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FRONTIER

STUDY

A guide to help you learn about the FRONTIER study and the use of Y-90 Glass Microspheres for patients with recurrent glioblastoma.

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A Patient's Guide to the FRONTIER Study

You are thinking about enrolling in the FRONTIER study, which uses Boston Scientific's Y-90 Glass Microspheres to treat recurrent glioblastoma (GBM). This booklet will help you learn about the study, how Y-90 glass microspheres work, and what to expect with the procedures and follow-up visits. It also includes a glossary with helpful information to explain medical terms.

You should talk to your doctor about potential risks and any questions you may have about joining the study.

Glossary

Blood Vessel: part of the circulatory system which carries blood through the body.

Clinical Trial: research study that tests new medical treatments on human volunteers (participants) to see how they work and to advance medical knowledge.

Early Feasibility Study: clinical trial with a small number of patients using a device early in development to test if it is safe and works well.

Informed Consent: written agreement to join a study, knowing the potential risks and benefits.

Microcatheter: small, flexible tube that goes into a blood vessel to reach a specific area of the body to inject fluids or deliver treatments like Y-90 glass microspheres.

TheraSphere™: a device that is made of tiny glass microspheres (beads) containing radioactive Yttrium-90 (Y-90) that is currently used for the treatment of hepatocellular carcinoma (liver cancer).

Yttrium-90 (Y-90): the radioactive material inside the glass microspheres that gives off radiation into the area surrounding the microspheres; once the Yttrium-90 gives off its radiation it is no longer radioactive.

Glioblastoma

Glioblastoma (GBM) is an aggressive form of brain cancer and is the most common type of cancer that begins in the brain. GBM is hard to treat because the cancer cells extend beyond what can be seen on clinical imaging. About 13,000 patients are diagnosed every year with GBM in the United States[1].

Treatment Options

When GBM is first diagnosed, standard treatment typically includes a combination of surgery, external radiation therapy, and chemotherapy.

If the tumor is in a part of the brain where surgery is possible, the surgeon will remove as much of the tumor as they can without removing healthy brain tissue. After recovering from surgery, patients usually have external radiation therapy and chemotherapy for six weeks to target any leftover tumor cells. Chemotherapy often continues for another six months after radiation therapy ends. Some patients may also receive tumor treating fields (TTF) along with their chemotherapy to help treat their cancer.

For GBM that has recurred (the cancer has come back), there is no standard treatment considered by medical professionals as best practice. Treatments depend on each patient's individual situation. Current options for treating recurrent GBM include more surgery, external radiation therapy, chemotherapy and tumor treating fields (TTF). Some patients might also qualify for investigational treatments in clinical trials, like the FRONTIER study.

You should talk with your doctor about your treatment goals, quality of life, benefits and risks of treatments to determine the right treatment option for you.

1. Ostrom, QT, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2015–2019. Neuro-Oncology, Volume 24, Issue Supplement_5, October 2022, Pages v1–v95.

FRONTIER
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The FRONTIER study is an early feasibility study looking at the use of Boston Scientific's Y-90 Glass Microspheres in patients with recurrent GBM. The goal of the study is to see if this therapy is safe to use in the brain. It will also look at the accuracy and effectiveness of using this technology for recurrent GBM. The study sponsor, Boston Scientific, has received approval from the FDA to conduct this study.

If you decide to join the study by providing informed consent, you will visit the hospital on separate occasions for imaging and a treatment planning procedure which will not require a hospital stay. You will come back to the hospital on the day of the procedure to get the Y-90 glass microspheres treatment, and will stay in the hospital until the next day discharge. After the treatment, you will come back to the hospital for follow-up visits at these times:

- 7, 14, and 21 days after treatment
- Once a month for the next 6 months
- After 6 months, visits will depend on your health status and the hospital's standard of care schedule

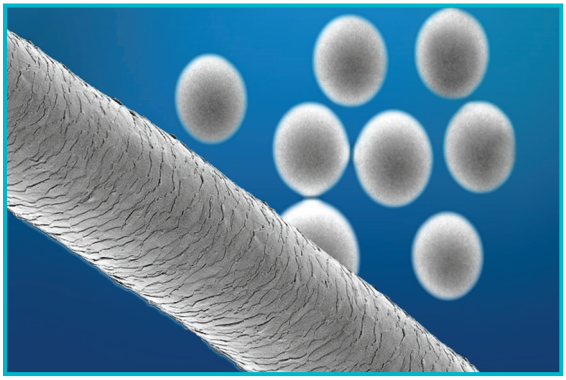
More information about the visits before the procedure, how the treatment is given in the administration procedure, and follow-up visits is provided in the next sections.

What are Y-90 Glass Microspheres and How Do They Work?

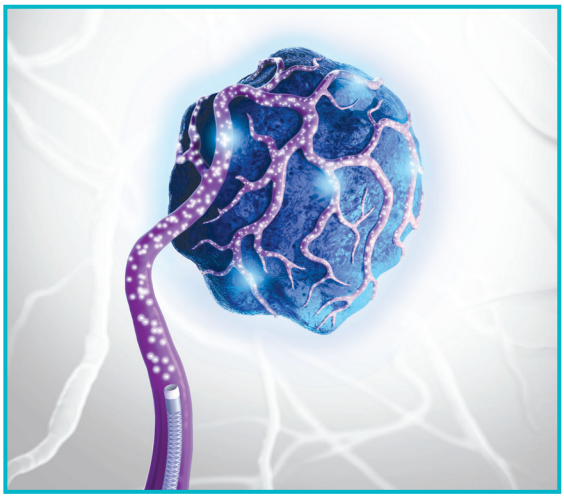
Boston Scientific's Y-90 Glass Microspheres for recurrent GBM is an investigational internal radiation cancer treatment that uses tiny glass beads, or microspheres, with radioactive Yttrium-90 (Y-90). The glass microspheres are approximately 0.001 inches in diameter – about a third of the width of a human hair. The glass microspheres are injected directly into the blood vessel feeding the tumor through a small flexible tube called a microcatheter. The glass microspheres enter the tumor's blood supply, lodge in the micro blood vessels of the tumor, and release radiation into the tumor. Unlike traditional radiation therapy, which delivers radiation from an external source, Y-90 therapy delivers radiation internally at the tumor site.

This treatment is called selective internal radiation therapy (SIRT). It uses radiation to destroy the tumor cells from the inside of the tumor. The goal of SIRT is to limit radiation to the healthy tissue that is near the tumor. The glass microspheres deliver most of the radiation (more than 95%) to the tumor in the first two weeks after the treatment. Even though the radiation decreases over time, the glass microspheres will stay in place permanently.

Boston Scientific's TheraSphere™ Y-90 Glass Microspheres have been used to treat hepatocellular carcinoma (liver cancer) in the United States for over 20 years. The FRONTIER study aims to find out if this technology can be safely used to treat patients with recurrent GBM.



Y-90 glass microspheres next to human hair.



Y-90 glass microspheres are delivered through a microcatheter to the blood vessel feeding the tumor where they become lodged and release radiation to the tumor.

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Before the Administration Procedure

Before getting the Y-90 glass microspheres treatment, your doctor will do diagnostic imaging to check the tumor characteristics, the anatomy of blood vessels in the brain, and blood flow. This helps the medical team guide the microcatheter to the tumor and decide how much Y-90 glass microspheres to administer. These visits will not require you to stay overnight in the hospital.

Visit #1: Pre-Procedural Diagnostic Imaging

TUMOR ON MRI

Images taken: MRI and CT Perfusion

MRI (magnetic resonance imaging): gives clear pictures of soft tissue like the brain and tumor, and can show inflammation and swelling using magnetic fields and intravenous (IV) contrast injection.

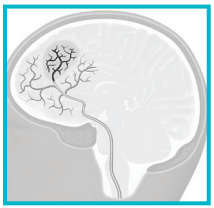
CT (computed tomography) Perfusion: shows detailed information about blood flow to the brain using x-ray and intravenous (IV) contrast injection.

Purpose: to check the starting tumor size, location and blood flow.

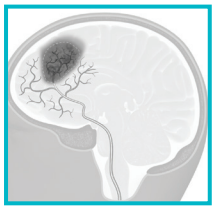
Timing: done within 21 days before the Y-90 glass microspheres administration procedure.

Visit #2: Treatment Planning

VESSELS TO THE BRAIN / TUMOR



VESSELS TO THE TUMOR



BLOOD FLOW VOLUME TO TISSUE

Images taken: Angiography and Cone-Beam CT (CBCT)

A small incision is made in the arm or leg and a microcatheter is guided into the brain to the blood vessels feeding the tumor to get these images.

Cerebral Angiography: shows images of blood vessels in the brain using x-ray and a contrast injection through a microcatheter.

CBCT (cone-beam computed tomography): provides 3D images of the treatment volume using x-ray and contrast injection through a microcatheter.

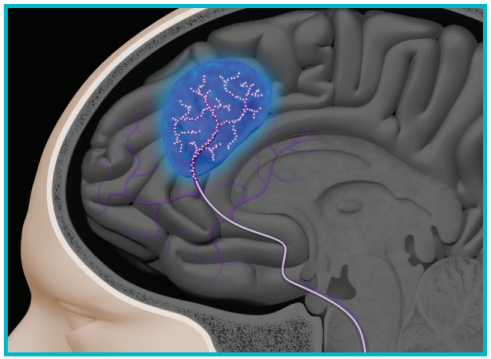
Purpose: to find the blood vessels feeding the tumor and the volume of tissue that will be treated.

Timing: done within 14 days before the Y-90 glass microspheres administration procedure.

After treatment planning, the medical team will combine the images to make sure the volume seen on the CBCT covers the recurrent tumor shown on the MRI. These images will also be used to calculate how much tissue needs to be treated and decide the amount of Y-90 glass microspheres to order. Each Y-90 glass microspheres order is specifically made for the patient being treated.

Y-90 Glass Microspheres Administration Procedure

Microcatheter navigated to the treatment location and repeat treatment planning imaging



Y-90 glass microspheres are delivered through the microcatheter to the tumor

On the day of the Y-90 glass microspheres administration procedure, the doctor will make a small incision in the leg or arm and insert a microcatheter into the blood vessel and guide the microcatheter to the brain's blood vessels using imaging guidance.

The doctor will take another CBCT and angiography to make sure the microcatheter is in the right spot and confirm the treatment volume.

The Y-90 glass microspheres will be delivered to the tumor through the microcatheter that is placed in a vessel that gives blood to the tumor.

The Y-90 glass microspheres will lodge in the micro blood vessels of the tumor and give off radiation from inside the tumor. The radiation from each microsphere will not reach farther than 0.5 inches, so the treatment goal is to give radiation to the tumor but limit radiation exposure to nearby healthy brain tissue.

Post-Procedure Imaging and Monitoring

After the Y-90 glass microspheres administration procedure, you will have an MRI to assess any changes from the procedure and you will be monitored with neurological assessments until you are able to be discharged from the hospital, usually 24 to 36 hours after treatment. A PET (positron emission tomography) image will be taken to show the Y-90 radiation activity, confirming that the glass microspheres are in the right place. The doctor will review these images and neurological tests before you are discharged from the hospital to go home.

Because the radiation from the glass microspheres has a very small radiation distance, the radioactive energy outside your body is very low. The hospital might give you instructions when you leave the hospital, as a precaution. The security screening equipment at some airports may detect radiation from the microspheres in the weeks after treatment. Ask your doctor if you need a letter explaining the treatment for travel.

PET image to identify the Y-90 radiation activity

Follow-up Visits

To keep track of how the therapy is working, you will go back to the hospital where you received treatment for FRONTIER study-required follow-up visits:

- Weekly for the first month post-procedure (no imaging will be done unless needed for medical reasons)
- Once a month for 6 months after the procedure (includes a monthly MRI)
- After 6 months, you'll follow the hospital's standard of care visit schedule

None of the planned follow-up visits will require surgery or an overnight hospital stay. These follow-up visits will include physical exams, neurological tests including NIHSS (National Institutes of Health Stroke Scale), and tests to check for negative side effects.

An MRI will be done at least once a month through the 6-month visit. After that, it is recommended to have an MRI every 2-3 months during regular care visits.

Potential Risks and Informed Consent

Participation in the FRONTIER study is voluntary. Your study doctor will talk to you about potential risks to participating in this study. You should refer to the Informed Consent for a list of potential risks. There may be additional risks related to the investigational procedure and follow-up testing that are not known.

Contact Information and Notes

HEALTH CARE TEAM	
NAME	
POSITION	
ADDRESS	
PHONE #	
E-MAIL	

NAME	
POSITION	
ADDRESS	
PHONE #	
E-MAIL	

SUPPORT TEAM/OTHER	
NAME	
POSITION	
ADDRESS	
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NAME	
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NOTES

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Helpful Brain Cancer Resources

In addition to resources discussed with your doctor, other helpful brain cancer resources include:

American Brain Tumor Association: **www.abta.org**

Brain Tumor Network: **www.braintumornetwork.org**

Glioblastoma Research Organization: **www.gbmresearch.org**

National Brain Tumor Society: **www.braintumor.org**

Watch a short video explaining the FRONTIER study:

Scan to watch explantation video

To learn more about FRONTIER and a list of participating sites:

Scan to learn more about FRONTIER

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