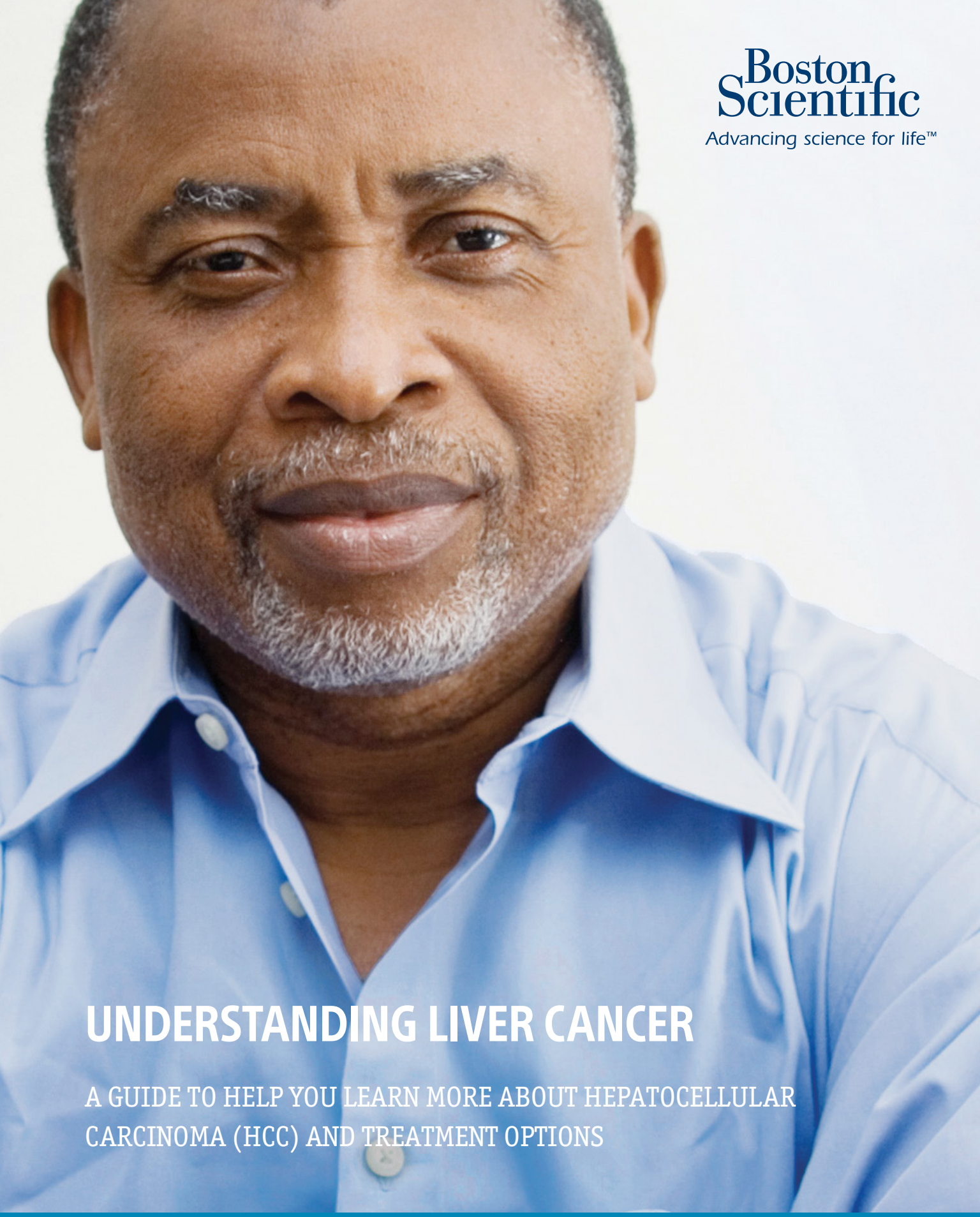

Boston Scientific

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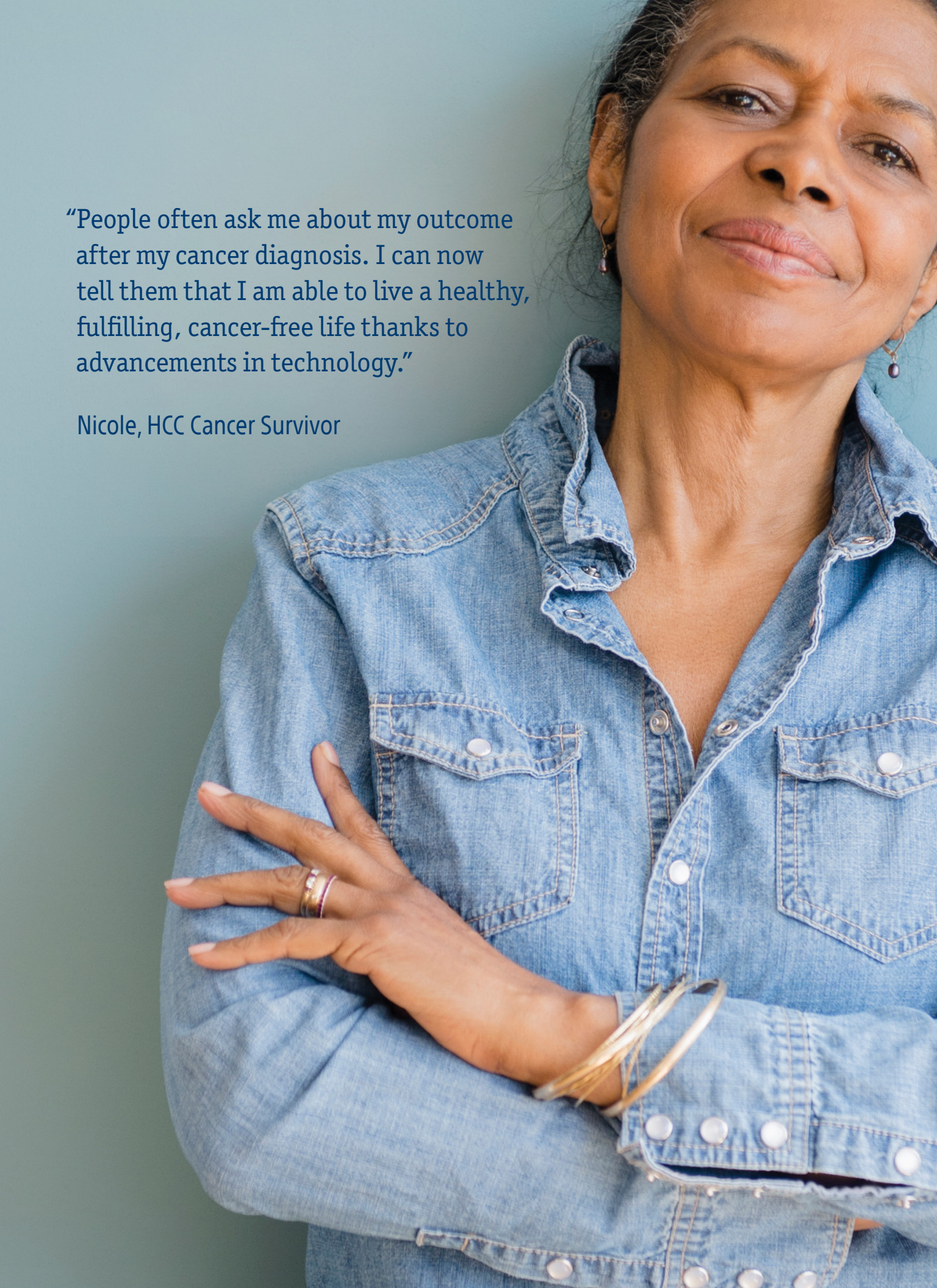
UNDERSTANDING LIVER CANCER

A GUIDE TO HELP YOU LEARN MORE ABOUT HEPATOCELLULAR CARCINOMA (HCC) AND TREATMENT OPTIONS



"People often ask me about my outcome after my cancer diagnosis. I can now tell them that I am able to live a healthy, fulfilling, cancer-free life thanks to advancements in technology."

Nicole, HCC Cancer Survivor

A CANCER DIAGNOSIS IS LIFE-CHANGING, AND THIS GUIDE CAN PROVIDE A HELPFUL PLACE TO START

You may have questions about your diagnosis. This guide can help you find answers, treatment information resources, and provide you with questions to ask your doctor. It is intended to offer practical support and information.

What you'll find inside:

What the liver does 4-5
How liver cancer develops 7
Treatment options 8-11
Questions to ask your doctor 12
Glossary 13
A closer look at the liver 14
Helpful resources 15

WHAT YOUR LIVER DOES

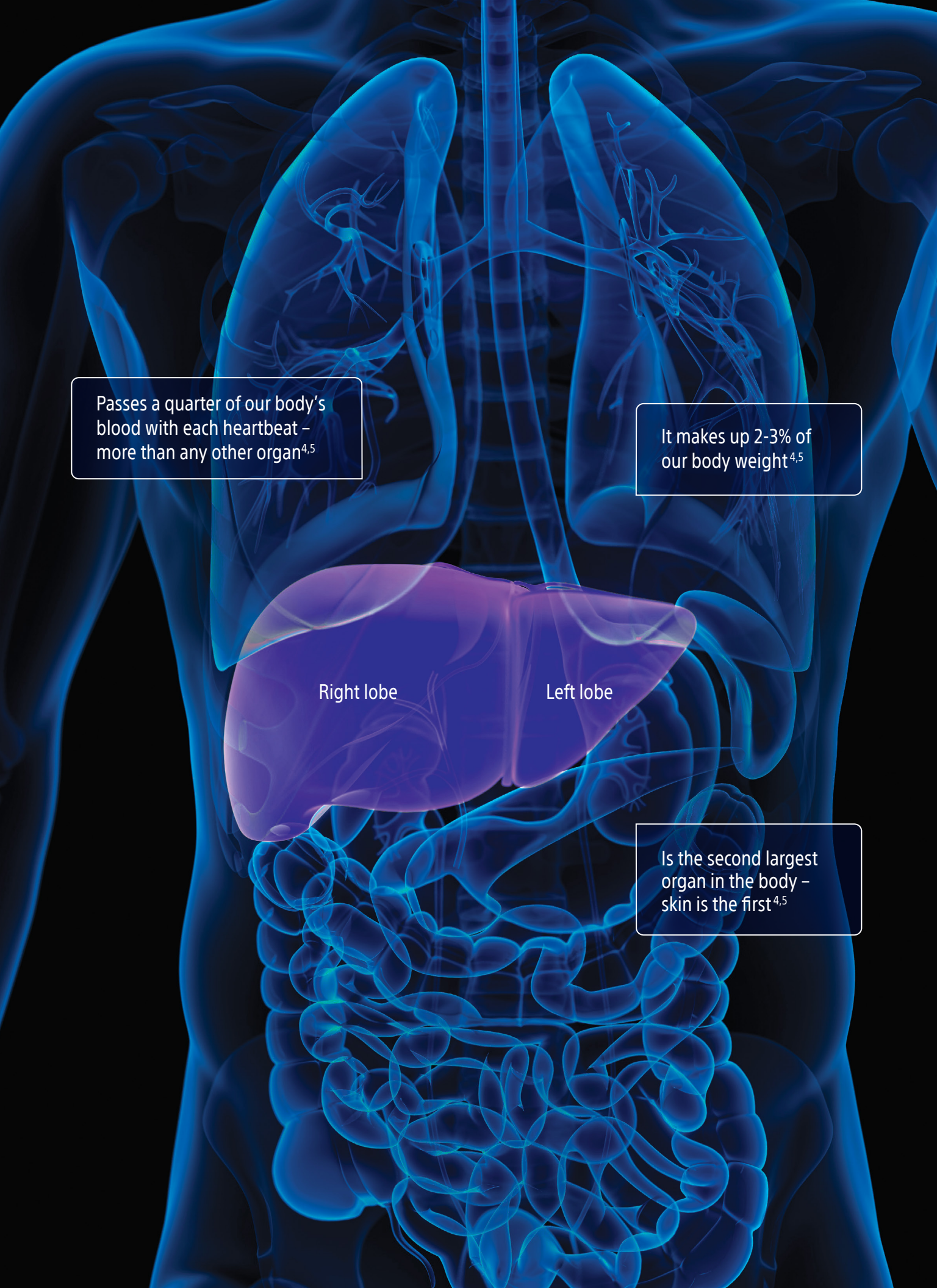
Before we discuss treatment options, it may be helpful to provide an overview of the liver. As one of the hardest-working organs in your body, the liver performs more than 500 vital functions.[1] The liver breaks down and processes nutrients in the blood and filters out harmful substances.[1,2,3]

Located in the upper right portion of the belly under the ribs, the liver is roughly the size of a football and has two large sections: the right lobe and the left lobe.[3] Its two main blood supplies are the hepatic artery and portal vein.[7]

The liver is a part of the digestive system and responsible for three main duties: producing hormones and nutrients, storing carbohydrates and filtering harmful toxins.[6]

Function	Hormone or Nutrient
Produces essential hormones and nutrients[1,2]	Cholesterol Bile Hormones Vitamin D Fats Nucleic acids (DNA/RNA) Proteins needed to: + Maintain body fluid balance + Assist with blood clotting + Immune function + Carry hormones and iron

Function	Details
Stores carbohydrates[2,3]	The liver stores carbohydrates to help control blood sugar levels and fats that can be broken down for energy.
Filters harmful toxins[1,2,3]	Alcohol, drugs and body waste are broken down and filtered by the liver.


Passes a quarter of our body's blood with each heartbeat – more than any other organ[4,5]
It makes up 2-3% of our body weight[4,5]
Right lobe
Left lobe
Is the second largest organ in the body – skin is the first[4,5]

A MATTER OF ORIGIN: OVERVIEW OF CANCER TYPES

There are two types of liver cancer: primary and secondary. Primary liver cancer starts in the liver. Secondary liver cancer starts somewhere else and spreads to the liver.

The most common type of liver cancer in adults is hepatocellular carcinoma, also known as HCC.[8] It develops when healthy liver cells start to multiply in overdrive in an effort to repair damage. However, this massive effort can sometimes do more harm than good, resulting in genetic mutation.[9] In other words, cancer cells are produced instead of healthy cells.

HOW HCC LIVER CANCER PROGRESSES

Over time, HCC cells form a lump (or multiple lumps) in the liver. This is called a tumor. As it develops, the tumor recruits blood vessels to feed it.[9] These blood vessels supply nutrients and oxygen to the tumor, allowing it to grow. If the tumor cells enter the blood stream, the tumor may spread to other parts of the body. This is called metastasis.[9]

HCC can form many small cancer tumors throughout the liver. This is seen most often in patients with cirrhosis (chronic liver damage). It can also begin as a single tumor that grows and spreads to other parts of the liver.

Testing[10]

Your doctor may request the following tests and procedures to diagnose liver cancer:[3]

+ Blood tests
+ Imaging exams, such as ultrasounds, CT and MRI
+ Liver biopsy, a procedure that removes a small sample of the organ's tissue for testing

Staging process[10]

Once HCC is diagnosed, your doctor will determine how much cancer is in your body. Staging of the cancer depends on size, location and if the cancer has spread. Treatment options and prognosis may vary based on test results, imaging results and your overall state of health

Your care team

Depending on the stage of the cancer and treatment options, your care team may include the following specialists:

+ Surgeon
+ Cancer specialist (Oncologist)
+ Liver specialist (Hepatologist)
+ Interventional Radiologist

AN OVERVIEW OF TREATMENT OPTIONS

There are various options and combinations of options for treating HCC. You and your medical team will determine the best treatment plan based on your stage of cancer, health and preferences. Your plan could be a combination of different treatments listed below. Be sure to ask your doctor about the benefits and potential risks associated with your particular treatment plan.[4]

SURGERY

Surgical resection involves removing a portion of the liver and is a common procedure if the HCC is in its early stages.[2,5,6] Resection surgery is possible if there is only one tumor that has not grown into blood vessels and there is a reasonable amount of liver function left once the tumor is removed.[9,11,12]

Liver Transplant involves removing the whole liver and replacing it with a healthy liver from a donor and may be most effective when the tumor cannot be removed through resection surgery. A transplant is used to treat patients who are within a set of criteria set by the United Organ Sharing Network.[13]

SYSTEMIC THERAPIES

Targeted drug therapy utilizes drugs that enter the blood stream and reach nearly all areas of the body, making it a useful therapy against cancers that have spread to distant parts of the body.[14]

Immunotherapy involves the use of medicines to help your own immune system find and destroy cancer cells.[15]

Chemotherapy ("chemo") uses drugs to destroy, shrink or slow the growth of cancer cells.[16]

MINIMALLY INVASIVE THERAPIES

Ablation uses radio frequency, microwave (heat) or cryotherapy (freezing) to destroy the liver tumor[8] and does not involve open surgery.[17]

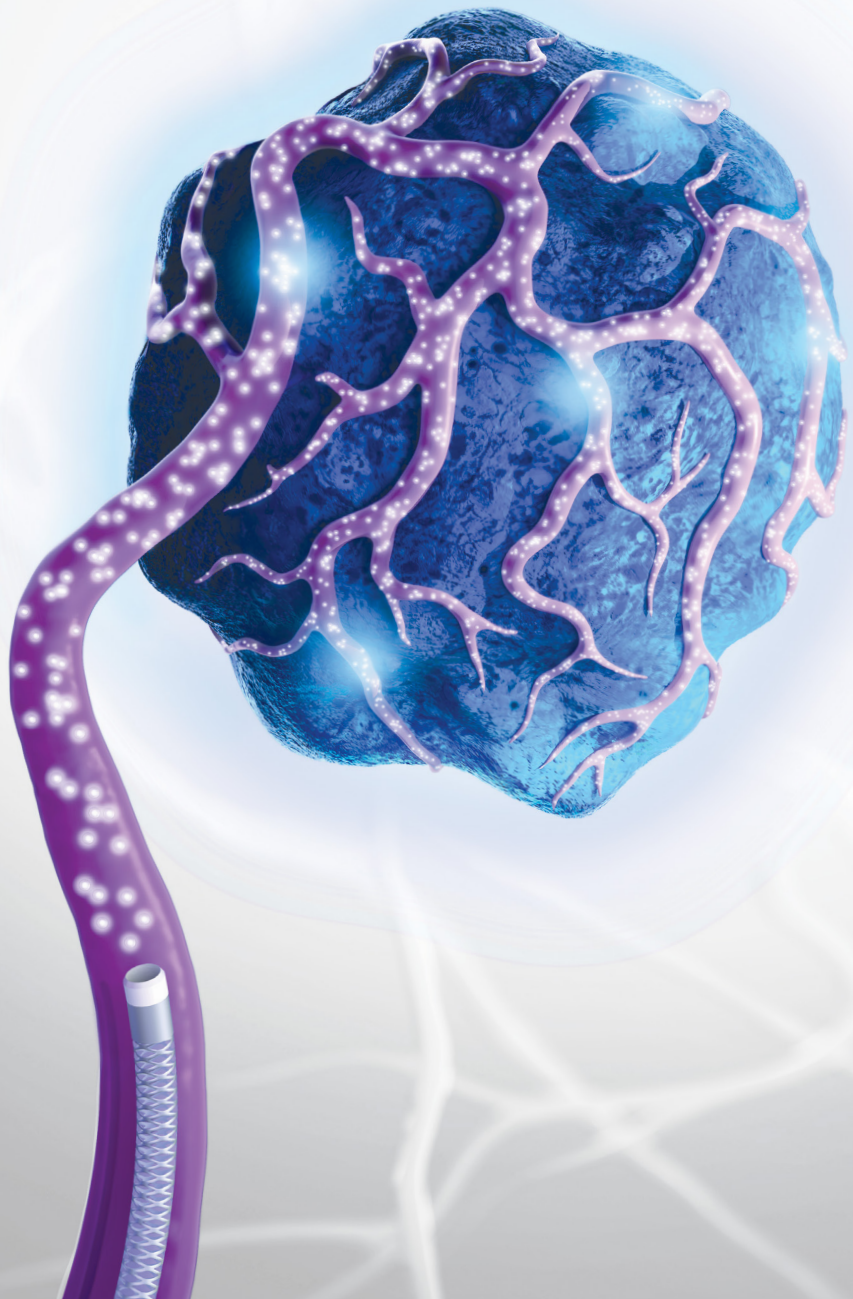
Embolization uses special techniques to close off blood flow to the tumor and does not involve open surgery.[18]

Radioembolization is a minimally invasive procedure that combines embolization and radiation therapy to treat liver cancer. Tiny glass or resin beads carrying radiation are placed inside the blood vessels that feed a tumor.[19]

YOU HAVE ANOTHER OPTION IN THE FIGHT AGAINST HCC

THE ONLY MINIMALLY INVASIVE MEDICAL DEVICE APPROVED BY THE FDA FOR THE TREATMENT OF HCC

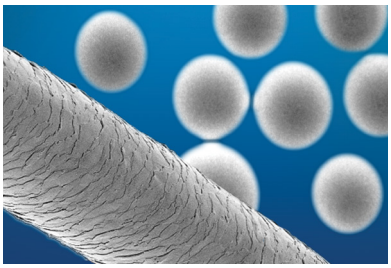
There is a proven radiation-based therapy available that has been developed to treat liver cancers, such as HCC. It's called **TheraSphere™ Y-90 Glass Microspheres**. In clinical trials, it's proven to shrink tumors and improve patient outcomes.[20] It's been used to treat HCC for more than 20 years, and it may help your fight against cancer.



HOW THERASPHERE™ WORKS[16]

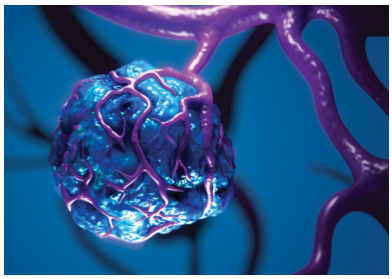
TheraSphere is a treatment consisting of millions of tiny glass beads — each thinner than a strand of hair — containing radioactive Yttrium-90. During the procedure, a doctor called an Interventional Radiologist, will make a tiny incision in your upper leg to deliver TheraSphere to the liver tumor through a microcatheter. Each glass bead delivers a highly concentrated dose of radiation that targets the HCC liver tumor. The radiation destroys the cancer cells within the tumor, with little damage to the surrounding healthy liver.

Treatment with TheraSphere is typically a single outpatient procedure that does not require a stay in the hospital. It is often well-tolerated by most patients with minimal side effects and doesn't preclude patients from other treatment options.

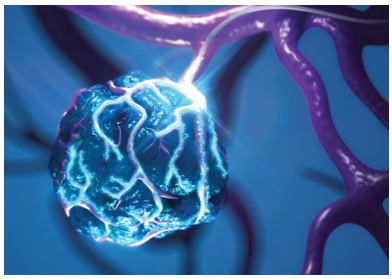


TheraSphere Y-90 Glass Microspheres compared to a strand of human hair

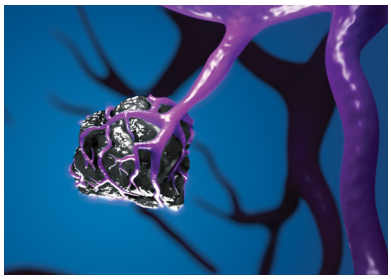
RADIATION TARGETS THE TUMOR WITH MINIMAL IMPACT TO THE SURROUNDING HEALTHY LIVER



Liver tumor before TheraSphere treatment



Liver tumor targeted with a high dose of radiation



Liver tumor after TheraSphere treatment

SIDE EFFECTS ARE USUALLY MILD AND MINIMAL

While patients may experience a variety of symptoms after TheraSphere treatment, the typical response is often described as common flu-like symptoms that may last for approximately one week. These symptoms may include mild to moderate fatigue, abdominal discomfort and nausea.

MORE THAN 100,000 TREATMENTS GLOBALLY AND GROWING

Thousands of patients have benefited from TheraSphere treatment for more than two decades. Talk to your physician to learn if TheraSphere may be a treatment option for you. You can learn more and read clinical trials by visiting www.TheraSphere.com.

THE BENEFITS OF THERASPHERE TREATMENT

IT'S PROVEN

In clinical trials, TheraSphere has been shown to reliably shrink and destroy tumors while being well-tolerated to optimize your quality of life.

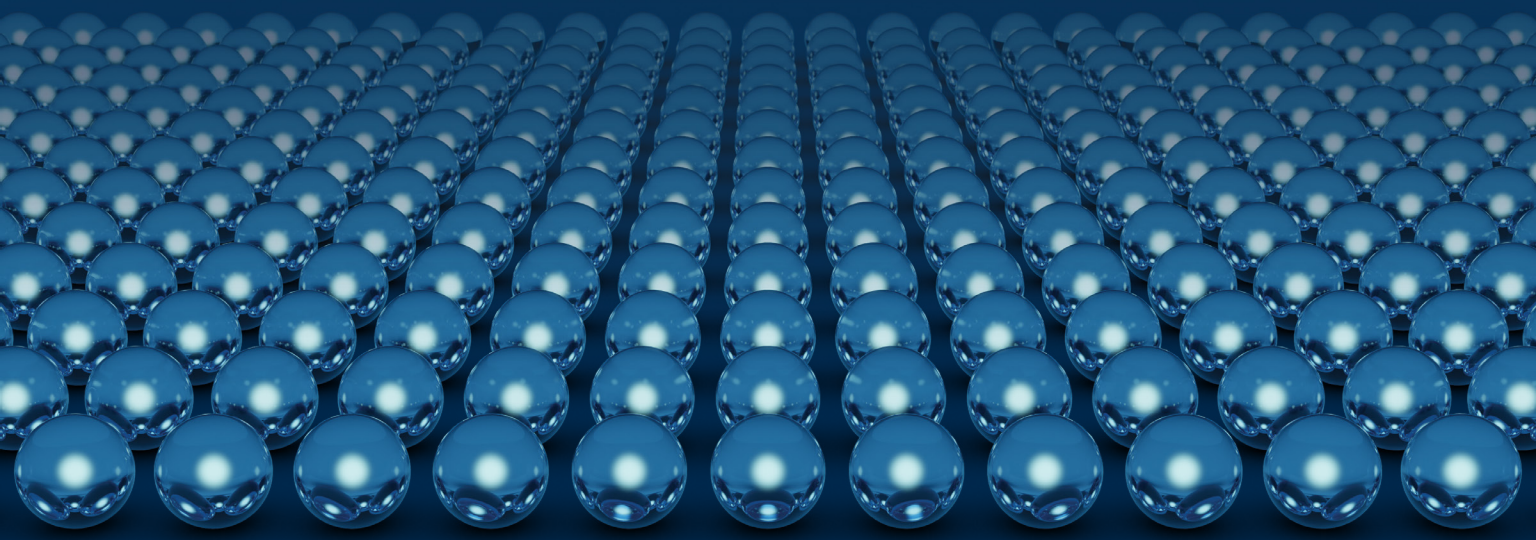
IT'S PERSONALIZED

Your physician calculates the radiation dose based on your unique needs to maximize the tumor's response.

IT'S PRECISE

There is minimal impact to surrounding healthy liver tissue because TheraSphere is precisely delivered to the tumor.

100% of the patients in the LEGACY study responded to TheraSphere treatment(s).[20]



QUESTIONS TO ASK YOUR DOCTOR

It is important to have open and honest conversations with your care team. These questions can help you get the information you need to make the best healthcare decision for yourself:

Who is on my cancer care team?

Who will be leading my overall treatment?

What are my treatment choices?

What treatment or treatments do you recommend and why?

What is the goal of each treatment?

Can the cancer be removed with surgery?

Will I need a liver transplant?

Should I get a second opinion? How do I do that? Can you recommend a doctor or cancer center?

What risks or side effects should I expect? How long are they likely to last?

How quickly do we need to decide on treatment?

Should I think about taking part in a clinical trial?

How soon do I need to start treatment?

What should I do to be ready for treatment?

How long will treatment last? What will it be like?

Where will my treatment take place?

Will the selected treatment affect my daily activities?

What will we do if the treatment doesn't work or if the cancer comes back?

If I have questions or problems, whom should I call?

NOTES

GLOSSARY

Artery: blood vessel that carries blood from the heart to the organs.

Benign: growth that is not cancer.

Catheter: a thin, flexible tube introduced through a blood vessel (used to access the treatment region) to inject fluids or to implant TheraSphere Glass Microspheres.

Cirrhosis: chronic liver damage.

Embolization: A procedure that uses particles such as radioactive glass microspheres to block a blood vessel.

Malignant: cancerous.

Metastasis: cancer cells that have spread elsewhere in the body.

Microcatheter: a thin, tiny, flexible tube introduced through a blood vessel (used to access the treatment region) to inject fluids or to implant TheraSphere Glass Microspheres or other treatments.

Prognosis: the expected outcome of a disease.

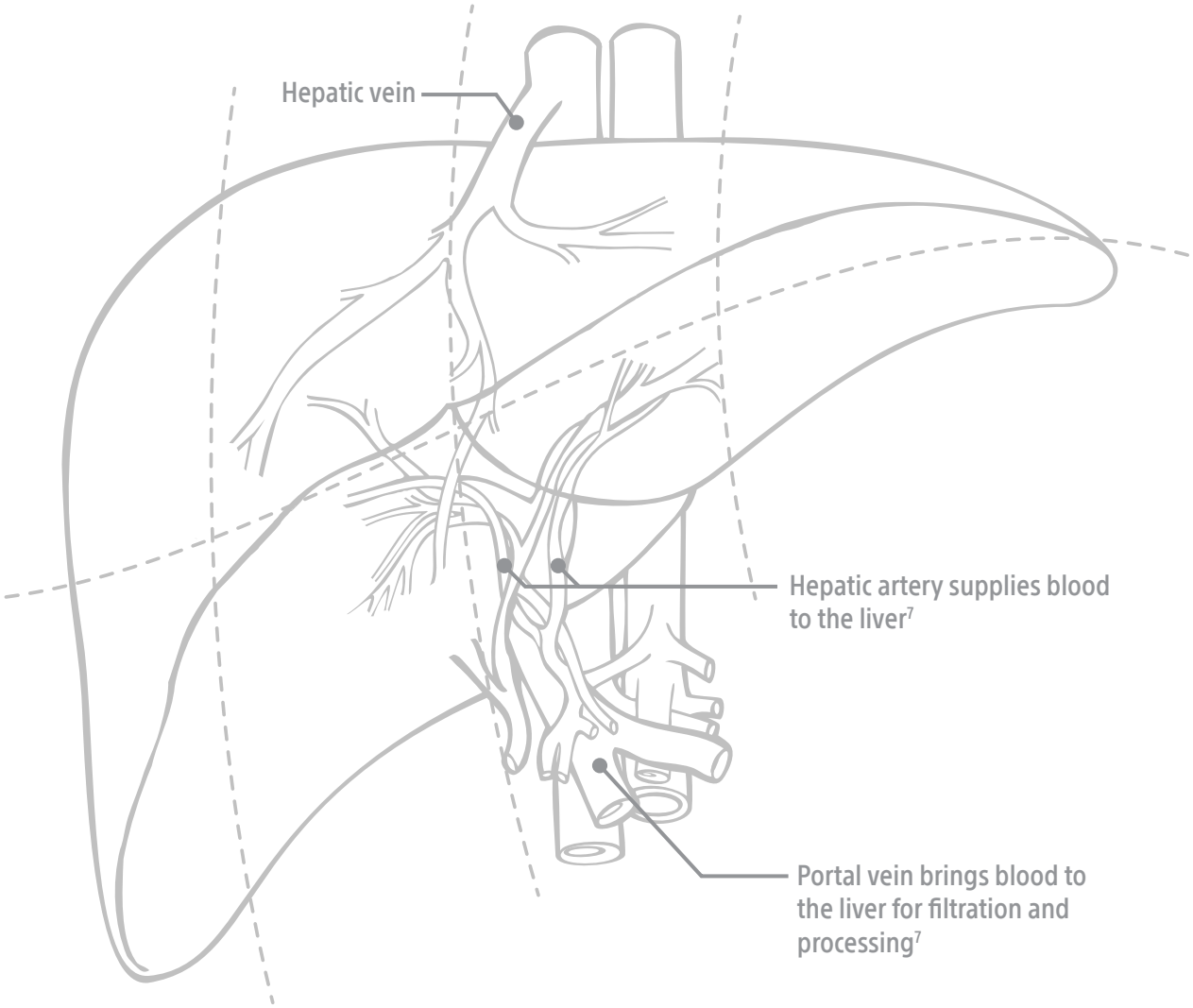
Radioembolization: a combination of radiation therapy and a procedure called embolization to treat cancer of the liver.

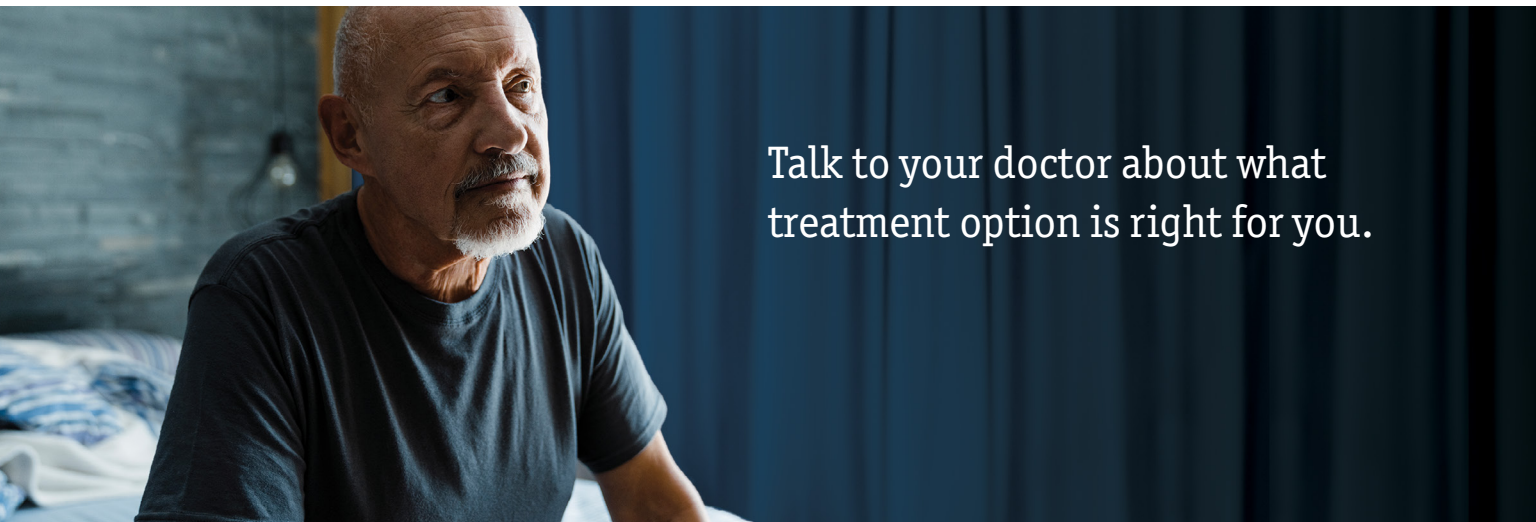
Resection: surgery to cut out the tumor.

TheraSphere: a liver cancer treatment that consists of tiny radioactive glass microspheres.

Yttrium-90: a radioactive isotope that is embedded within TheraSphere beads.

A CLOSER LOOK AT THE LIVER





RESOURCES TO HELP SUPPORT YOU

Here are some general resources available for you and your family.

CANCER INFORMATION & SUPPORT

The National Cancer Institute (NCI)
cancer.gov

American Cancer Society (ACS)
cancer.org

LIVER FOUNDATIONS

American Liver Foundation (ALF)
liverfoundation.org

SUPPORT GROUPS

Cancer Care
cancercare.org

Cancer Hope Network (CHN)
cancerhopenetwork.org

OTHER RESOURCES

The Interventional Initiative
theii.org

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20. LEGACY study. Hepatology. 2021

TheraSphere™ Yttrium-90 Glass Microspheres

INDICATION FOR USE: TheraSphere is indicated for use as selective internal radiation therapy (SIRT) for local tumor control of solitary tumors (1-8 cm in diameter), in patients with unresectable hepatocellular carcinoma (HCC), Child- Pugh Score A cirrhosis, well-compensated liver function, no macrovascular invasion, and good performance status.

CONTRAINDICATIONS: TheraSphere is contraindicated in patients: whose Tc-99m macroaggregated albumin (MAA) hepatic arterial perfusion scintigraphy shows any deposition to the gastrointestinal tract that may not be corrected by angiographic techniques • who show shunting of blood to the lungs that could result in delivery of greater than 16.5 mCi (0.61 GBq) of Y-90 to the lungs. Radiation pneumonitis has been seen rarely in patients receiving doses to the lungs greater than 30 Gy in a single treatment. • in whom hepatic artery catheterization is contraindicated, such as patients with vascular abnormalities or bleeding diathesis • who have pulmonary insufficiency (conventionally defined by an arterial oxygen pressure (Pa,O2) of < 60 mmHg, or oxygen saturation (Sa,O2) of < 90%) or severe liver dysfunction, including hepatic encephalopathy, clinically evident ascites or treatment with diuretics for ascites • with portal vein thrombosis (PVT) Type 4 involvement and lack of Tc-99m MAA deposition on the PVT seen on the Tc-99m MAA imaging with >70% tumor replacement in the liver • with comorbidities or poor overall health (e.g., ECOG performance status rating > 2) which may make the patient a poor candidate for locoregional radiation treatment. • who are pregnant.

WARNINGS: The following pre-treatment, high-risk factors (disease characteristics) have been associated with serious adverse events deemed possibly related to use of the device: infiltrative tumor type • tumor nodules too numerous to count • AST or ALT > 5 times ULN • bilirubin > 2 mg/dL • tumor volume > 50% combined with albumin < 3 g/dL. Keep the TheraSphere dose vial upright and stored in its lead pot before and during patient treatment, except as required for radiation measurement. Do not open the dose vial acrylic shield prior to patient treatment. Post-treatment, waste materials require caution to prevent contamination and beta shielding due to residual glass microspheres.

PRECAUTIONS: GENERAL PRECAUTIONS: As in any intra-arterial procedure, aseptic technique should be practiced, and care should be taken to ensure minimum patient anesthesia exposure extraneous to therapeutic objective. • Consideration of patient comorbidities should be used when determining the type and volume of fluid to infuse via catheter to avoid electrolyte imbalance, fluid shift, and hyperglycemia. • It is important to avoid any aggressive arterial procedure that may lead to arterial spasm that impairs TheraSphere distribution into the perfused liver target volume which may lead to underdosing or non- target deposition of TheraSphere. PRECAUTION IN PATIENTS WITH IMPAIRED LIVER FUNCTION: No efficacy or safety data from the LEGACY study are available to support the use of the device in patients with Child-Pugh score B or C cirrhosis. PRECAUTION IN VULNERABLE PATIENTS: No effectiveness or safety data are available to support the use of the device in children or breast- feeding women. ENDOCRINE DISRUPTION, CARCINOGENICITY, MUTAGENICITY, TOXICITY TO REPRODUCTION: Ideally the use of this radioactive device in women of childbearing capability should be performed during the first few (approximately 10) days following the onset of menses. RADIATION SAFETY: Radioactive products should be used only by healthcare professionals who are qualified by specific training in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides. • As in the use of any radioactive material, ensure minimum radiation exposure to the patient extraneous to the therapeutic objective, and to minimize radiation exposure to workers and others in contact with the patient. RELEASE AND POST-TREATMENT PRECAUTIONS: Post treatment patient care: use universal precautions for body fluid contact. Trace Y-90 may be detectible in blood and urine; handle with gloves and dispose as normal body fluids. The radiation field is expected to be less than 1 mrem/h (10 µSv/h) at 3 ft (1 m) from the patient's abdomen. Supplemental shielding and segregation of the patient are not required to maintain exposure to others below regulated limits. • Release instructions: The patient should follow good hygiene (e.g., proper hand washing). Caregivers, family, and others do not require restrictions on patient contact; however, they can minimize their radiation exposure by avoiding prolonged time (>12 hours per day) within 1 ft (0.3 m) of the patient's abdomen for the first week post therapy. Patients should be advised that radiation emitted from the patient may be detectible at security screening (e.g., international travel). • Special precautions post-administration: If the patient requires hospitalization, surgery, medical assessment or treatment regarding any part of their thorax or abdomen within first 2 weeks of treatment, the patient should advise the hospital and treating physician of the Y-90 TheraSphere implant. The physician should consult their radiation safety staff for handling and disposal of liver tissue. • Special liver tissue handling: Special liver tissue handling may be required for post-treatment surgery, explant, or transplant since the glass microspheres remain permanently implanted in the liver tissue. Disclosure of the treatment will be required if cremation is considered.

POTENTIAL ADVERSE EVENTS: The use of this product leads to irradiation of both tumorous and normal liver tissue. As a result, patients with compromised liver function may be at greater risk of liver function impairment and hence could experience complications. Clinical side effects usually occur within the first 4 to 6 weeks after treatment. Based on clinical trial data, literature reviews and post market surveillance, adverse events potentially associated with treatment using Y-90 microspheres, including TheraSphere, may include the following: Allergic reaction • Altered liver function, acute or chronic • Anorexia • Anxiety • Ascites • Bile Duct injury • Bleeding/hemorrhage • Chills / rigors • Cholecystitis (inflammatory or infectious) • Colitis • Death • Dehydration • Diarrhea • Dizziness • Dyspnea • Edema (any location) • Electrolyte abnormalities • Elevated BUN/creatinine • Fall • Fatigue • Fever • Gastrointestinal bleeding / hemorrhage • Gastrointestinal ulcer or ulceration • Hepatic encephalopathy • Hepatorenal failure • Hiccups • Hypertension • Hypotension • Infection (any location) • Liver failure, acute or chronic • Lymphopenia • Malaise • Mood alteration • Muscle weakness • Nausea • Neutropenia • Pain (any location) • Pancreatitis • Platelet count abnormalities • Pleural effusion • Portal hypertension • Pre-existing chronic liver disease decompensation • Pulmonary edema • Pulmonary fibrosis • Radiation hepatitis • Radiation induced disease, acute • Radio Embolization Induced Liver Disease (REILD) • Sepsis • Supraventricular arrhythmia • Thrombosis (arterial or venous) • Tumor inflammation (including tumor edema) • Tumor-lysis syndrome • Vomiting • Weight loss. Complications related to the administration procedure itself may include: Allergic reaction: Arterial injury including vessel dissection • Aspiration pneumonia • Bruising/bleeding/hematoma at site • Constipation/abdominal distension • Fatigue • Flushing • Infection • Nausea • Nerve damage.

CAUTION: Federal (USA) law restricts this device to sale by or on order of a physician

Patient side effects statement

All medical treatments have risks or discomforts and may cause side effects. Common side effects that may occur within approximately
1 week after TheraSphere treatment are generally mild to moderate and include:

- fatigue
- mild stomach discomfort
- nausea
- vomiting
- fever

Doctors describe these symptoms as like those of the common flu. You may experience loss of appetite and temporary changes in liver blood tests that may or may not be associated with symptoms. Many side effects disappear shortly after treatment and completely within one week of treatment. Tell your doctor if these symptoms continue or worsen. Be aware that some side effects may last longer or, rarely, become permanent.

More severe side effects are rare but possible, and most of them are completely reversible. Very rarely there may be deterioration of the liver function that could lead to death.

Even after safety screening, there is still a small risk that some of the microspheres could go to other organs, resulting in injuries such as:

- radiation damage to the lungs
- fluid collection around the lungs
- injury or radiation to the gallbladder
- stomach or intestinal ulcer
- bleeding from the stomach or intestines
- kidney damage

Everyone responds differently to their treatment. These are not all the possible side effects you may feel. Contact your doctor if you experience any side effects.

Content of this guide is for Information purposes only and does not constitute medical advice. BSC strongly recommends that you consult with your physician on all matters pertaining to your health or to address any questions.

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