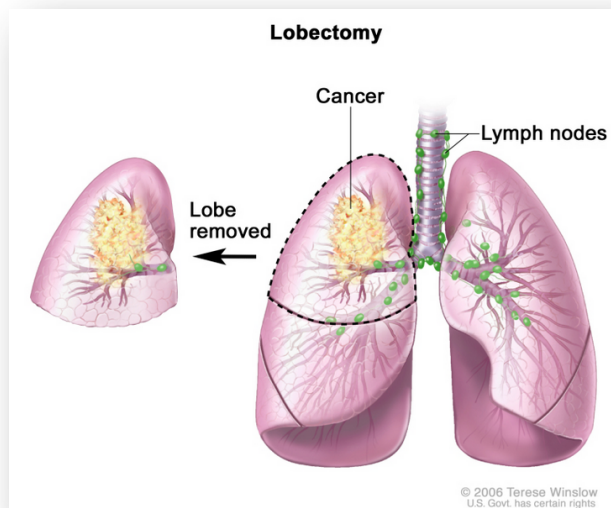
Wedge resection is a surgical procedure to remove a triangle-shaped slice of tissue in order to remove a tumour. These types of surgeries remove only the cancer and a small portion of the lung along with it and the technique is used most often when the tumours are small.



Source: National Cancer Institute. <https://nci-media.cancer.gov/pdq/media/images/466555.jpg>

b) Lobectomy

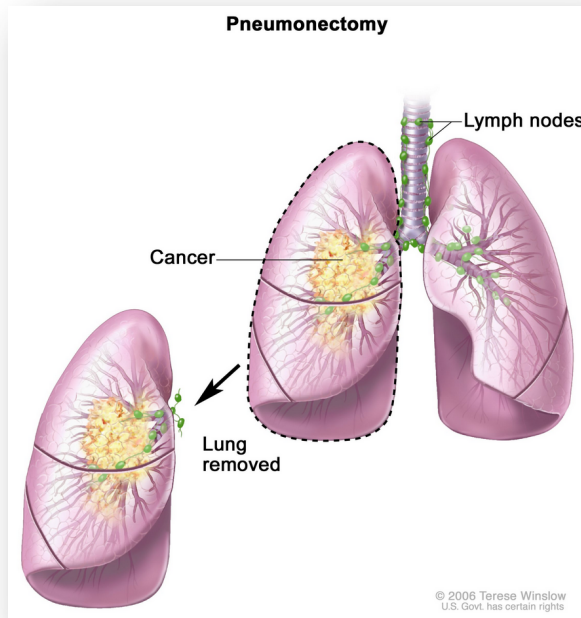
A lobectomy may be done when a tumour is found in just part of a lung. The right lung has 3 lobes and the left lung has 2 lobes. After the surgery, the remaining healthy lung tissue expands to fill the space left by missing section.



Source: National Cancer Institute. https://www.ncbi.nlm.nih.gov/books/NBK65917/figure/CDR0000062956_298/

c) Pneumonectomy

A pneumonectomy is the surgical removal of the entire affected lung.



Source: National Cancer Institute. <https://nci-media.cancer.gov/pdq/media/images/466556.jpg>

Radiation Therapy Options for Lung Metastases

Beyond surgery and chemotherapy, two radiation therapy techniques are used to treat colorectal cancers in the lung.

a) Stereotactic Body Radiation Therapy (SBRT) is a specialized external beam radiation treatment which can accurately target some lung tumours that cannot be removed surgically. It delivers extremely precise, very intense doses of radiation to cancer cells while minimizing damage to healthy tissue. SBRT involves the use of sophisticated image guidance that pinpoints the exact three-dimensional location of a tumour so that the radiation can be more precisely delivered to cancer cells.

Conventional radiation is typically delivered in relatively small doses each day over several weeks. This can delay or interfere with other cancer treatments, such as chemotherapy. By contrast, SBRT can usually be given in five or fewer daily sessions and requires no anaesthesia. SBRT also can lead to better outcomes and fewer side effects than conventional radiation therapy.

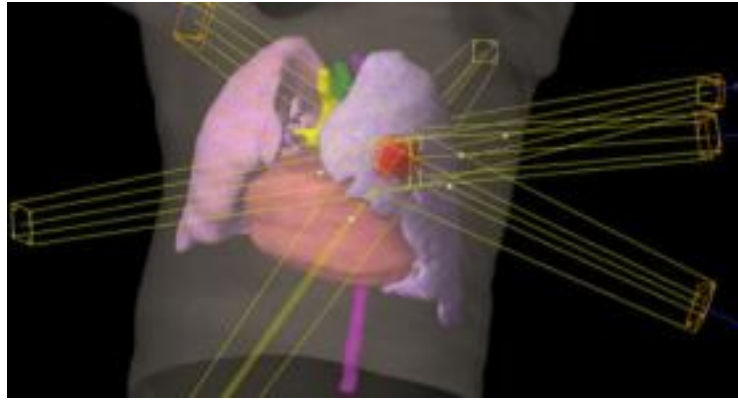
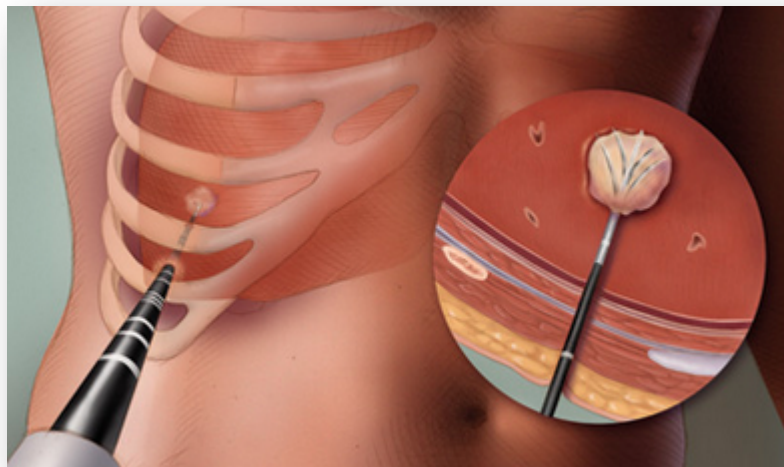


Image Source: Healthimaging.com

b) Radiofrequency Ablation (RFA) uses electromagnetic energy to kill the tumour by heating it to greater than 50°C for more than 5 minutes. The energy waves are delivered to the tip of a small needle that penetrates the skin and is guided to the tumour under CT (computerized tomography) imaging.

Illustration of Radiofrequency Ablation of a Lung Tumour



Source: Oncology Nurse Advisor. <https://www.oncologynurseadvisor.com/home/departments/radiation-and-your-patient/tumor-ablation-treatment-a-review-of-modalities/>

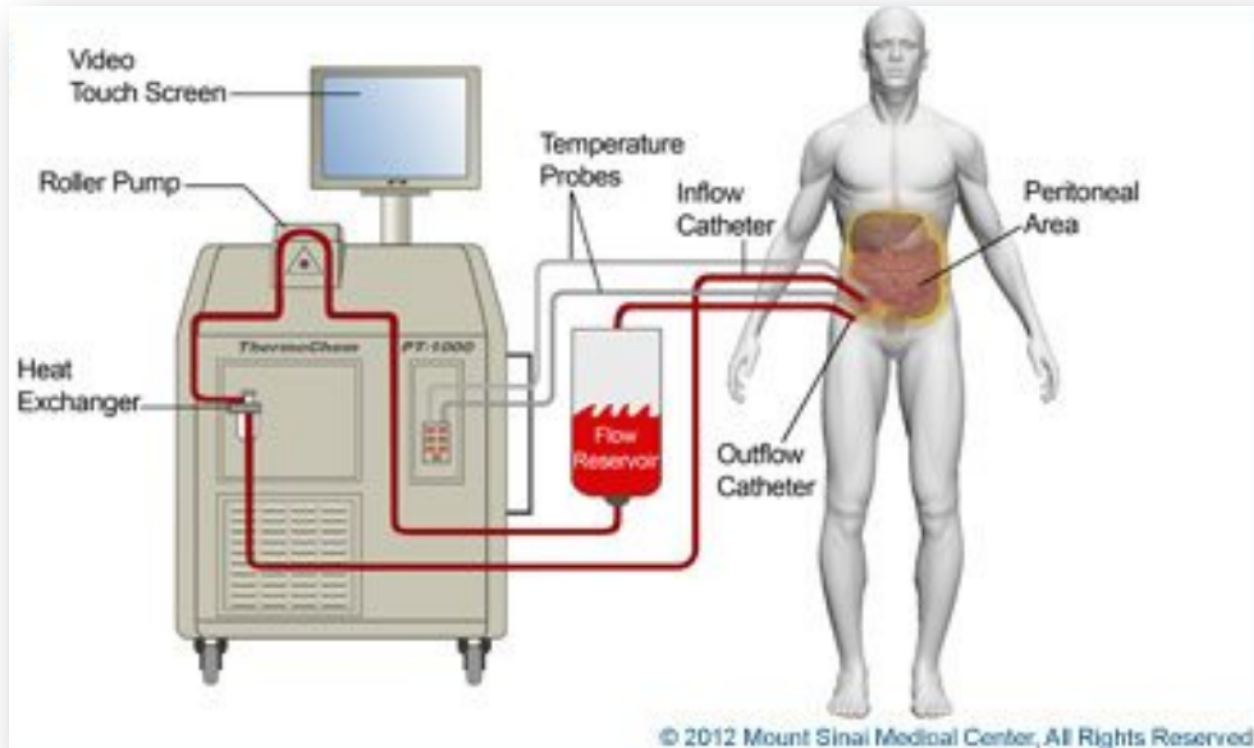
iv. Treating Peritoneal Metastases

The peritoneum is a membrane lining the cavity of the abdomen and covering the abdominal organs. It is a common site for metastases from colorectal cancer.

In recent years, the combination of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have improved both disease-free survival and overall survival. CRS can be a long and challenging procedure, therefore, it is essential for patients undergoing this treatment to have generally good health.

HIPEC is usually performed directly after surgical cytoreduction. The abdominal cavity is perfused with a heated chemotherapeutic drug solution (generally 42° C) for 30 to 60 minutes. The anti-cancer drugs are applied heated to increase their penetration depth and cytotoxic effect, making them more effective against the tumour.

Illustration of HIPEC Apparatus



Source: HIPEC Treatment Center. <https://hipectreatment.com/hipec/>

v. Considerations for patients who have other medical conditions

Although surgery is a mainstay of treatment for later stages of colorectal cancer, there are some situations where it may not be the best option for you.

The American Society of Clinical Oncologists offers the following advice.

Before surgery, you and your doctor should think about the following:

Heart function. Surgery may make heart problems worse. It is important to consider your heart function before you have surgery. Older adults have heart disease or an irregular heartbeat more often than younger people. Also, your heart might not tolerate changes in blood pressure as well. This can happen during surgery.

Kidney function. Surgery can involve many drugs. You might also get a lot of fluids to keep your body working. Your kidneys need to process the drugs and fluids. If your kidneys do not work as well as they used to, surgery can cause problems.

Liver function. As you get older, less blood flows to your liver to help it work. Your liver breaks down drugs. If it does not work as well as it should, you are more likely to have a reaction to the drugs needed for surgery.

Lung function. As you get older, your lungs do not hold as much air. And they might not work as well to move air in and out of your body. If you have a lung condition such as emphysema or chronic obstructive pulmonary disease (COPD), you may have problems recovering from anesthesia. This includes medications you get before and during surgery. Lung problems raise your risk of getting pneumonia after surgery, which can be very serious.

Source: Cancer.Net <https://www.cancer.net/navigating-cancer-care/older-adults/cancer-care-decisions-older-adults>

Questions to ask your surgeon before and after surgery

Please consult the list of questions in the previous section (on stage II/III colorectal cancer).

Interventional radiology for stage IV and recurrent colorectal cancer

Interventional radiology is a less invasive way than surgery to treat colorectal tumours that have spread to the liver and lungs. Where radiation therapy kills cancer cells by exposing them directly to a high-energy x-ray beam, interventional radiological techniques use different methods to attack the tumour.

In **embolization** procedures, the interventional radiologist places a catheter into the affected organ (usually through an artery) guided by imaging techniques, such as x-rays, CT, MRI, to deliver therapies directly to the tumour site. We saw an example of this approach in the description of ALPPS surgery, above, where the portal vein of one lobe of the liver was blocked by an embolus in order to divert blood flow to the other lobe, thus allowing it to regenerate.

Another example is chemoembolization where micro-beads coated with an anti-cancer drug are infused into the tumour's blood supply, thus directly targeting the tumour.

Radiofrequency ablation (RFA) uses electromagnetic energy to kill the tumour by heating it to greater than 50°C for more than 5 minutes. The energy waves are delivered to the tip of a small needle that penetrates the skin and is guided to the tumour under CT (computerized tomography) imaging.

vi. Chemotherapy for Stage IV and Recurrent Colorectal Cancer

Chemotherapy refers to a course of treatment with anti-cancer medications, which are designed to interfere with the molecular pathways that promote cell growth and division, causing the tumour to shrink.

Also referred to as systemic therapy, chemotherapy is different for each type of cancer and may consist of a single drug or a combination of different drugs. They may be taken orally or administered intravenously (IV) – by injection, by infusion over 30 minutes, or by prolonged infusion over several days using a pump.

The prescribed plan for the drugs, dosages, and the methods and timing of administration is referred to as the treatment regimen. Each regimen has been extensively tested to achieve the maximum destruction of cancer cells with the minimum of side effects for the patient. The choice of treatment will depend on the characteristics of your tumour, how healthy you are, and the availability of particular drugs at your cancer centre or hospital.

Which patients receive chemotherapy?

Most patients with stage IV or recurrent colorectal cancer will have had surgery to remove the primary tumour. While this procedure will remove the visible cancer at the primary site, there is a risk that cancer cells have spread into the lymphatic system or blood stream and been transported to other organs where they lodge and begin to grow as metastatic tumours. Chemotherapy is often used as an additional line of attack (adjuvant therapy) to slow down or halt this growth. Typically, chemotherapy begins five or six weeks after surgery and continues for six months or longer.

Chemotherapy also can be used when it is not possible to remove the tumour by surgery or radiation therapy and has a role in reducing the bulk of the tumour, either before surgery or radiation therapy (neoadjuvant).



How is chemotherapy given?

A course of chemotherapy is delivered over several treatment cycles. Periods of receiving the medications are alternated with times of rest. Because normal tissues and organs are also affected by the chemotherapy, the rest period allows the body to recover its normal functions.

Depending on the regimen you have been prescribed, the cycle may be daily, weekly, every 2 weeks or monthly. Treatment may be given at your doctor's office, at a cancer centre or in an in-patient or out-patient clinic in a hospital.

What are the side effects of chemotherapy?

It is a reality that most chemotherapy regimens cause side effects. The high doses of anti-cancer drugs needed to kill the tumour cells are also toxic to normal cells, especially those that are dividing rapidly, such as the lining of the gut and blood cells. These effects tend to be experienced most acutely during the initial cycles and to diminish over the course of treatment.

The prospect of having to endure multiple cycles of chemotherapy can be daunting to even the most resilient of patients. If, however, you are prepared and well informed about the drugs you are administered, the experience can be less frightening.

Fortunately, there are medications available that can reduce most side effects. Reducing anxiety in anticipation of chemotherapy may, through relaxation techniques, also help. The periods of rest between cycles enable the body to recover and, once the course of treatment is completed, your organ systems will resume their normal functions.

More detailed information can be found in the section on “Help with Treatment-Induced Side Effects”.

https://drive.google.com/file/d/1RLeiG03X6BcC0WW2BGzNH_TPeVqvjDmW/view?usp=sharing

Commonly Used Chemotherapy Regimens for Colorectal Cancer

The chemotherapies in the following table are the most commonly used regimens to treat all stages of colorectal cancer. They may be used as single agents or in combinations. The abbreviations are often used to describe combination chemotherapy regimens. Unless stated otherwise, these are given intravenously, either by injection, infusion or through a port (surgically implanted catheter).

Patients are normally started on a standard, first-line regimen following surgery or radiation therapy. If the side effects cannot be tolerated, or if there are other health-related reasons, an alternative first-line option may be substituted. In some patients the chemotherapy eventually stops working because the tumour has developed mutated cells that are resistant to the drugs (in much the same way as bacteria develop resistance to antibiotics). In these cases, a second-line treatment is offered that works through a different molecular mechanism and is thus effective against the resistant mutated cancer cells.

Common Chemotherapy Regimens for Colorectal Cancer	
Single Agents	
5-fluorouracil (5-FU) and folinic acid (leucovorin)	This treatment is the most common one used to treat colorectal cancer. 5-FU is given together with folinic acid (a vitamin derivative), which makes the drug 5FU more active or effective.
capecitabine (Xeloda®)	This oral agent may be taken at home and is as effective as infusions of 5-FU, with a somewhat different side effect profile.

irinotecan (Camptosar [®] ; CPT-11)	Irinotecan is usually given either as initial (first-line) therapy or as an alternative when other treatments have ceased to work. It may be given on its own or in combination with other chemotherapy drugs.
oxaliplatin (Eloxatin [®])	Oxaliplatin is a platinum-based chemotherapy drug which is given in a similar way to irinotecan, as a single agent or in combination.
raltitrexed (Tomudex [®])	Raltitrexed is most often used as an alternative to 5-FU and folinic acid because it has a different side effect profile. It is seldom prescribed in Canada.
Combination Chemotherapies	
FOLFOX	This combination of 5-FU, folinic acid and oxaliplatin is frequently used as a first-line treatment.
FOLFIRI	5-FU, folinic acid and irinotecan in combination is an alternative to the FOLFOX regimen.
FOLFOXIRI	This more intensive combination therapy, which includes 5-FU, folinic acid, oxaliplatin and irinotecan, is most often used in patients with more advanced colorectal cancer.
XELOX or CAPOX	XELOX (also referred to as CAPOX) is a combination of capecitabine and oxaliplatin.
XELIRI	Combination of capecitabine and irinotecan, used as a second-line alternative.

vii. Targeted therapy for stage IV and recurrent colorectal cancer

Traditional chemotherapy regimens, as described above, work by killing cells – both cancerous and normal. Targeted therapies are designed to attack molecular pathways within cancer cells that are responsible for uncontrolled growth. Because they are more selective, they cause less damage to healthy tissues and have fewer side effects.

Targeted therapy can be used in combination with chemotherapy, enhancing its ability to reduce tumour size and extend the length of time before the tumour recurs. In some cases, the combination treatment allows the tumour to shrink so that surgery becomes an option.

A targeted therapy can be a small molecule or a biological therapy. Small molecule drugs are chemically synthesized and may be administered in pill form or intravenously. They work inside the cell to interfere with processes that govern cell survival and division. Biological therapies are proteins harvested from cultures of living cells and are given intravenously. They generally work by inhibiting the function of receptors on the surfaces of cancer cells.

Small molecule targeted therapies

Regorafenib (Stivarga[®]) works inside the cancer cell, blocking tyrosine kinase molecules which send signals to promote cell growth and division. It is unique in its class because it inhibits several kinase proteins at once, not only blocking cancer cell growth, but also stopping the development of new blood vessels to feed the cancer (angiogenesis). Regorafenib is effective in KRAS mutant and wild-type tumours.

Trifluridine and Tipiracil (Lonsurf®): This oral drug has been approved by Health Canada as an option for patients with colorectal cancer who did not respond to treatment with chemotherapy, anti-VEGF or anti-EGFR therapies.

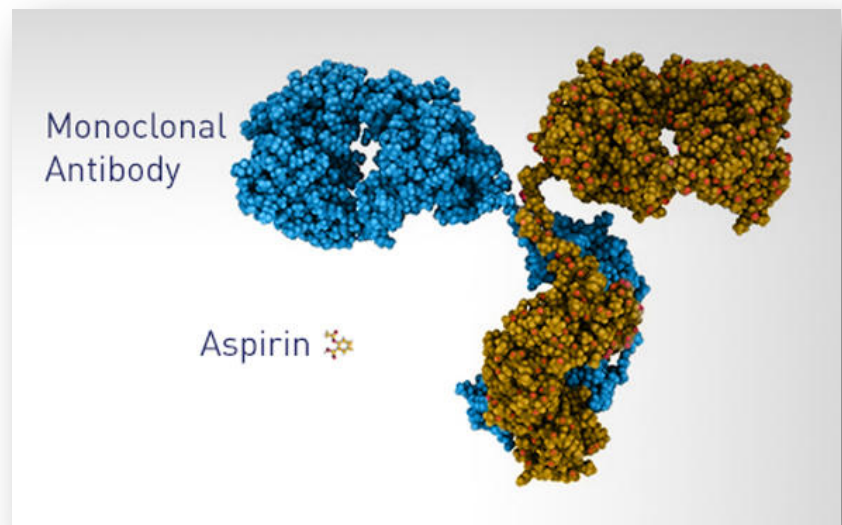
Larotrectinib (Vitrakvi®)

Larotrectinib is approved in Canada for Tyrosine Receptor Kinase (TRK) fusion protein-driven childhood and adult cancers. TRK fusion cancer is rare in colorectal cancer. The TRK fusion proteins act as oncogenic drivers promoting cell growth and survival, leading to TRK fusion cancer, regardless where it originates in the body.

Biological therapies

Monoclonal antibodies are made in the laboratory from a single type of immune system cell. These antibodies can identify molecules called receptors on the surface of cancer cells that may help them grow. The antibodies attach to the receptors and kill the cancer cells, block their growth, or keep them from spreading.

An important receptor regulating the growth and multiplication of cancer cells is the epidermal growth factor receptor (EGFR). Biological therapies that block EGFR include panitumumab (Vectibix®) and cetuximab (Erbix®).

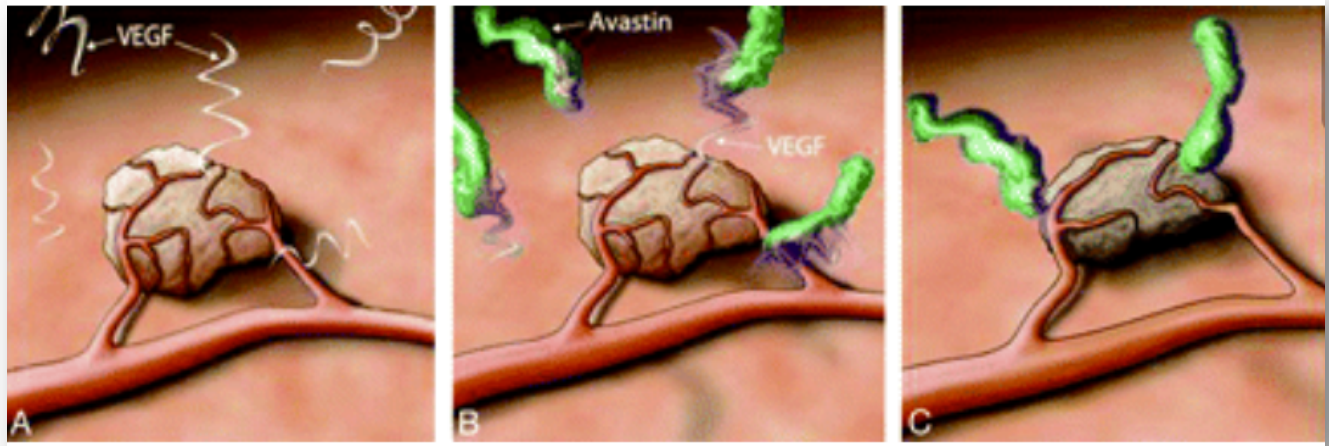


Size comparison of monoclonal antibody and small molecule drug (Aspirin®)

Source: Food and Drug Administration

The receptor may also send signals to other types of cells. For example, tumour cells release a chemical signal called vascular epithelial growth factor (VEGF) which is picked up by receptors on the surfaces of surrounding blood vessels and causes them to grow. This mechanism, called 'angiogenesis', feeds the tumour and allows it to enlarge. The biological therapy bevacizumab (Avastin®, Mvasi®) blocks the chemical from attaching to the receptor, causing the blood vessels to wither and thus starving the tumour of oxygen and nutrients.

Illustration of the mechanism of bevacizumab



A, There is a hypervascular tumour surrounded with VEGF protein. B, The bevacizumab compound binds to the free VEGF and reduces the concentration of the free VEGF. C, The reduction of available VEGF results in diminished blood supply to the tumour and tumour shrinkage.

Source: <http://www.ajnr.org/content/31/2/235/F1>

Choosing the right biological therapy

Patient selection is very important in choosing the right biological therapy to treat your colorectal cancer. Some types of genetic mutations within the tumour may make it resistant to treatment with certain biological agents. Therefore, it is crucial that your tumour has been tested to know its 'biomarker profile'.

The '**sidedness**' of the colorectal cancer (whether the tumour is on the right or left side of the body) is also an important determinant of which therapies may work best. Further information is contained in the Biomarkers section of the website

<https://drive.google.com/file/d/1DNkdQfH3qWZXH3INU9T9UgpREIFdndiy/view?usp=sharing>

Examples of Biological Targeted Therapies	
bevacizumab (Avastin [®] , Mvasi [®])	A monoclonal antibody administered together with chemotherapy. Chemotherapy attacks the tumour while bevacizumab blocks the growth of the tumour's blood supply.
panitumumab (Vectibix [®])	A fully human monoclonal antibody. Used as initial therapy in combination with chemotherapy. Can be used as a single-drug therapy when previous treatment has failed. Blocks the signals required for cancer cell growth and division.
cetuximab (Erbix [®])	A human/mouse (chimeric) monoclonal antibody. Used in combination with chemotherapy or as a single agent. Blocks the signals required for cancer cell growth and division.

Biosimilars

A biosimilar drug is nearly, but not quite, identical to an already-approved biological drug. Because biologics are complex protein-based molecules, they cannot be copied exactly and may have slightly different compositions than the original drugs. Biosimilar drugs are approved by Health Canada based on meeting certain manufacturing standards. Because they are not required to undergo extensive clinical testing, they are cheaper to produce and can be cost saving to the health system. An example is Mvasi[®] (bevacizumab) which is a biosimilar of Avastin[®].

Side effects of biological therapies

Although biological therapies are targeted at cancer cells, they can also have side effects. Most of these are reduced or disappear entirely as treatment progresses, however you should inform your doctor if you experience any symptoms during or after treatment.

Each biological therapy has a different side effect profile. The section on 'Help with Treatment-Induced Side Effects' https://drive.google.com/file/d/1RLeiG03X6BcC0WW2BGzNH_TPeVqvjDmW/view?usp=sharing in this website provides more details and ways to cope with side effects.

viii. Immunotherapies for Stage IV and Recurrent Colorectal Cancer

Like many forms of cancer, the outlook for people with colorectal cancer has improved as our understanding of the disease has increased. **Checkpoint inhibitors**, a type of immunotherapy that can kick start the immune system into fighting cancer, have recently emerged as a treatment option for a small subset (3-5%) of people with advanced colorectal cancer. People with these tumours have a biology described as “microsatellite instability-high” (MSI-H), which increases the likelihood that the body’s own immune system is able to detect the tumour. The remaining group, accounting for around 95% of people with advanced colorectal cancer, has disease commonly described as “microsatellite stable” (MSS). For these people, the immune system is most often not able to engage with the tumour and monotherapy checkpoint inhibitors have currently not been shown to be effective. Researchers are now exploring how they could expose colorectal cancer to the immune system by designing combination treatments that trigger an immune response.

Immune checkpoint inhibitors are showing promise in treating MSI-H or MMR-D tumours:

- Pembrolizumab (Keytruda[®])
- Nivolumab (Opdivo[®])

Knowing your MSI status is extremely important prior to selecting a treatment. MSI or MMR testing is recommended especially for colorectal cancer patients suspected to have a hereditary syndrome.

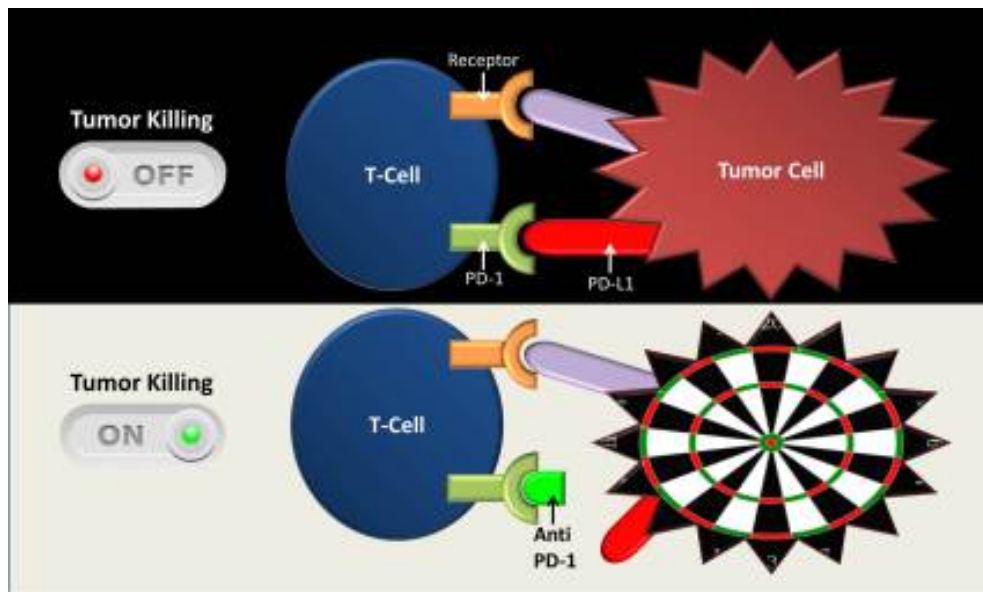
How immune checkpoint inhibitors work

Immune checkpoint inhibitor drugs work by allowing the body's immune response to do its job of attacking and killing abnormal cells, to stop them from multiplying and causing cancer.

This immune response involves T cells, which are activated when they recognize an abnormal or mutated cell. PD-1 is a checkpoint protein on the surface of T cells which normally acts as a type of "off switch" to help keep the T cells from attacking other cells in the body. It does this when it attaches to PD-L1, a protein on some normal (and cancer) cells. When PD-1 binds to PD-L1, it basically tells the T cell to leave the other cell alone. Some cancer cells have large amounts of PD-L1, which helps them hide from an immune attack.

Monoclonal antibodies that target either PD-1 or PD-L1 can block this binding and boost the immune response against cancer cells. These drugs have shown a great deal of promise in treating certain cancers.

Illustration of How Checkpoint Inhibitor Drugs Work



In the diagram above, before immunotherapy (top), the tumour cell's PD-1 ligand, or PD-L1, molecule (red) binds to a type of white blood cell called a T cell in a way that enables the tumour cell to evade destruction by the immune system. During immunotherapy (bottom), an anti-PD-1 inhibitor drug (bright green) blocks PD-L1 binding, enabling the T cell to target the tumour cell for destruction.

Availability of targeted medications and immunotherapies

All of the medications mentioned have been approved by Health Canada for the treatment of colorectal cancer. However, since each province has its own list of the drugs that it covers, some of these treatments may not be available or may not be reimbursed by your health system. If you have private insurance, your plan may cover

these treatments. Some pharmaceutical manufacturers offer patient assistance programs that provide financial support to obtain the medications. If none of these options are available, you may have to pay for certain drugs out of pocket. Contact us, we are happy to help advocate on your behalf.

Questions to Ask Your Oncologist About Chemotherapy and Targeted Drugs

Goals of treatment

What can I expect from my therapy?
Can the cancer spread, even though I am on chemotherapy?

My treatment plan

What are the names of the drugs that will be used in my treatment?
Is there evidence that they are more effective than other chemotherapy drugs?
How many treatments will I need?
How will the treatments be given?
Do I qualify for biological therapy in conjunction with chemotherapy? If so, which do you recommend?
Can I be treated according to the side in which my primary tumour originated?
Do I have an MSI-High tumour or MSS tumour?
Is immunotherapy a potential treatment for me?
Do I require genomic profiling for my tumour?

How will the chemotherapy affect me?

Will I be able to go home afterwards?
What will I feel like after my treatments?
Will I be able to work? Will I be able to take care of my family?
If I am taking chemotherapy, can I eat all kinds of foods?
Will I be able to take multi-vitamins or antioxidant therapy during chemotherapy?
Can I drink alcohol?
Will chemotherapy affect my sex life?
Will chemotherapy affect my fertility?
How often will CEA testing be done?
How often will ct scans be performed?
Will any other tests be done regularly while I am receiving chemotherapy?

Side effects of chemotherapy

What are the possible side effects of these treatments and how long do they last?
Will my hair fall out?
Will I be nauseated? If so, how can that be treated?
Will I be fatigued? How will you address that?
Will I get mouth sores? If so, how will that be addressed?
Is there anything I can do to lessen the side effects?

Outcomes of chemotherapy

How will I know if the treatment is working?

What are the chances for remission or for a longer life?

D. Remission/Cure

If the treatment has successfully eliminated all traces of cancer, the patient is said to be in remission. During the 5-year follow-up period after treatment, patients are actively monitored by physical examinations and routine testing.

Regular tests include:

- Medical history, physical examination and CEA laboratory test every 6 months for 5 years
- Abdominal CT imaging annually for 5 years
- Pelvic CT imaging annually for 3 years, if primary tumour was located in the rectum
- Chest CT imaging annually for 5 years
- Colonoscopy at 1 year following surgery; frequency dictated by findings; every 5 years of findings are normal

If no recurrence has been detected after 5 years, the patient is deemed to be no evidence of disease (NED) for their cancer. Regular screening is still recommended, however. The chances of developing a new colorectal tumour are the same as for other people with the same health status and medical history.

E. Working with Your Oncology Team

Your doctor and the rest of your health care team are there to help you and support you through what can be a difficult time. Building good relationships with your treating physician and other members of the team doesn't just happen – it takes care and effort on both sides. As in any relationship, clear and honest communication is the key to success.



Being informed, forthright and respectful is a great starting point. Ensure that all your concerns and questions, no matter how small, have been addressed. It may require more than one visit to discuss all of your questions and you can be sure that new concerns will arise at a later time.

Preparing for appointments with your doctor

Given that this is an emotionally stressful time and you are trying to absorb a lot of facts at once, it may be difficult to remember everything your doctor says to you. This is why most patients find it helpful to do any or all of the following:

- Bring a family member or friend with you to the appointments. The other person will hear what is said and may think of questions to ask
- You may wish to tape record the conversations with your physician (with their permission) so you can replay the information later
- Ask the other person to take detailed notes during the appointment so that you can concentrate on what is being said to make sure you understand everything. Ask for clarification if necessary
- Write out your questions or concerns before the appointment so that you will not forget what to ask. Some people find it helpful to keep a small notebook handy so they can write down questions as they come up from day to day
- Don't be afraid to ask where you can find more information about what you are discussing. You are most certainly entitled to know.

Asking for Copies of Your Medical Records



This may be the last thing on your mind as you gather information, think through all the decisions, and undergo stressful treatments. But, it's a very important step to take!

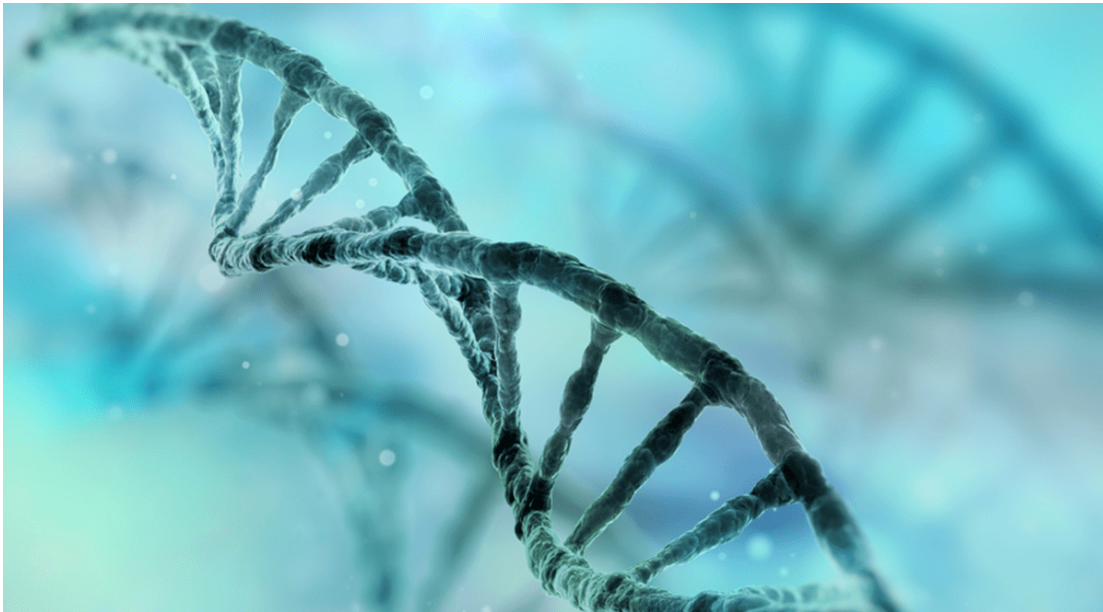
If your Centre does not have electronic access to medical records for their patients, then the following information may be helpful. Every patient should ask for copies of all medical records related to their diagnosis, treatment and follow up. In the future, it is quite likely that you will be under the care of a new doctor – either because of a staff change, because your treatment plan requires you to see a new specialist, or because you are being followed up by your family doctor or other medical practitioner. It is important that you are able to give your new doctor the exact details of your diagnosis and treatment. This will not only save time for the new doctor but also ensure that your set of records is complete.

We recommend that you obtain two copies of the following documents – one to give to a new doctor and one to keep for yourself:

- The pathology report from any biopsy or surgery
- The surgical report (if you have had surgery)
- The hospital discharge summary (if you were admitted to hospital)
- A final summary of the dose and field of any radiation therapy you have received
- A list of all your drugs, drug doses, and when you took them (including over-the-counter drugs and natural medicines). This may be helpful if long term side effects are later discovered.

Staff in your treating doctor's office can provide you with copies. It is best to ask for your records as soon as they are generated. If the treatment or test took place in a hospital, you may need to contact the hospital's medical records department to determine how to go about securing your records.

PART V: NEW & EMERGING DEVELOPMENTS IN COLORECTAL CANCER TREATMENTS

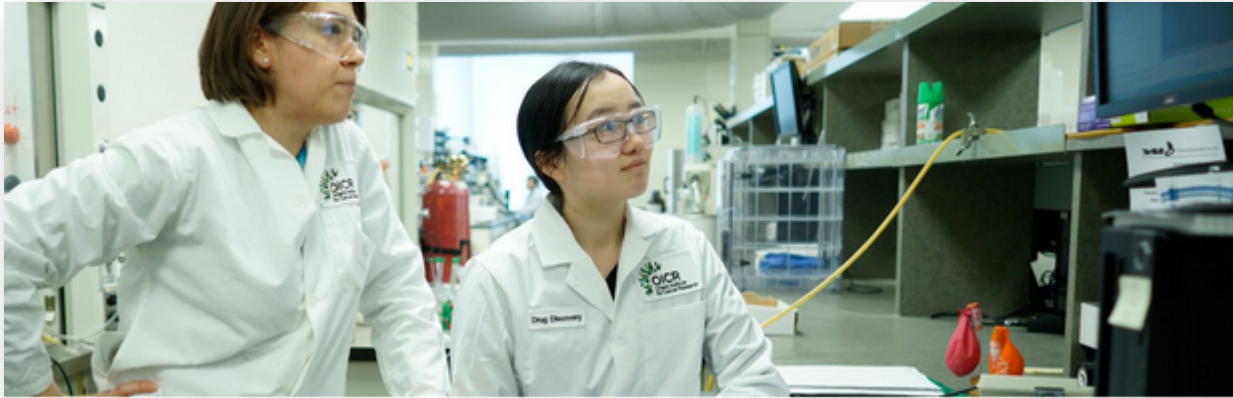


Research continues for better ways to prevent and treat colorectal cancer. A major focus of new developments is on metastatic disease – eliminating the spreading of the primary tumour and treating metastatic tumours that appear in other organs. New therapies require clinical testing before being made available on a widespread basis.

As new options for surgery and radiation therapy are developed, they are usually available at first only in research-based facilities. Over time, the new procedures may be adopted by other treatment centres if there is sufficient demand and if the resources are available. Specialized equipment may be required and doctors trained in these techniques need to perform the procedure regularly. The ALPPS procedure, described earlier, is an example of this process. Developed in the United States, it is now becoming available in Canada. Other examples of emerging surgical techniques include robotic surgery and laparoscopic lateral pelvic lymph node dissection.

New drug treatments are developed on a world-wide basis and Canadian cancer centres may participate in various phases of discovery and testing. Patients may gain access to experimental drug treatments through clinical trials or on a compassionate basis if no other treatment options are available and the patient is in a life-threatening situation. Once a new drug is approved by Health Canada and each province has decided whether and how they will fund it, most treatment centres will begin to use the new medication immediately. For further information, consult the sections on ‘What are Clinical Trials?’

https://drive.google.com/file/d/1RLeiG03X6BcC0WW2BGzNH_TPeVqviDmW/view?usp=sharing
and ‘Help me Find a Clinical Trial’ [\[insert hyperlink\]](#).



Source: Ontario Institute for Cancer Research

An example of a new development in drug treatment is immunotherapy (discussed in the section on 'Biomarkers' <https://drive.google.com/file/d/1DNkdQfH3qWZXH3INU9T9UgpREIFdndiy/view?usp=sharing> . New immunotherapies such as pembrolizumab (Keytruda[®]) and nivolumab (Opdivo[®]) stimulate the patient's own immune system to fight cancer cells. These treatments are currently being used by oncologists across Canada to treat skin and lung cancers and clinical studies are underway to study their effects in colorectal cancer. An exciting development is that they have shown activity in colorectal cancer patients whose tumours exhibit microsatellite instability – a characteristic that can be measured by lab testing.

If you would like additional information on the management of the disease or would like to discuss any of the information appearing in this guide, please call us, we are eager to assist. Contact us, we are eager to help!

Toll Free: 1 833 79 CCRAN (22726) or

Email us at info@ccran.org

SCREEN IT! TREAT IT! BEAT IT!

TOGETHER, ANYTHING IS POSSIBLE!

PART VI: ONLINE SOURCES & REFERENCES:

American Cancer Society.

<https://www.cancer.org/treatment/treatments-and-side-effects.html>

Canadian Cancer Society.

<https://www.cancer.ca/en/cancer-information/cancer-type/colorectal/treatment/?region=on>

Cleveland Clinic.

<https://consultqd.clevelandclinic.org/surgery-opens-new-possibilities-for-treating-liver-metastases-from-colorectal-cancer/>

Healthline.

<https://www.healthline.com/>

Johns Hopkins Website:

http://www.hopkins-gi.org/GDL_Disease.aspx?CurrentUDV=31&GDL_Cat_ID=AF793A59-B736-42CB-9E1F-E79D2B9FC358&GDL_Disease_ID=A6D10E80-887D-49A7-B3BB-0517D38CE757

Moffitt Cancer Center.

<https://moffitt.org/cancers/liver-hepatocellular-cancer/treatment/surgery/alpps/>

National Cancer Institute.

<https://www.cancer.gov/types/colorectal/patient/colon-treatment-pdq>

National Comprehensive Cancer Network (NCCN).

<https://www.nccn.org/patients/default.aspx>

National Institutes of Health

<https://directorsblog.nih.gov/2015/06/09/a-surprising-match-cancer-immunotherapy-and-mismatch-repair/>

Oncolink (information about rectal cancer).

<http://oncolink.com/types/article.cfm?c=5&s=11&ss=605&id=9457&p=3>

Ostomy Canada Society.

<https://www.ostomycanada.ca/>

Radiation Therapy Answers.

www.rtanswers.org

Sunnybrook Health Sciences Centre

<https://health.sunnybrook.ca/navigator/when-cancer-spreads-and-standard-therapy-no-longer-works/>