Boston Scientific
Advancing science for life™

THERASPHERE™
Y-90 Glass Microspheres

STRIKE FIRST





THERASPHERE™
Y-90 Glass Microspheres



Your precision strike. Arming you to target HCC tumors directly and hit them hard with high-dose radiation therapy.

With TheraSphere, you have a powerful, well-tolerated precision HCC therapy to give your patients a fighting chance. Maximizing outcomes. Improving quality of life.

Proven
evidence-based HCC liver cancer therapy

Personalized
dosing dialed in, ready to deploy

Precise
delivery of targeted radiation therapy

HCC Liver Cancer:
We're coming for you.

A rich legacy of clinical evidence.
Based on 20+ years of real-world data.

2021

TARGET: GLOBAL REAL-WORLD STUDY CONFIRMS TUMOR ABSORBED DOSE IS CRITICAL FOR PREDICTABLE TUMOR RESPONSE AND OS IN BROAD POPULATION[9]

PMA: 1ST AND ONLY Y-90 THERAPY APPROVED BY FDA FOR HCC

2020

LEGACY CONFIRMS NEOADJUVANT OR STANDALONE TREATMENT IN HCC[8]

DOSISPHERE-01 PERSONALIZED DOSIMETRY APPROACH IMPROVES OVERALL SURVIVAL[7]

2018

CURATIVE INTENT: EARLY HCC AND LOW TUMOR BURDEN[6]

2014

RADIATION SEGMENTECTOMY THRESHOLD DOSE DEFINED[5]

2011

RADIATION SEGMENTECTOMY: HIGH-DOSE RADIATION DELIVERED TO < 2 HEPATIC SEGMENTS[4]

2009

RADIATION LOBECTOMY: LOCAL TUMOR SHRINKAGE AND HYPERTROPHY OF NORMAL LIVER[3]

2006

DOWNSTAGING AND BRIDGING TO TRANSPLANT[2]

2004

ADVANCED HCC WITH OR WITHOUT PVT[1]

1999

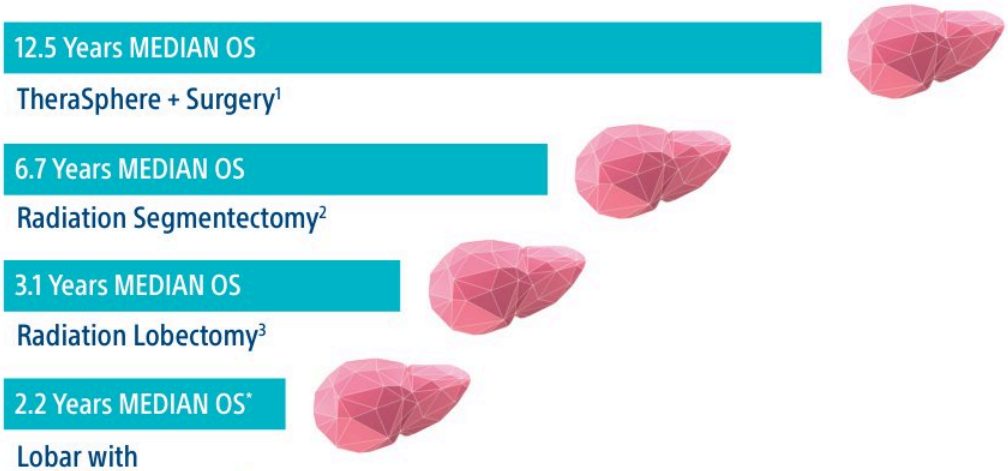
THERASPHERE RECEIVES FDA HDE APPROVAL

1. Salem R, Lewandowski R, Roberts C et al. J Vasc Interv Radiol. 2004; 15(4) 335-45 **2.** Kulik LM, Atassi B, van Holsbeeck L et al. J Surg Oncol. 2006;94: 572-586 **3.** Gaba RC, Lewandowski RJ, Kulik LM et al. Ann Surg Oncol. 2009 Jun;16(6):1587-96 **4.** Riaz A, Gates VL, Atassi B et al. Int J Radiat Oncol Biol Phys. 2011 Jan 1;79(1):163-71 **5.** Vouche M, Habib A, Ward TJ et al. Hepatology. 2014;60(1):192-201 **6.** Lewandowski RJ, Gabr A, Abouchaleh N et al. Radiology. 2018;287(3) epub **7.** GarinE, Tselikas L, Guiu B et al. Personalized versus standard dosimetry approach of selective internal radiation therapy in patients with locally advanced hepatocellular carcinoma (DOSISPHERE-01): a randomised, multicentre, open-label phase 2 trial. Lancet Gastroenterol Hepatol. 2021, 6: 17-29 **8.** 3020.2: Yttrium-90 Glass Microspheres in the Treatment of Hepatocellular Carcinoma: The LEGACY Study," CIRSE 2020 Virtual Summit, September12-15, 2020; Salem R, Johnson GE, Kim E, RiazA, BishayV, Boucher E, Fowers K, Lewandowski R, PadiaSA. Yttrium-90 Radioembolization for the Treatment of Solitary, Unresectable Hepatocellular Carcinoma: The LEGACY Study. Hepatology. 2021 Mar 19. doi: 10.1002/hep.31819. **9.** Lam, Marnix. A Global Study of Advanced Dosimetry in the Treatment of Hepatocellular Carcinoma with Yttrium-90 Glass Microspheres: Analyses from the TARGET Study. Presented at SIR. March 25, 2021.

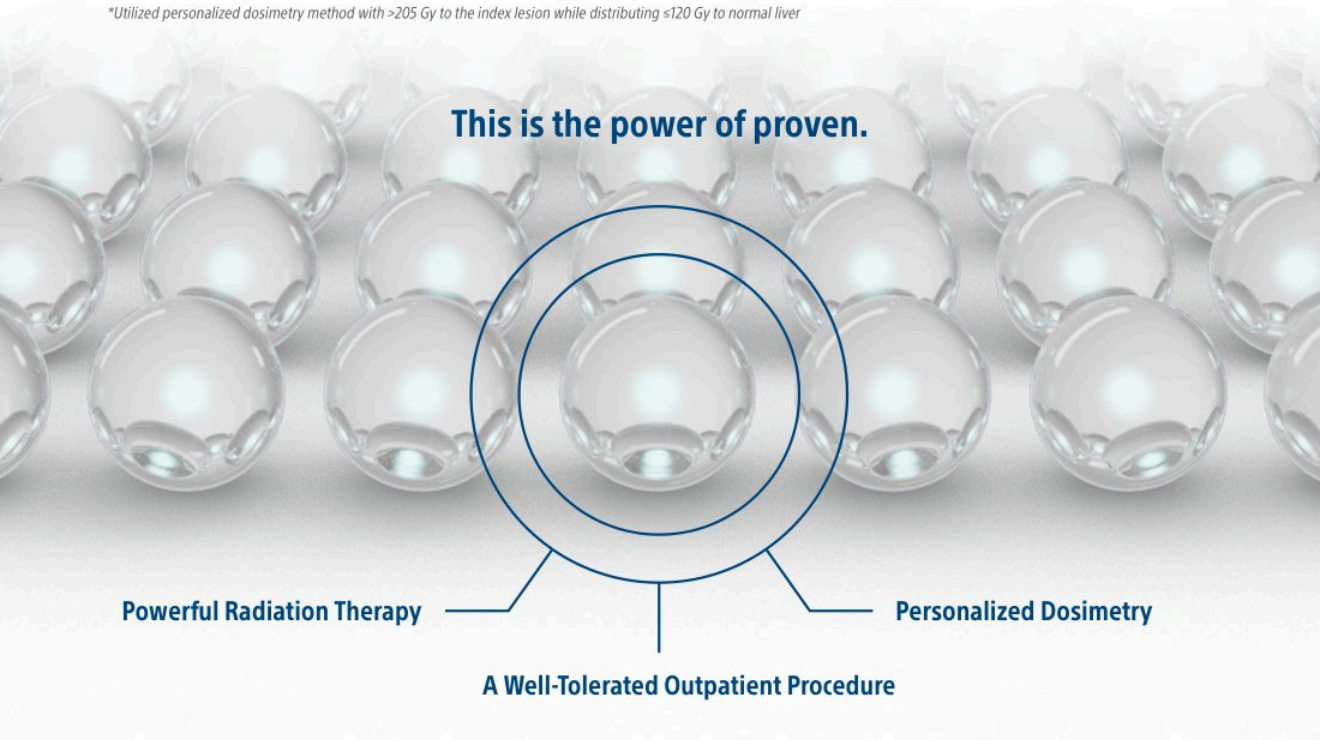
THE EVIDENCE IS IN.

TheraSphere™ Y-90 Glass Microspheres are a proven, evidence-based HCC therapy that hits tumors hard.

TheraSphere is proven across a variety of treatment approaches to ensure repeatable outcomes in HCC patients.[1]



**Utilized personalized dosimetry method with >205 Gy to the index lesion while distributing ≤120 Gy to normal liver*



1. Gabr, A., Kulik, L., Mouli, S., Riaz, A., Ali, R., Desai, K., Mora, R.A., Ganger, D., Maddur, H., Flamm, S., Boike, J., Moore, C., Thornburg, B., Alasadi, A., Baker, T., Borja-Cacho, D., Katariya, N., Ladner, D.P., Caicedo, J.C., Lewandowski, R.J. and Salem, R. (2020), Liver Transplantation Following Yttrium-90 Radioembolization: 15-year Experience in 207-Patient Cohort. Hepatology. Accepted Author Manuscript. doi:10.1002/ hep.31318 >=30% hepatic reserve. **2.** Lewandowski RJ, Gabr A, Abouchaleh N et al. Radiation segmentectomy: potential curative therapy for early hepatocellular carcinoma. Radiology. 2018; 287(3): 1050-1058. **3.** Gaba RC et al. Ann Surg Oncol 2009;16:1587–96. **4.** Garin E, Tselikas L, Guiu B et al. Personalized versus standard dosimetry approach of selective internal radiation therapy in patients with locally advanced hepatocellular carcinoma (DOSISPHERE-01): a randomised, multicentre, open-label phase 2 trial. Lancet Gastroenterol Hepatol. 2021, 6: 17-29.

PROVEN

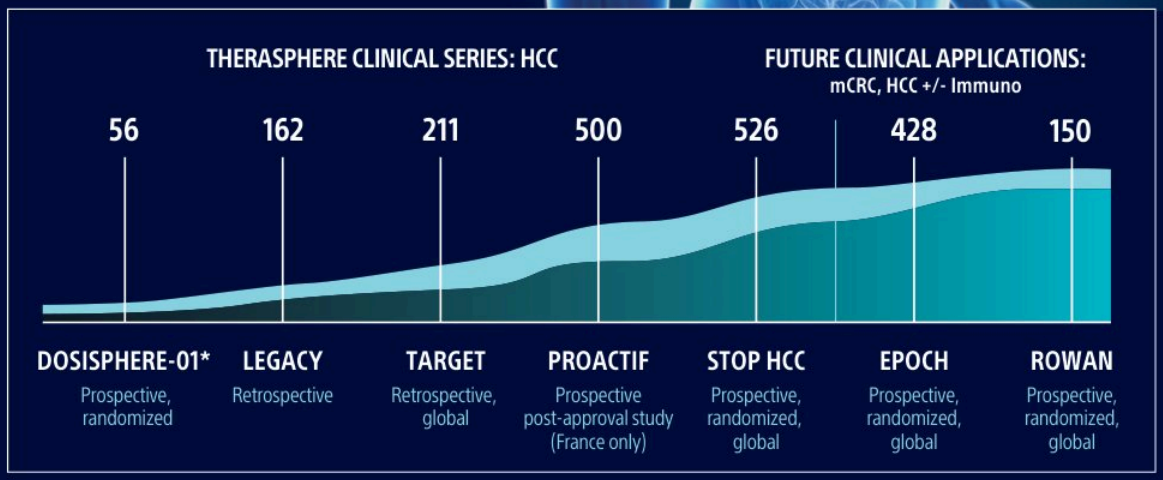
EVIDENCE-BASED. TO FIGHT HCC.

Now you have the power to reliably shrink and destroy tumors and enhance outcomes. It's been used to successfully treat HCC for over 20 years.

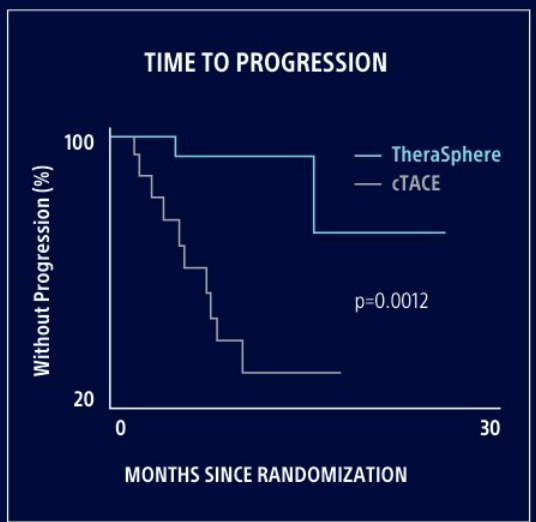
100 global studies. 500 publications. 70,000 treatments globally. Together, we will further unlock the future of targeted radiation therapy.



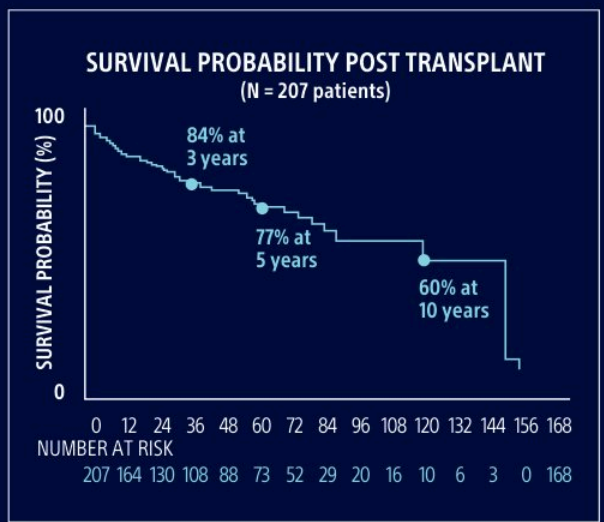
TheraSphere™ clinical program enrolling more than 2,000 patients worldwide.



Significantly prolongs time to progression.[1]



Median overall survival after liver transplant was 12.5 years.[2]



*This investigator-sponsored study is supported by grant funding from Boston Scientific. 1. Salem R, Gordon AC, Mouli S, et al. Y90 radioembolization significantly prolongs time to progression compared with chemoembolization in patients with hepatocellular carcinoma. Gastroenterol. 2016; 15: p. 1155-1163. 2. Gabr, A., Kulik, L., Mouli, S., Riaz, A., Ali, R., Desai, K., Mora, R.A., Ganger, D., Maddur, H., Flamm, S., Boike, J., Moore, C., Thornburg, B., Alasadi, A., Baker, T., Borja-Cacho, D., Katariya, N., Ladner, D.P., Caicedo, J.C., Lewandowski, R.J. and Salem, R. (2020), Liver Transplantation Following Yttrium-90 Radioembolization: 15-year Experience in 207-Patient Cohort. Hepatology. Accepted Author Manuscript. doi:10.1002/hep.31318

PERSONALIZED

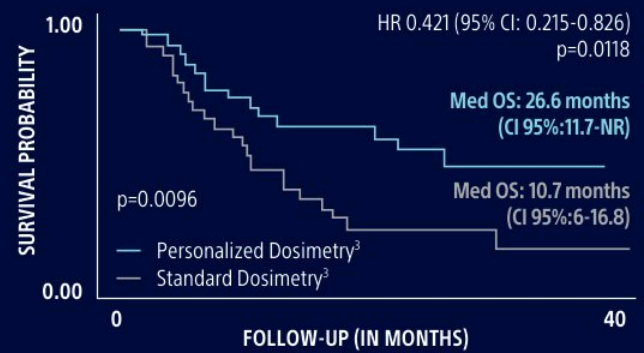
HIGHLY POWERFUL TARGETED DOSE. MAKE A CALCULATED FIRST MOVE.

Each dose is precisely calculated for each patient, every time.

TheraSphere™ is the only radiation therapy with Level 1 randomized data to demonstrate efficacy in large tumors (mean tumor size of 10.5 cm)[1], while also validating reproducible dosimetry planning with Simplicit^{90}Y™ Personalized Dosimetry Software[2].

Optimizing outcomes with a personalized dosimetry approach.[3]

MEDIAN OVERALL SURVIVAL
(ITT POPULATION) (INVESTIGATOR ASSESSMENT)



16 MONTH
Survival Improvement
(personalized vs. standard dosimetry)

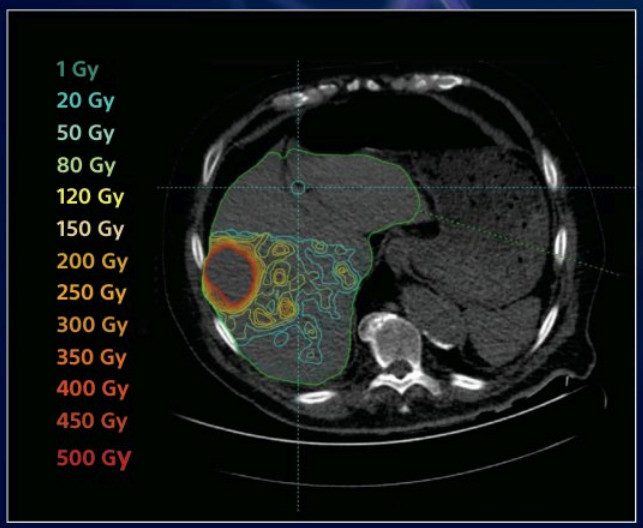
1. TheraSphere™ Y-90 Glass Microspheres DOSISPHERE-01 Study. Data on file. **2.** Lam, Marnix. A Global Study of Advanced Dosimetry in the Treatment of Hepatocellular Carcinoma with Yttrium-90 Glass Microspheres: Analyses from the TARGET Study. Presented at SIR. March 25, 2021. **3.** Garin E, Tselikas L, Guiu B et al. Personalized versus standard dosimetry approach of selective internal radiation therapy in patients with locally advanced hepatocellular carcinoma (DOSISPHERE-01): a randomised, multicentre, open-label phase 2 trial. Lancet Gastroenterol Hepatol. 2021, 6: 17-29.

PRECISE

TAKE AIM AT HCC.
HIT TUMORS HARD WITH THERASPHERE™.

Precisely formulated glass microspheres deployed with pinpoint precision to shrink and destroy tumors, making TheraSphere a highly versatile, targeted radiation therapy.

Highly powerful radiation precisely targets cancer* cells while preserving healthy tissue.[1]



TheraSphere's unique ability to deliver high-dose radiation with fewer spheres allows for maximum absorbed dose, and increased tumor response while preserving healthy tissue.

*Refers to HCC (liver cancer)

1. Pasciak AS, Abiola G, Liddell RP et al. The number of microspheres in Y90 radioembolization directly affects normal tissue radiation exposure. Eur J Nucl Med Mol Imaging. 2019 Nov 18. doi: 10.1007/s00259-019- 04588-x. 9

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. PI-992004-AA

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

TheraSphere is a registered trademark of Theragenics Corporation used under license by Biocompatibles UK Ltd. All trademarks are the property of their respective owners.

To place an order for TheraSphere™ Y-90 Glass Microspheres, please contact your TheraSphere consultant at TherasphereCustomerSupport@bsci.com

or call Customer Service (US/CANADA): 1-866-363-3330.

Visit our website at www.therasphere.com

Boston Scientific
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Peripheral Interventions
300 Boston Scientific Way
Marlborough, MA 01752-1234
www.bostonscientific.com

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PI-865105-AC