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VO90YAGER STUDY

A guide to help you learn about the VO90YAGER Study and the use of TheraSphere™ PCa Y-90 Glass Microspheres for the treatment of prostate cancer (PCa).

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Table of Contents

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A Patient's Guide to the VO^{90}YAGER Study

You are considering enrollment in the VO^{90}YAGER Study, which will use TheraSphere™ PCa Y-90 Glass Microspheres to treat localized prostate cancer (PCa). This booklet contains information to help you learn about the VO^{90}YAGER Study design, the TheraSphere PCa technology, and what to expect with the procedures and follow-up visits. It also contains some helpful information with medical terms found in the glossary section.

You should have a detailed discussion with your doctor about potential risks and address any questions you may have regarding your participation in the study. TheraSphere PCa potential risks are covered in the study's Informed Consent Form, which you will have to sign if you choose to take part in this study.

Glossary

Blood Vessel: a channel of the circulatory system which carries blood throughout the body.

Clinical Trial: a research study that tests medical treatments and evaluates their effects on human volunteers (participants) to advance medical knowledge and improve patient care.

Early Feasibility Study (EFS): is a clinical trial conducted in a small number of patients using a non-commercial new treatment that is early in the development stage. The objective of an EFS is to evaluate the initial clinical safety of the new treatment. It also looks at how the device functions and any potential benefit or risk to patients.

First-in-Human (FIH) study: is a study where a new treatment is used in human population for the first time.

Informed Consent Form (ICF): also referred to as Informed Consent, is a document that describes a clinical trial. It explains the type of treatment you will receive, how the treatment will be performed, what will be the follow-up, the known potential risks and potential benefits of the new treatment. After reading the information without any pressure from your study team, you may choose to sign the consent to participate in the study. Participation in this study is completely voluntary. You can decide whether or not to participate at any time without any penalty to you or loss of benefit to which you are entitled. A signed written agreement (the ICF) is required for all participants in this study.

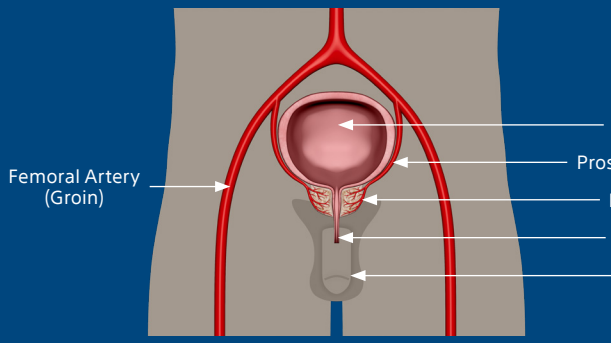
Microcatheter: a thin, flexible tube introduced through a blood vessel to access the treatment region to inject fluids or implant Therasphere PCa.

TheraSphere: is a treatment for hepatocellular carcinoma (liver cancer) made up of tiny glass spheres (also called microspheres or beads) that contain high doses of radiation called Yttrium-90 or Y-90 inside each bead. It will be referred to as TheraSphere PCa or the TheraSphere administration procedure for the VO^{90}YAGER Study.

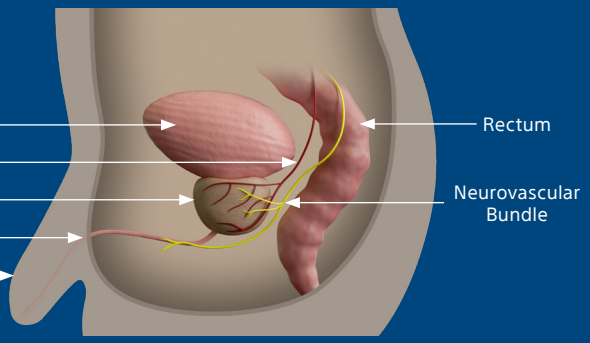
Yttrium-90 (Y-90): is the radioactive material inside the TheraSphere glass microspheres that releases radiation into the treatment area surrounding the microspheres. A radioactive element emits radiation while transitioning from yttrium 90 (unstable element) to Zirconium 90 (stable element). After emitting its radiation, Y-90 decays to undetectable levels in the body within 14 days post treatment. Following the treatment, the microspheres stay in the body permanently.

Prostate Cancer

Prostate cancer (PCa) is a type of cancer that originates in the prostate gland. The prostate gland is a small walnut-shaped gland in the male reproductive system located below the bladder. The current data estimates that about 288,300 new PCa cases will be diagnosed in the U.S. in 2023, making PCa the most common male cancer in the U.S.[1]



Frontal view of the prostate gland and nearby organs.



Side view of the prostate gland and nearby organs.

Treatment Options

Depending on your type of prostate cancer, the current standard treatment options might include the following:

- Observation (sometimes called watchful waiting) and active surveillance – are two ways of monitoring prostate cancer without treating it. The difference is that observation is meant to manage symptoms and improve quality of life, while active surveillance is intended to cure the cancer if it becomes more aggressive.
- Surgery – the removal of a part of, or the whole, prostate gland.
- Radiation therapy – uses a high-powered energy source (radiation) to kill cancer cells. Prostate cancer radiation therapy may involve internal (also called brachytherapy) or external radiation.

These possible treatment options are chosen based on your specific prostate cancer. Usually, doctors use the Gleason score, a grading system, to determine how abnormal the prostate cancer cells look. Doctors also consider your age, overall health status, and, most importantly, your opinion to decide on the best treatment option. Therefore, you should consult with your doctor regarding the benefits and risks and the effect of the treatment on your quality of life as you choose the appropriate treatment.[2]

1. Cancer of the Prostate – Cancer Stat Facts. National Cancer Institute. SEER. Accessed from: https://seer.cancer.gov/statfacts/html/prost.html#
2. Treating Prostate Cancer - American Cancer Society. Accessed from: https://www.cancer.org/cancer/types/prostate-cancer/treating.html

Treatment Team

During your prostate cancer diagnosis, treatment, and follow-up care, you will likely be working with several different types of physicians. The main types of doctors who treat prostate cancer may include:

- Medical Oncologist – a doctor who specializes in treating prostate cancer with medications such as chemotherapy, hormone therapy, and immunotherapy.
- Urologist – a surgeon trained specifically to diagnose and treat prostate cancer. A urologist also deals with other conditions of the male reproductive organs (e.g., kidneys, ureters, bladder, and urethra).
- Radiation Oncologist – a specialized physician who uses radiation techniques and methods to treat cancers, including prostate cancer.

Other specialists involved in your care may include nurse practitioners, physician assistants, nurses, nutritionists, etc. For the VO^{90}YAGER Study, an Interventional Radiologist (IR) will administer the TheraSphere PCa treatment to each participant.

- An IR is a specialized physician that diagnoses and treats a wide range of conditions in the human body using image-guided techniques (e.g., CT scan and ultrasound). IRs use minimally invasive tools, such as catheters or wires through the blood vessels which feed into a particular organ or location inside the body. The IR, along with the Urologist and the Radiation Oncologist will form part of your treatment team in this study.

VO90YAGER STUDY

The VO90YAGER Study is a first-in-human, early feasibility study assessing the use of TheraSphere™ PCa Y-90 Glass Microspheres in patients with localized prostate cancer. The purpose of the VO90YAGER Study is to evaluate the safety of using TheraSphere PCa to treat prostate cancer patients. Additionally, the study will evaluate the accuracy and effectiveness of the therapy.

TheraSphere PCa is an investigational device limited by United States law for investigational use only. It is not an approved treatment for prostate cancer and is not for sale.

Boston Scientific (study Sponsor) has gathered data on TheraSphere in liver cancer that indicates that this treatment could be suitable for other types of cancers, such as prostate cancer. Boston Scientific has also obtained approval from the FDA to conduct this experimental research study using TheraSphere PCa in patients with localized prostate cancer.

The VO90YAGER Study will enroll up to 36 patients at up to 5 hospitals at major academic and prostate treatment centers in the United States.

If you agree to participate in this study by providing informed consent, you will be expected to continue in this research study for about 5 years. You will visit the research hospital on separate occasions for imaging and treatment planning. You will return to the hospital on the day of the treatment procedure to receive the TheraSphere PCa administration. These visits will not require a hospital stay. Each participant who agrees to be in this study will visit the research hospital as follows:

- Pre-treatment: 60 days before TheraSphere PCa treatment to sign the Informed Consent Form (ICF) and complete screening tests and procedures for your doctor to determine if you are a good fit to participate in this study. These tests and procedures may occur over multiple days, as determined by your doctor.

VO90YAGER STUDY

- Treatment day: to receive the TheraSphere PCa treatment and complete any required tests and imaging assessments on the same day.
- Post-treatment: you will complete about 15 study contacts and follow-up visits over your 5 years duration on the study (e.g., visits post treatment include: at 36 hours; at 7, 15, and 30 days; at 3 months; and at every 6 months until 60 months or 5 years).

Participants will not be paid to take part in this study. Boston Scientific will pay for any special test or examinations that is required by this study. However, each participant's insurance company will be charged for the health care services that make up the standard medical care. You should check with your study doctor and insurance company regarding any potential medical services cost.

More information on the VO^{90}YAGER Study, including the pre-procedural visits, the treatment administration procedure, the follow-up visits and participant's responsibility can be provided by your study doctor.

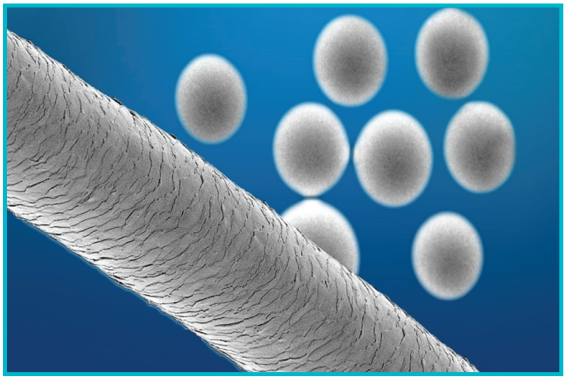
What is TheraSphere™ and How Does it Work?

TheraSphere™ Y-90 Glass Microspheres are a targeted hepatocellular carcinoma (HCC) therapy consisting of tiny glass beads (microspheres) containing radioactive Yttrium-90 (Y-90). The glass microspheres are approximately a third of the width of a human hair (0.001 inches in diameter). The glass microspheres are injected directly into the blood vessel feeding the tumor through a small flexible tube called a microcatheter using advanced imaging guidance. The glass microspheres enter the tumor's blood supply, lodge within the blood vessels feeding the tumor, and release radiation to the tumor. The radiation works to destroy the tumor cells from within. This process is referred to as selective internal radiation therapy (SIRT).

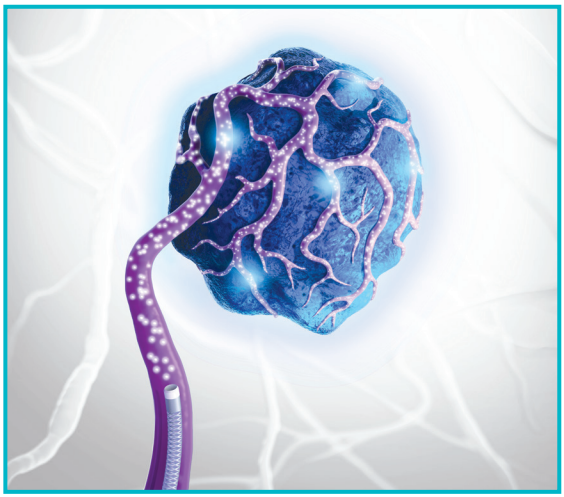
The intention of SIRT is to limit radiation exposure to surrounding normal tissues. The majority (90%) of the radiation from a TheraSphere glass microsphere is deposited in tissue within 5mm (5mm is about the thickness of two nickels stacked). The glass microspheres will deliver most of the radiation (>95%) to the tumor in the first two weeks following the TheraSphere administration procedure. Although the amount of radiation released decreases over time, the glass microspheres will remain permanently in the treated location in the patient's body and cannot be removed.

TheraSphere is approved by the Food and Drug Administration (FDA) to treat HCC, a type of liver cancer. TheraSphere has been used to treat liver cancer in over 20,000 patients in the U.S.and 100,000 patients worldwide for over 20 years.

Each TheraSphere PCa dose is made uniquely for each patient being treated.



TheraSphere microspheres next to human hair.



TheraSphere 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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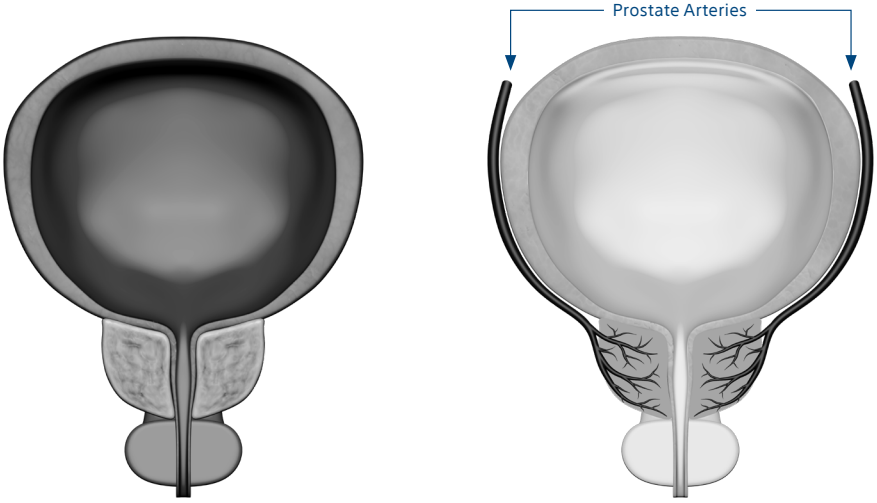
Before the Administration Procedure

Prior to the TheraSphere™ PCa administration procedure, you will need to have some imaging tests (MRI and CT) to make sure you are eligible for the VOY^{90}AGER trial and determine how much TheraSphere PCa will be needed to treat your prostate. The diagnostic imaging visits usually do not require a hospital stay.

Visit 1: Pre-procedural Diagnostic Imaging



MRI **CT Angiography**

Images acquired: MRI and CT Angiography

MRI (magnetic resonance imaging): provides detailed images of soft tissues such as the prostate and bladder via magnetic fields and intravenous (IV) contrast injection.

CT (computed tomography) Angiography: provides detailed information about prostate blood vessels via x-ray and intravenous (IV) contrast injection.

Purpose: MRI provides size of prostate to determine how much TheraSphere PCa is required. CT Angiography maps prostate blood vessels.

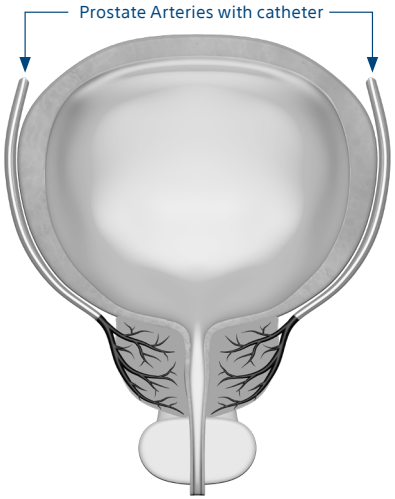
Timing: MRI within 90 days and CTA within 60 days of TheraSphere PCa administration procedure.

Note: A single microcatheter will be used to check the left side of the prostate, then the right side, or as preferred by your physician.

Before the Administration Procedure

Once a patient is considered a candidate for the VOY^{90}AGER trial based on diagnostic imaging, the doctors will perform a treatment planning angiography procedure. During this procedure the doctor will insert a microcatheter into the femoral (groin) or radial (wrist) artery and use angiography imaging to guide it to the blood vessel that feeds one side of the prostate. The doctor will check blood flow in the vessel with angiography and also use Cone-Beam CT to make sure that the TheraSphere™ PCa treatment will cover the prostate only and not reach any surrounding organs. These scans will then be repeated in the blood vessel on the other side of the prostate to ensure the whole prostate gland will be treated.

Visit 2: Treatment Planning



Angiography

CBCT

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

A microcatheter will be placed in each blood vessel supplying the prostate to acquire angiography and CBCT.

Angiography: provides images of blood vessels and blood flow in the prostate via x-ray and a microcatheter contrast injection to areas being examined.

CBCT (cone-beam computed tomography): provides 3D images of the treatment region via x-ray and microcatheter contrast injection to areas being examined.

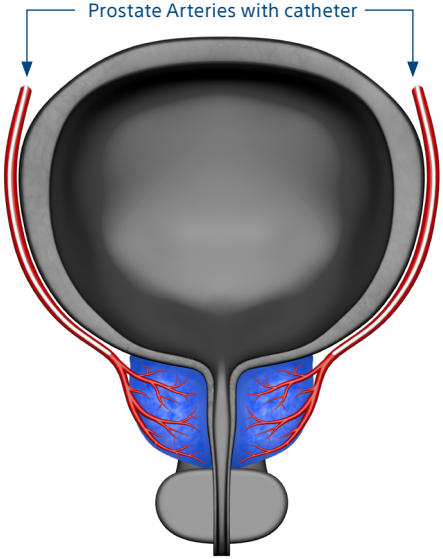
Purpose: Confirm the whole prostate gland will be treated.

Timing: within 21 days prior to TheraSphere PCa administration procedure.

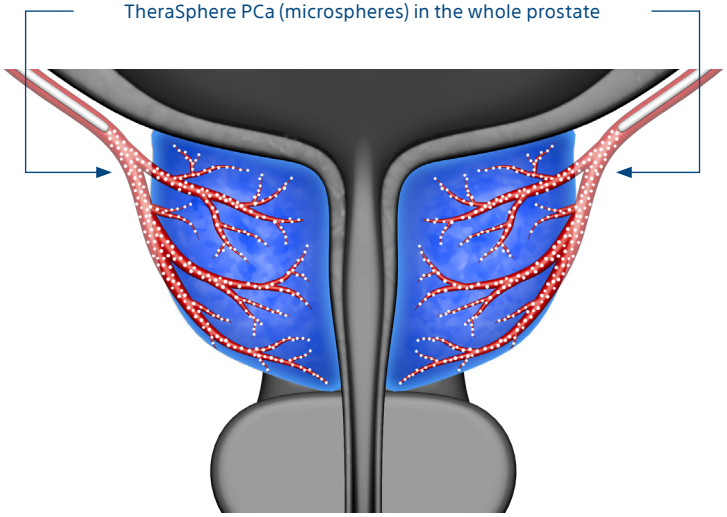
TheraSphere™ PCa Administration Procedure

On the day of the TheraSphere PCa administration procedure, the doctor will again use imaging scans to insert a microcatheter into the femoral or radial artery and guide it to the blood vessel supplying one side of the prostate gland (e.g., the right side). A CBCT scan will be taken to confirm the treatment area and then TheraSphere PCa will be delivered to this side of the prostate through the microcatheter.

Following delivery of TheraSphere PCa to one side of the prostate (e.g., the right side), the microcatheter will be removed and a new microcatheter will be guided to the blood vessel supplying the other side of the prostate (e.g., the left side). Another CBCT scan will be taken to confirm the treatment area and then TheraSphere PCa will be delivered to this side of the prostate gland (e.g., the left side) through the microcatheter.



Microcatheter navigated to the treatment location



Closeup showing TheraSphere PCa (Y-90 Glass Microspheres) delivered to the whole prostate through microcatheters (one side at a time)

The glass microspheres will be trapped in the prostate and deliver radiation throughout the prostate and covering the tumor. The majority (90%) of the radiation from one TheraSphere glass microsphere is deposited in tissue within 5mm of the glass microsphere (5mm is about the thickness of two nickels stacked). Therefore, the TheraSphere PCa treatment is intended to provide radiation to the entire prostate and the tumor, while limiting radiation exposure to nearby tissues and organs.

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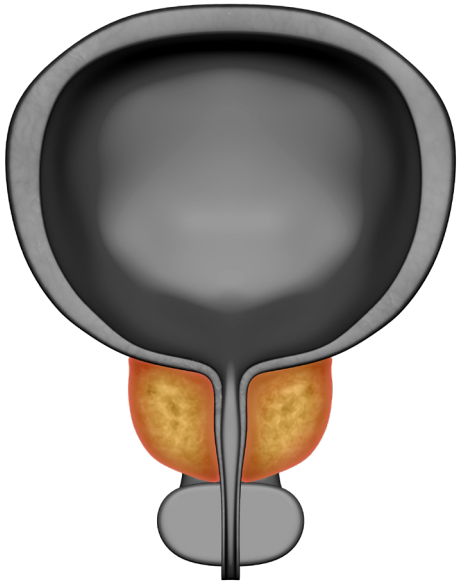
Post TheraSphere™ Administration Procedure Imaging and Monitoring

Following the TheraSphere PCa administration procedure*, you will have another imaging test called a PET (positron emission tomography)-MRI or PET-CT scan to verify that the treatment has been delivered as planned. This scan is used to confirm that the Y-90 glass microspheres were delivered to and are irradiating the intended treatment location (the whole prostate gland). You will be monitored until you are discharged from the hospital (within 24 to 36 hours post-treatment).



PET scan showing TheraSphere PCa in the whole prostate after being delivered through microcatheters to each side of the prostate (one side at a time)

Because the radiation produced by the Y-90 glass microspheres has a very small range of action, the radioactive energy outside your body is very low. The hospital may give you instructions when you are discharged as a precaution. No radiation safety restrictions are required for visitors, family, or caregivers after your TheraSphere PCa administration procedure.

*usually on the same day

Post TheraSphere™ Administration Follow-Up Visits

As a participant in the VO^{90}YAGER Study, you will return to the research hospital at the following visit intervals for on-going evaluation after the TheraSphere PCa administration procedure:

- Within 36 hours; at 7, 15, and 30 days; at 3 months; and at every 6 months for 5 years following TheraSphere treatment procedure.

These follow-up visits will include physical exams, gastrointestinal and genitourinary (GI/GU) assessments, and adverse events (AEs) assessments. An MRI scan will be performed at months 3, 6, 12, 24, 36, 48 and 60 during the 5-year follow-up period. A PSMA PET scan will be performed at 60 months to check the status of the tumor.

Potential Risks and Informed Consent

Participation in the VO^{90}YAGER Study is voluntary. Your study doctor will discuss potential risks of participating in this study with you. Additionally, you should refer to the Informed Consent Form for a list of potential risks for the study.

There may be additional risks linked to the investigational procedure and follow-up testing that are unknown. Your study doctor will discuss these risks (known and unknown) and others with you.

Diversity, Inclusion, And Equity in Prostate Cancer

While there are considerable racial and ethnic disparities in prostate cancer incidence and mortality in the U.S., clinical trials often do not reflect disease incidence across racial and ethnic subgroups. The VO^{90}YAGER Study seeks to enroll participants that reflect the prostate cancer population the investigational TheraSphere PCa therapy is likely to treat if approved. Therefore, Boston Scientific is partnering with the study team at each research center to engage all men, including those from diverse backgrounds (i.e., people from racial and ethnic minority and other diverse groups) about participation in the VO^{90}YAGER Study. Together with your study team, Boston Scientific is committed to closing the health equity gap in clinical trials.

Helpful Prostate Cancer Resources

In addition to your doctor's research center website, other helpful prostate cancer (PCa) resources include:

www.zerocancer.org: national nonprofit with the mission to end prostate cancer.

www.pcf.org: philanthropic organization dedicated to funding prostate cancer research.

www.prostatehealthed.org: eliminating prostate cancer disparity for all men.

www.pcri.org: dedicated to educating patients and their families about prostate cancer.

www.cdmrp.health.mil/pcrp: US Government's initiative on prostate cancer research funding.

www.cancer.gov/types/prostate: US Government's prostate cancer educational initiative.

Study Team Contact Information and Notes

HEALTH CARE TEAM	
NAME	
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E-MAIL	

NAME	
POSITION	
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E-MAIL	

SUPPORT TEAM/OTHER	
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POSITION	
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NAME	
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NOTES

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