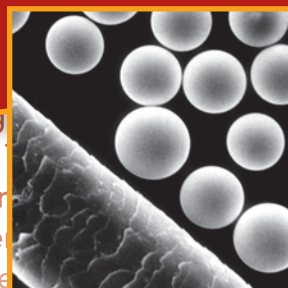


TheraSphere®

An Innovative Treatment for Liver Cancer

Powerful • Targeted • Safe



A Patient's Guide

Important Information
for People with Liver Cancer

www.therasphere.com

U.S. Market

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TheraSphere®

A Patient's Guide

This booklet contains information about **TheraSphere®**, also called radioembolization, what to expect from typical treatment activities and possible side effects. It also contains some helpful information such as common medical terms (found in the Glossary) and patient resources.

Ask your doctor if **TheraSphere** is right for you.

www.therasphere.com

Manufactured by  **MDS**
Nordion



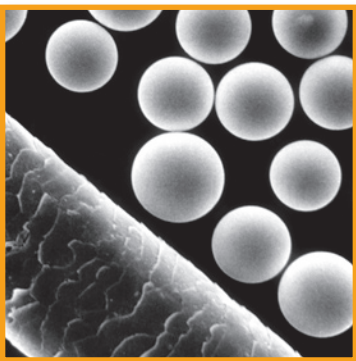
Introduction

What is TheraSphere and how does it work?

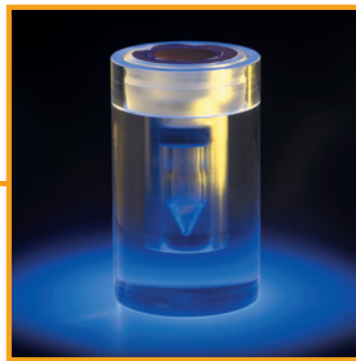
TheraSphere is a low toxicity, targeted liver cancer therapy that consists of millions of tiny glass beads containing radioactive **yttrium-90**.

The glass radioactive beads (20-30 **micrometers** in diameter – about a third of the width of a human hair) are delivered directly to the liver tumors.

Your doctor injects **TheraSphere** into the **hepatic artery** of your liver through a small flexible tube known as a **catheter**. The tiny radioactive glass beads flow directly into the liver tumor via its own blood vessels and become permanently lodged in the small blood vessels of the tumor. The radiation destroys the tumor cells from within the tumor, with minimal impact to the surrounding healthy liver tissue. The radioactive microspheres will continue to emit radiation over the course of several weeks after **TheraSphere** treatment and radiation levels will decrease to insignificant levels. **TheraSphere** treatment is commonly referred to as radioembolization or selective internal radiation therapy (SIRT).



TheraSphere microspheres next to a human hair



TheraSphere dose vial

TheraSphere treatment is typically an outpatient procedure that does not require hospitalization. It is well tolerated by patients, with side-effects that are normally milder than with many other liver cancer treatments. Because the procedure is directed to the liver tumor, there is minimal impact to non-targeted tissue. After treatment, most **TheraSphere** patients are eligible for further therapeutic options because the procedure does not block the vessels of the liver.

TheraSphere treatment has some common side effects, including mild to moderate fatigue, pain and nausea for about a week. Physicians describe these symptoms as similar to those of the common flu. Some patients may experience loss of appetite and temporary changes in liver blood tests. For details on side effects, please refer to section [What side effects may I have?](#) (page 11).

TheraSphere is a **humanitarian use device (HUD)** for treating cancer that started in your liver (**hepatocellular carcinoma or HCC**). It can be used to **downstage** tumors to become eligible for surgery or transplantation. It is also the only medical device approved in the United States to treat primary liver cancer patients with **portal vein thrombosis (PVT)**. **TheraSphere** has been approved as an HUD based upon its safety and probable benefit.

Over 5000 treatments have been performed with **TheraSphere** in both routine liver cancer treatment and at research centers of excellence around the world.

When can my doctor use TheraSphere?

- Your doctor may use **TheraSphere** to treat your liver cancer if it cannot be removed by surgery.
- Your doctor may use **TheraSphere** to treat your liver cancer while you wait for a liver transplant. **TheraSphere** has demonstrated the potential for **downstaging** patients, making them eligible for **Radiofrequency Ablation (RFA)**, surgery or a liver transplant.

Who is TheraSphere suitable for?

TheraSphere is suitable for patients where either the liver is the only site of disease or the liver is the major site of disease. **TheraSphere** has no effect on tumors outside the liver.

Before **TheraSphere** can be offered as a treatment option, your doctor will take into consideration several factors such as liver performance status, medical history and the liver blood flow to minimize side effects and optimize therapy to your liver. Do not hesitate to ask your doctor or nurse about the tests they will perform.

How can I benefit from TheraSphere treatment?

Since every patient is different, it is difficult to know how much you may benefit from **TheraSphere**. If your doctor thinks **TheraSphere** may be suitable for you, your doctor can treat your liver cancer with **TheraSphere**, possibly stabilizing your liver disease or increasing your chance of having RFA or surgery to remove the tumor or getting a liver transplant (some physicians refer to this as downstaging to transplant).

Will insurers pay for TheraSphere treatment?

TheraSphere is approved for Medicare reimbursement. It is assigned to Ambulatory Payment Classification (APC 2616) and is billed to Medicare under HCPCS code C2616. To date, all Medicare cases have been reimbursed.

In addition to Medicare coverage, **TheraSphere** has been reimbursed by United Healthcare, Anthem Wellpoint and a variety of commercial insurance plans. These plans include HMO, PPO, indemnity, and self-insured employers. Government sponsored programs such as state Medicaid programs, Veterans Administration and Tri-Care for military personnel have also provided coverage. For those insurance plans that require it, your health care provider will work with you to achieve pre-certification for **TheraSphere** treatment.

A Practical Guide to TheraSphere Treatment

At MDS Nordion, we care about the lives and families our products touch. We hope you will be reassured by the information that is provided for your consideration.

What to expect with a typical TheraSphere treatment

You can expect different types of doctors to be involved with **TheraSphere** treatment. Interventional Radiologists, Radiation Oncologists and Nuclear Medicine Physicians are some of the specialists who may be working with you during your treatment. Typically, you will continue seeing your Medical Oncologist while undergoing treatment.

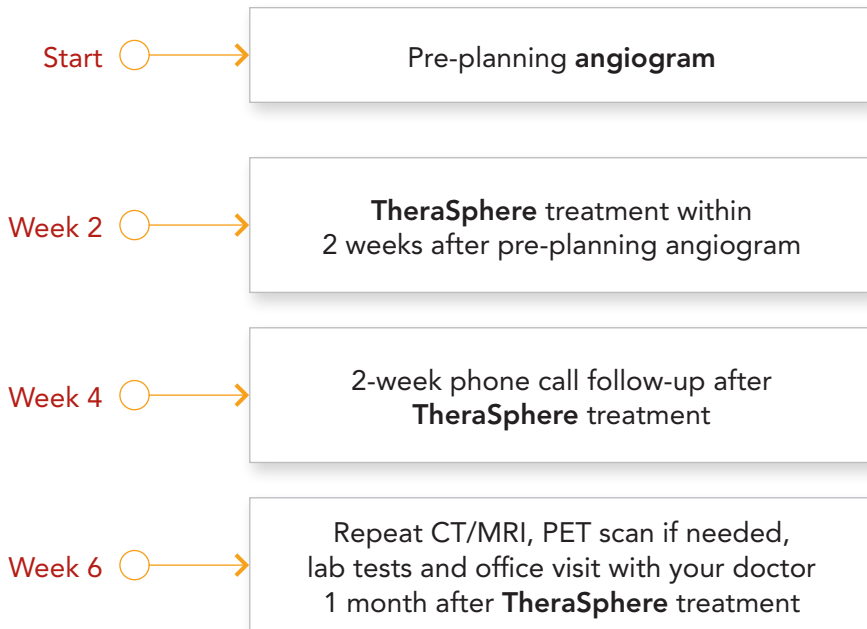
The actual **TheraSphere** administration is performed by an Interventional Radiologist.

Although all of the procedures are done on an outpatient basis, they require several visits to the hospital and your follow-up treatments will span several months.

Will I have to stop my other therapy treatments to receive TheraSphere?

Generally, most patients' therapy is stopped before receiving **TheraSphere**. However, your Oncologist will determine if your therapy needs to be stopped during the treatment period.

TheraSphere Treatment Summary

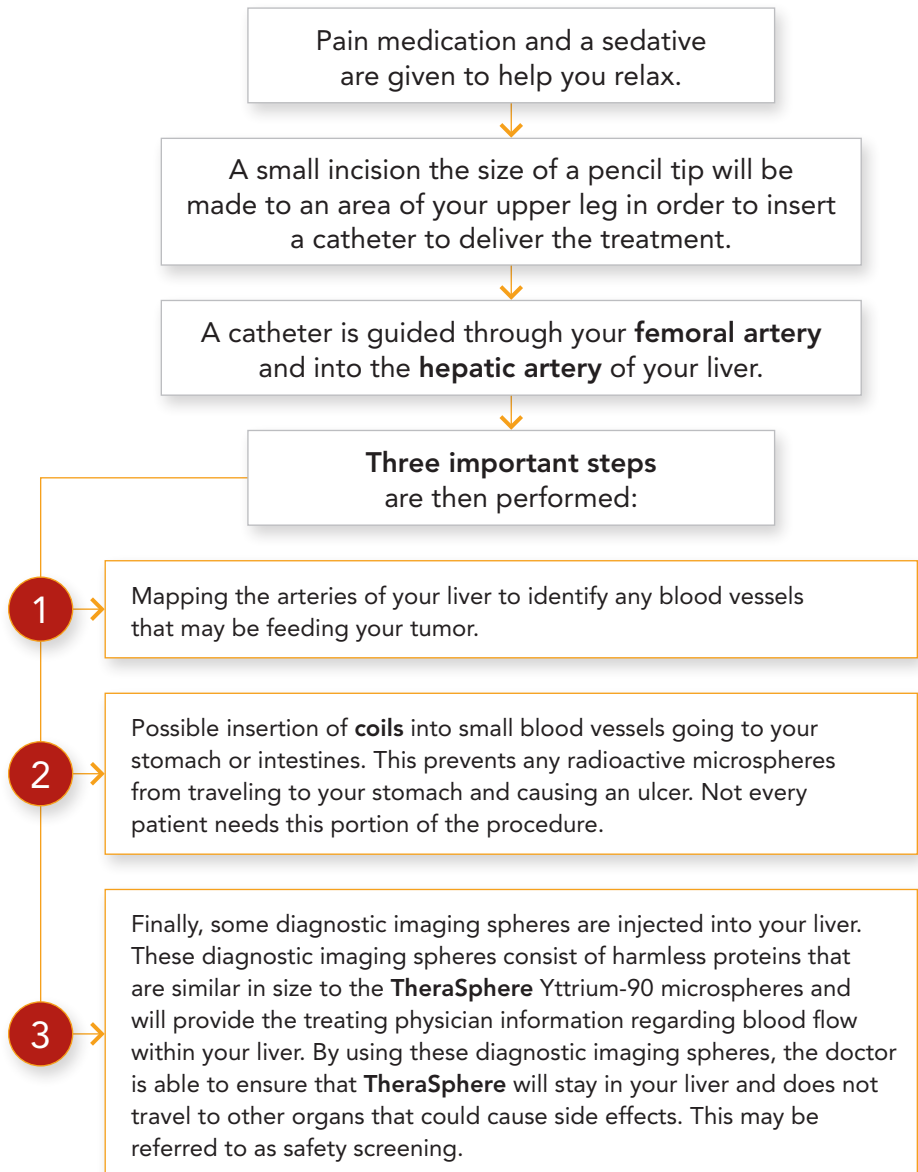


If a second **TheraSphere** treatment is needed, the same schedule will be repeated. To maximize the safety of **TheraSphere** treatment, only one lobe of the liver is treated at a time. Therefore, if you have tumors in both lobes of your liver, you may need a second treatment.

These steps are described in further detail below. See [Follow-Up Appointments](#) (page 13).

Preparation and Pre-Planning Angiogram

This is the first step to prepare you for your treatment (this is not the radiation treatment). The angiogram helps determine if you are a candidate for **TheraSphere**. If you are a candidate, you will return 2 weeks later for your radiation treatment. Once you are in the procedure room, the following steps occur:



A small bruise or marble-sized lump may be present at the site where the catheter was inserted. You should notify your doctor if you notice any bleeding or additional swelling at the site.

The angiogram takes up to 2 hours. You will then be transferred to the Nuclear Medicine Department for a scan to see the location of the diagnostic imaging spheres. This scan takes approximately 2 hours. Following your Nuclear Medicine scan you will typically be discharged.

Discharge Instructions

On the day of discharge, limit your activities:

- No physical exercise or heavy lifting (greater than 10 pounds/4.5 kilos) for the next 3 days.
- Do not drive for 24 hours after the procedure.
- You may resume all other daily activities 24 hours after the test.
- You should drink at least 6 glasses of water (8 oz.) over the next 24 hours. Water helps to clear the dye used during the pre-planning angiogram.

TheraSphere Treatment Day

Typically, your treatment day will be 1–2 weeks following your pre-planning angiogram. You will be at the hospital for approximately 4–6 hours. The treatment requires another angiogram, but you typically will not need to have another scan in the Nuclear Medicine Department.

What will TheraSphere treatment be like?

Once you are taken into the procedure room, the following steps occur:

1

Pain medication and a sedative are given to help you relax. You will be sleepy but able to communicate with your doctor and the team if you choose.

2

A topical numbing agent is applied to an area of your upper leg, a small incision made and the catheter inserted into your **femoral artery**.

3

The catheter is guided to the **hepatic artery** using an x-ray method (**fluoroscopy**) to position the catheter.

4

TheraSphere is infused, the blood flow carries **TheraSphere** to the targeted tumor and radiation is emitted from the glass beads. **TheraSphere** infusion takes several minutes but due to catheter placement time, you will typically be in the room for about 1 hour.

5

The catheter is removed and you are taken to the recovery room for approximately 2–6 hours.

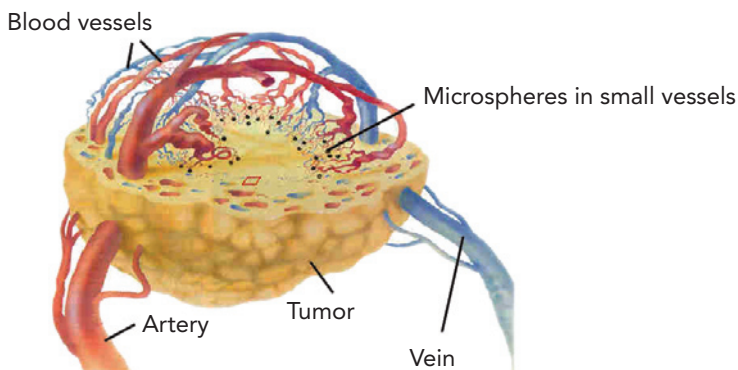


Figure 1: Typical Liver Tumor with Microspheres Lodged in Small Vessels
(catheter placed in artery)

Will the incision site be different from the pre-planning angiogram?

The procedure for inserting the catheter is similar for both **TheraSphere** infusion and the pre-planning angiogram. Please refer to **Preparation and Pre-Planning Angiogram** for information (page 7).

Prescription Medications

The following prescription medications may be given to you the day of treatment:

- A low-dose steroid (i.e. Medrol dose pack) is given to help combat fatigue.
- An anti-ulcer medication is given to help protect your stomach.
- An antibiotic to take for 5 days to reduce potential for infection.

Not all patients require medications. All prescriptions will be reviewed with you prior to discharge.

Please take your medications as prescribed.

On the day of treatment, you may be discharged with an information packet containing items such as your scheduled follow-up appointments, prescriptions and emergency contact phone numbers. **Please put these in a safe place, as you may need to bring them with you to your follow-up appointments.**

Post-treatment Discharge Instructions

Discharge instructions will be similar to the pre-planning angiogram. Any additional considerations may be provided by your treatment team.

Do I need to do anything differently when I go home after treatment?

As with any surgical procedure, on the day of discharge, limit your activities. You should not do any physical exercise or heavy lifting (greater than 10 pounds/4.5 kilos) for the next 3 days, but you may resume all other daily activities 24 hours after treatment. Please refer to **Radiation Safety Precautions** (page 14) for additional considerations.

When can I return to work?

Every patient has different recuperative needs. Generally, patients that have no symptoms prior to the procedure recover more quickly. The type of work you do should also be taken into consideration before returning to work as physical exercise and heavy lifting (greater than 10 pounds/4.5 kilos) should be considered. Consult your physician if you have any questions.

What side effects may I have?

Typical side effects are mild to moderate after **TheraSphere** treatment. These may include abdominal/stomach pain, nausea, vomiting, fever or fatigue and generally resolve within 48 hours. If these signs and symptoms last more than 7–10 days, tell your doctor. You may receive additional medications with your treatment to minimize these side effects.

TheraSphere releases radiation that affects liver tissue. As a result, your physician will routinely test your blood to monitor liver function and identify any potential risks that might occur. Rarely there may be loss of liver function which could lead to death. Many side effects disappear shortly after the delivery of treatment. Other side effects may last longer or become permanent.

Even after safety screening, there is still a small risk that **TheraSphere** could be delivered to your lungs and/or digestive tract, possibly resulting in:

- Lung damage, which could include swelling, scarring or shortness of breath
- Irritation of the gastrointestinal tract, which could result in chronic pain, nausea, vomiting, ulcers, bleeding or pancreatitis (swelling of the pancreas)

As possible with every treatment, rare, serious side effects may occur and since every patient is different, your doctor can best describe any possible side effects you may experience.

Further information is also described in the **TheraSphere Package Insert** (available at www.therasphere.com).

What should I do if I experience a side effect?

It is important that you contact your doctor or nurse if you experience a side effect. Your doctor may prescribe medications to ease any discomfort. Although it is rare that side effects become life threatening, it is important to tell your doctor as soon as you experience any side effects.

Does TheraSphere treatment cause hair loss?

There are no reported side effects of hair loss due to treatment with **TheraSphere**.

Follow-Up Appointments

- Your doctor may follow up with you 2 weeks after your treatment to evaluate how you are feeling after the procedure.
- Approximately 4 weeks after your treatment, you will return to your hospital for a repeat CT/MRI or PET scan if needed, and blood tests. You will then have a one-month post treatment visit with your doctor to review your scans and blood tests.
- At your one-month follow-up appointment it will typically be determined if you need a second treatment. To maximize the safety of **TheraSphere** treatment, only one lobe of the liver is treated at a time. Therefore, if you have tumors in both lobes of your liver, you may need a second treatment.
- Your doctor or nurse will advise you about your specific follow-up appointments or routine monitoring. Typically they will occur at 3 month intervals.

Radiation Safety Precautions

Radiation safety is a natural concern for many patients being discharged from the hospital following **TheraSphere** treatment, however no special safety precautions are required. It has been established that patients leaving the hospital are not at risk to those around them; the radiation field outside their body is sufficiently low to be deemed not a radiation safety issue. As a precaution, many hospitals have general instructions as suggested guidelines. You will be provided with further information on these precautions when you leave the hospital.

If you anticipate traveling across international borders, the security screening equipment may detect low radiation levels as a result of your **TheraSphere** treatment. Your physician can provide you with a letter explaining the circumstances and it is available upon request.

Please note: Although **TheraSphere** radioactivity continues to diminish over time, **TheraSphere** will remain permanently implanted in the liver tissue. Special liver tissue handling may be required at the time of surgery or if cremation is considered.

MDS Nordion Cares

First hearing the words “you have liver cancer”, can be a life altering experience and can start a cascade of emotions. By spending time researching treatment options for either yourself or a loved one, you are ensuring you will be receiving the best care available today based on individual needs. We hope the information provided on **TheraSphere** has been helpful. Should you have any questions, please don't hesitate to contact your doctor.

About MDS Nordion

MDS Nordion is a global leader in providing products and services for medical imaging and radiotherapeutics, and sterilization technologies for the prevention, diagnosis and treatment of disease. MDS Nordion's products and services are used on a daily basis by pharmaceutical and biotechnology companies, medical-device manufacturers, hospitals, clinics and research laboratories and benefit the lives of millions of people in more than 70 countries around the world. Learn more at www.mdsnordion.com.

Glossary

Please note that the terms defined in this glossary are commonly used terms for the treatment of liver cancer with TheraSphere.

Albumin is a serum protein that is mostly produced by the liver. Decreases in albumin levels can be an indication of advanced liver disease.

ALT stands for alanine amino-transferase which is an enzyme found in large amounts in the liver. High ALT can be a sign of toxic hepatitis. The AST/ALT ratio is sometimes used in the diagnosis of different liver diseases (see AST below).

Angiogram – is a medical imaging technique used to visualize the inside of blood vessels and organs of the body.

An **Artery** is any blood vessel that carries blood from the heart to the body.

AST stands for aspartate amino-transferase which is an enzyme found in large amounts in the liver. High levels of both ALT and AST

is a sign of viral hepatitis or liver damage caused by drugs. High AST without a change in ALT is a sign of active cirrhosis of the liver or metastatic tumor to the liver, among other possibilities.

Bilirubin is the major pigment of bile and is removed from the blood by the liver. Bilirubin levels in the blood levels rise when the liver is unable to metabolize it. Rises in serum bilirubin levels are a sign of liver disease.

A **Catheter** is a flexible tube used to deliver or withdraw fluids from the body.

Coil – a small twisted wire that is inserted into a vessel to block blood flow.

Downstaging is a situation in which a patient with a previously inoperable tumor or large number of tumors is now eligible for surgery or liver transplant following treatment.

The **Femoral Artery** is the chief artery of the thigh supplying blood to the groin and legs.

Fluoroscopy is an x-ray procedure that takes continuous pictures to study moving structures within the body.

The **Hepatic Artery** is a blood vessel to the liver, stomach, small intestine and pancreas.

Hepatocellular Carcinoma (HCC) (or Primary Liver Cancer) is a type of liver cancer which has started in the liver.

A **Humanitarian Use Device (HUD)** is a medical device that is available in the United States on the basis of established safety coupled with probable benefit.

An **Infiltrative Tumor** is a type of tumor that has grown into the surrounding tissue so much that there are no clear edges.

A **Micrometer** is a unit of measurement of length. One micrometer is equal to one millionth of a meter (approximately one 25 thousandth of an inch).

Portal Vein Thrombosis (PVT) is a blockage, by a blood clot, of the portal vein, which brings blood to the liver.

RFA – Radiofrequency Ablation (RFA) is a medical procedure where a probe is placed inside the tumor, radiofrequency waves pass through the probe and increases the temperature within tumor tissue that results in destruction of the tumor.

TheraSphere is a liver cancer treatment that is made up of microscopic glass beads containing radioactive Yttrium-90.

TheraSphere Package Insert is a document which fully describes the **TheraSphere** product, its indication, contraindications, precautions/warnings, adverse events and other important product related information. The TheraSphere Package Insert can be found on the website **www.therasphere.com**.

ULN is a short form for Upper Limit of Normal and is the largest value of a test result before the result is considered high.

Yttrium-90 is a radioactive isotope that emits energy in the form of beta radiation as it decays to stable Zirconium-90.

Zirconium-90 is a stable element that is produced from the decay of Yttrium-90.

Patient Resources

These resources may help you find information and support:

Cancer Information & Support

The National Cancer Institute (NCI)

For valuable cancer related health information. You may call 1 800 4 CANCER (1 800 422 6237), 9:00 a.m. to 4:30 p.m. local time, Monday through Friday; TTY 1 800 332 8615
www.cancer.gov

American Cancer Society (ACS)

For support and information – includes an online planner to better participate in your treatment. For immediate assistance, call the National Cancer Information Center at 1 800 ACS 2345. Trained Cancer Information Specialists are available 24 hours a day, seven days a week to answer your questions.
www.cancer.org

Liver Foundations

American Liver Foundation (ALF)

Provides research, information on clinical trials, advocacy and support through local chapters. 75 Maiden Lane, Suite 603
New York, NY 10038
Tel: 212 668 1000

Toll-free: 1 800.go.liver (465 4837)
Toll-free: 1 888.4hep.usa (443 7872)
Fax: 212 483 8179
E-mail: info@liverfoundation.org
www.liverfoundation.org

Support Groups

Cancer Care

National Office
275 7th Avenue, Floor 22
New York, NY 10001
Toll-free: 1 800 813 HOPE (813 4673)
www.cancercares.org

Cancer Hope Network (CHN)

Two North Road – Suite A
Chester, NJ 07930
Toll-free: 1 877 HOPENET (467 3638)
www.cancerhopenetwork.org

Yttrium 90 Microspheres Education and Support (YES)

791 Arnold Paul Road
Canton, TX 75103
Toll-free: 1 877 937 7478
www.beatlivetumors.org
www.y90support.org

