HISTOSONICS™

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HISTOTRIPSY SYSTEM

USER GUIDE
Software Version 3.2

REF	
EDNTC1001	TREATMENT CART
EDNTH12	12 CM TREATMENT HEAD
EDNTH14	14 CM TREATMENT HEAD
EDNSA1001	SUPPORT ARM
EDNCK2001	COUPLING KIT



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1 Introduction

Introduction to the system and this user guide.

General Description

The Histotripsy System (system) allows physicians to target, plan, and deliver histotripsy while using live ultrasound imaging to visualize the targeted tumor in real-time. Treatment parameters are customized based upon the properties of the acoustic pathway and the targeted tissue. The system ensures that the treatment parameters confine the histotripsy tissue effect to the planned treatment volume (PTV) to help prevent damage to tissue and structures outside of the PTV.

Caution
Do not attempt to use the system with components other than those provided or specified by HistoSonics.

Principle of Operation: Histotripsy

The technology underlying the system is histotripsy—a mechanical process of focused ultrasound that utilizes a non-ionizing and non-thermal mechanism of action to destroy targeted liver tissue by delivering high amplitude, very short (microsecond), focused ultrasound pulses. Histotripsy pulses are engineered to induce controlled acoustic cavitation at a known focal zone in the form of a “bubble cloud” – a cluster of micro-bubbles – which rapidly expands, then collapses to impart significant tissue stress and strain and ultimately, mechanical tissue destruction, reducing the targeted tumor into a non-viable homogeneous acellular lysate.

Caution	
Rx ONLY	Federal law (USA) restricts this device to sale by or on the order of a physician.

Clinical Benefits

To non-invasively destroy targeted liver tumors deemed harmful to the patient by the treating physician.

User Training

Contact HistoSonics for information about company provided training options.

Warning

The system is for use only by persons who have completed formal training from HistoSonics on the use of the system and are familiar with the instructions, warnings, and precautions provided in this user guide.

Contact Information

Additional technical and customer service information is available from HistoSonics. Please visit HistoSonics.com or contact HistoSonics at:

Manufacturer	**HistoSonics, Inc.**
Address	16305 36th Avenue North, Suite 300 Plymouth, MN 55446-4273 (USA)
Phone	612-351-0361 Toll free (US only): 877-740-0543
Email	info@HistoSonics.com
European Union Authorized Representative	Obelis S.A. Boulevard Général Wahis, 53 1030 Brussels BELGIUM

About this User Guide

Software Version

This user guide is specific to software version 3.2.

Navigating the PDF

- Contents: Select any entry in the table of contents to go directly to the corresponding page.
- Index: An alphabetical list of key topics is provided at the end of this user guide. Select a page number to go directly to that page.
- Bookmarks: The PDF is equipped with predefined bookmarks with drop-down menus that help you quickly navigate through chapters and sections.
- Cross-references: Selecting cross-references will take you directly to the referenced content.
- Search Function: To quickly find specific information, you can utilize the search function in your PDF reader. Press 'Ctrl + F' (or 'Cmd + F' on macOS) to open the search bar.

Printed User Guides

Printed versions of this user guide are available upon request at no charge.

Conventions Used

The following conventions are used to draw attention to safety information and other types of important information.

Warning

Indicates a potentially hazardous situation that, if not avoided, could result in death or serious injury.

Caution

Indicates a potentially hazardous situation that, if not avoided, could result in minor to moderate injury or product damage.

Important

Used to draw attention to important information and to provide additional context, details and operational tips.

Symbols

Definitions for labeling symbols.

Symbol	Meaning
	Manufacturer
	Country and date of manufacture
	Use-by date
	Lot number
	Catalog number
	Serial number
	Distributor
	This side up (indicates the correct upright orientation for transport and storage)
	Fragile (handle with care)
	Temperature limitation
	Humidity limitation
	Do not re-use (single use)
	Consult electronic instructions for use

	Caution — Consult instructions for use for specific warnings or precautions associated with the medical device
	Medical device
	Caution: Federal law (USA) restricts this device to sale by or on the order of a physician
	Two people are required to transport the treatment cart over inclines
	Protective earth (ground) The ground point and symbol are located inside the treatment cart
	Alternating current
	Electrostatic sensitive device Note: This hazard and symbol are only inside the treatment cart
	Non-ionizing electromagnetic radiation
	Emergency stop
	Type B applied part
	Waste from Electrical and Electronic Equipment (WEEE) indicates the product should be collected separately and not disposed of as unsorted municipal waste
IP20	System degree of protection against ingress (excludes treatment head)
	Follow instructions for use
EU REP	European Union representative
CE	CE mark

Terminology

Key terminology and concepts.

acoustic aberration	Distortion of therapeutic ultrasound that results when there is significant variation of the sound speed within the acoustic pathway.
acoustic cavitation	A phenomenon where high acoustic pressure results in the formation of micro-bubbles within tissue.
acoustic pathway	The field in which therapeutic ultrasound travels from the therapy transducer to its focal point (target tissue). The boundaries of the acoustic pathway are represented by the acoustic field indicator overlay in the live ultrasound imaging.
bubble cloud	A group of micro-bubbles formed by focused ultrasound pressure waves. The bubble cloud location is fixed relative to the therapy transducer in the treatment head.
coupling kit	A kit that contains single-use accessories required to perform a histotripsy procedure. Includes the patient membrane (membrane), membrane cradle, coupling oil, coupling band, inspection mirror, and bubble removal tool.
crosshairs	An overlay on the live ultrasound imaging that designates the expected location of the bubble cloud.
Fluidics System	An inclusive term that refers to the fluidics cart and daily disposable kit which are used to collect and process water from a clinical water source and transfer ultrasound medium to support a histotripsy procedure. For more information about HistoSonics' Fluidics System, refer to the Fluidics System User Guide.
focal zone	The focal location and volume where therapeutic ultrasound is concentrated to produce a bubble cloud.
fusion	Optional workflow in the Plan phase that aligns and registers reference images (MR or CT) to live ultrasound imaging. Fusion provides multi-modal visualization to enable the user to identify the targeted tumor and other critical anatomy in the region of interest.
histotripsy	The mechanical destruction or disruption of tissue caused by a specific form of controlled acoustic cavitation.
Histotripsy System (system)	An inclusive term that refers to the treatment cart, treatment head, support arm, and coupling kit. Also referred to as the "system."

imaging transducer	A curvilinear ultrasound transducer that connects directly to the ultrasound system to display live ultrasound imaging on the treatment cart. Both a handheld and treatment head–integrated imaging transducers are used as part of a histotripsy procedure.
lysate	A fluid containing the contents of lysed tissue and cells and any disrupted extra-cellular materials remaining after histotripsy.
margin/ margin contour	Additional treatment volume prescribed by the physician. The margin contour is the larger, outer ellipsoid surrounding the target contour and is the maximum outer boundary of the PTV. The margin contour is displayed as a red 2D ellipse in the live ultrasound imaging.
maximum treatment depth	The deepest possible treatment depth as measured from the patient's skin to the furthest extent of the PTV.
membrane cradle	Webbing that helps prevent the membrane from excessively bulging or shifting on the patient.
minimum treatment depth	The shallowest possible treatment depth as measured from the patient's skin to the nearest edge of the PTV. Dependent on patient's body wall thickness and target tissue depth.
patient membrane (membrane)	A malleable, impermeable barrier that conforms to the patient and holds ultrasound medium. Visually transparent and acoustically transparent to ultrasound. Inserts in the frame to create a reservoir.
plan points	Seven discrete locations in the PTV (-X, +X, -Y, +Y, -Z, +Z, and center) where the physician establishes a threshold voltage—the voltage required to generate a sustained bubble cloud. The system uses the seven voltage settings as input, computing the necessary voltage to establish a bubble cloud for every focal zone within the PTV.
planned treatment volume (PTV)	An ellipsoidal volume consisting of the target contour and margin contour. Comprised of a predetermined number and spacing of focal zones based on the size and shape of the volume.
pre-focal cavitation	Unwanted acoustic cavitation that occurs proximal to the intended focal zone, includes tissue surfaces such as skin.
reference images	MR and CT images imported from a study.
region of interest	A volume that encompasses the targeted tumor and may also include critical anatomy and relevant landmarks.
reservoir	An assembly of the membrane and frame. Used to contain the ultrasound medium during the histotripsy procedure.

support arm	Multi-joint articulating arm with frame and bed rail clamp. Secures on a bed rail and holds the reservoir (frame with installed membrane) in the desired position above the patient.
system check container	An integrated basin at the top of the fluidics cart designed for collecting, processing, and temporarily storing ultrasound medium before transferring it to the reservoir above the patient. Its name is derived from the fact that during the treatment cart system check, the treatment head is submerged in the system check container.
target contour	A 3D ellipsoidal volume aligned and positioned over the targeted tumor. Displayed as part of the PTV as an orange 2D ellipse on the live ultrasound imaging.
therapeutic ultrasound	Histotripsy ultrasound pulses emitted from the therapy transducer in the treatment head for the non-invasive mechanical destruction of targeted liver tumors.
therapy transducer	The component in the treatment head that delivers focused therapeutic ultrasound. Designed to produce controlled acoustic cavitation (histotripsy bubble cloud).
threshold voltage	The minimum voltage required to generate a sustained bubble cloud.
treatment	The process of using the System to perform a histotripsy procedure to destroy targeted liver tumors.
treatment arm	Micropositioning arm used to position and move the treatment head during all phases of the procedure.
treatment head	Houses the therapy transducer and ultrasound imaging transducer. Mounts and interfaces on the distal end of the treatment arm.
treatment zone	Volume of tissue that was mechanically destroyed or disrupted via the histotripsy procedure (resulting treatment volume).
ultrasound imaging	The live ultrasound displayed in the user interface for localizing the region of interest, planning and real-time monitoring of the histotripsy procedure. The Samsung R20 Ultrasound System (ultrasound system) streams real-time ultrasound images via the handheld imaging transducer (when localizing) and via the treatment head imaging transducer (when planning and monitoring treatment).
ultrasound medium	Water prepared to the required specifications (dissolved oxygen level and temperature) for a histotripsy procedure. Creates efficient acoustic coupling between the treatment head and the patient.

2 Safety and Standards

General use information, summary of safety notices, and information about manufacturing and testing.

Indications for Use

The Histotripsy System is indicated for the non-invasive destruction of liver tumors, including unresectable liver tumors, using a non-thermal, mechanical process of focused ultrasound.

Contraindications

None known.

Intended Use

The Histotripsy System is intended for the non-invasive mechanical destruction of liver tumors, including the partial or complete destruction of unresectable liver tumors via histotripsy.

Caution

Rx ONLY Federal law (USA) restricts this device to sale by or on the order of a physician.

Histotripsy Procedure Considerations

Important

The system was used in a study population that included patients with liver tumors that an independent multidisciplinary tumor board determined to be unresectable, as well as patients who were intolerant of surgery. Study results confirmed the safety and effectiveness of the system when compared to other ablation methods.

The system has not been evaluated by regulatory authorities for the treatment of cancer, any cancer outcomes (such as local tumor progression, 5-year survival or overall survival), or any other specific disease. The use of this device in all instances should be guided by the clinical judgment of an appropriately trained physician.

Warning

The system is for use only by persons who have completed formal training from HistoSonics on the use of the system and are familiar with the instructions, warnings, and precautions provided in this user guide.

Warning

Histotripsy is used to destroy targeted liver tumors. Consequently, histotripsy should only be considered in patients with sufficient functional liver reserve to withstand the destruction of the planned volume of liver tissue. Functional liver capacity can be impacted by multiple factors, including prior focal therapies, chemotherapies and/or immunotherapies. Loss of liver function below a critical threshold can lead to patient harm, including liver failure and death. Only the physician can determine if a treatment plan is safe and medically appropriate.

Since sufficient functional liver reserve following treatment is a requirement for any focal liver therapy, patients who are Child-Pugh class C or have decompensated liver cirrhosis prior to treatment should not be considered candidates for histotripsy. Histotripsy of the liver has only been evaluated in patients who are Child-Pugh class A and B, without evidence of decompensated cirrhosis.

Clinical Considerations

Anesthesia

It is expected that anesthesia will typically be used during histotripsy treatments to help mitigate the risk of patient/target tissue movement during treatment. Ensure potential histotripsy patients can undergo the planned anesthetic as part of the patient selection process.

Multiple Treatments

The system supports delivery of more than one distinct treatment within a single anesthetic session. Physician judgment should be informed by review of the treatment plan before treatment and by ultrasound assessment of the treatment zone following completion of each treatment. Because the system displays treatment volume only for the current PTV, physicians must account for the cumulative volume of tissue destruction when considering additional treatments.

Patient Populations Not Evaluated

The system has not been evaluated in patients who are pregnant or breastfeeding, or in pediatric patients defined as individuals under 18 years of age.

Known and Potential Side Effects

The following list includes known and potential side effects associated with the system, the procedure, and similar procedures (local focal therapies). Adverse Device Effects (ADEs) and Serious Adverse Device Effects (SADEs) as reported in #HOPE4LIVER are included in the Appendix.

- Abdominal pain or tenderness
- Damage to adjacent normal liver
- Petechial hemorrhage
- Elevated/abnormal liver function tests
- Pain
- Damage to targeted non-tumor tissue included in PTV which may result in clinical sequelae specific to the damaged tissue
- Damage to the ribs
- Dyspnea/shortness of breath
- Failure to thrive
- Fatigue
- Hematoma
- Hemoglobinuria
- Hemolysis
- Leukocytosis
- Post-ablation syndrome (low-grade fever, malaise, chills, myalgia, delayed pain, systemic inflammatory response, nausea, vomiting, anorexia)
- Peripheral perfusion defects
- Skin erythema
- Thrombocytopenia
- Unnecessary exposure to anesthesia
- Vertigo/lightheadedness
- Anemia
- Decline in functional status
- Hemoptysis
- Pulmonary embolism
- Venous thrombosis
- Constipation
- Dehydration
- Diarrhea
- Dysuria
- Fluid or blood collection (abdominal, perihepatic, or renal)
- Hematuria
- Hypervolemia
- Pseudoaneurysm
- Post-procedural discomfort
- Rash
- Rise in creatinine
- Skin burn
- Unintended tissue damage outside of target organ
- Bile duct stricture
- Hypertension/hypotension
- Infection
- Jaundice
- Neutropenia
- Oliguria
- Residual tumor
- Abscess
- Acute kidney injury (AKI)
- Hepatic artery stenosis/obstruction (partial or complete)
- Lung hemorrhage
- Pancreatitis
- Fistula in organ or abdominal wall
- Intestinal injury/leak/obstruction
- Biloma
- Post-procedural edema
- Subcutaneous or intervening tissue damage
- Ascites
- Bacteremia
- Chest pain
- Gastrointestinal inflammation
- Pleural effusion/pleuritic pain
- Pneumothorax
- Bile duct obstruction
- Cholangitis
- Cholecystitis
- Encephalopathy
- Hemothorax
- Major blood vessel stenosis
- Renal dysfunction/failure
- Hemorrhage/bleeding
- Gastric leak
- Myocardial infarction
- Death
- Intrahepatic segmental necrosis
- Elevated C-reactive protein
- Hypothermia
- Hematemesis
- Cardiac arrhythmias
- Gastrointestinal perforation
- Hemodynamic instability
- Liver failure
- Peritonitis
- Seeding of tumor
- Sepsis
- Multisystem organ failure

The following list includes known and potential side effects associated with delivery of general anesthesia.

- Cough/sore throat
- Confusion
- Headache
- Lung edema/atelectasis
- Rhinorrhea
- Hypoxia
- Urinary retention
- Deep vein thrombosis
- Delirium
- Pneumonia
- Cardiac arrest
- Dental or vocal cord injury
- Pneumatosis
- Psychosis
- Blocked lung artery
- Respiratory failure
- Stroke

Technical Considerations

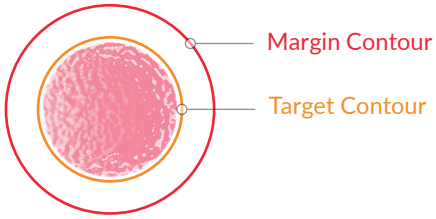
The following scenarios prohibit the use of the system to destroy tumors:

- Tumor is beyond the reach of the system
- Physician cannot visualize the bubble cloud to perform in vivo crosshair calibration
- Acoustic blockage prevents the ability to sustain the bubble cloud
- Plan parameters exceed the thermal safeguards of the system

Plan Volume Considerations

The system enforces a minimum and maximum PTV:

- Minimum dimensions: 15 mm diameter sphere (resulting in a volume of 1.8 cm^3)
- Maximum dimensions: 40 mm diameter sphere (resulting in a volume of 33.5 cm^3)



Target Contour + Margin Contour = Planned Treatment Volume

Procedure Room – Space Considerations

To ensure the feasibility of performing a histotripsy procedure at your site, assess if there is a procedure room that can accommodate all of the necessary equipment. Take into account the:

- Equipment dimensions
- Required placement and orientation of equipment in relation to other equipment
- Space required for personnel to move safely around equipment as needed during setup and operation
- Space required in the event of a patient emergency where the ultrasound medium must be rapidly evacuated

Equipment	Width	Depth
Treatment cart	100 cm	65 cm
Samsung R20 ultrasound system	63 cm	94 cm
Fluidics cart	82 cm	65 cm

Dimensions are approximate

*The waste basin in the HistoSonics Fluidics Cart can function as an EEC

Important

For information on how HistoSonics equipment must be oriented during System Check and during the procedure, refer to Chapter 6: Operation. For assistance evaluating whether your procedure room can accommodate a histotripsy procedure, contact HistoSonics.

Summary of Safety Notices

This section contains important information about the safe use of the system. Read and understand this section prior to setting up and using the system.

Warnings

The following warnings apply to the system and its use.

Warning
The system is for use only by persons who have completed formal training from HistoSonics on the use of the system and are familiar with the instructions, warnings, and precautions provided in this user guide.
Histotripsy is used to destroy targeted liver tumors. Consequently, histotripsy should only be considered in patients with sufficient functional liver reserve to withstand the destruction of the planned volume of liver tissue. Functional liver capacity can be impacted by multiple factors, including prior focal therapies, chemotherapies and/or immunotherapies. Loss of liver function below a critical threshold can lead to patient harm, including liver failure and death. Only the physician can determine if a treatment plan is safe and medically appropriate.
Consider patient-specific risk factors for acute kidney injury (AKI) and/or renal failure based on clinical history and procedural scenarios that may increase stress on kidney function. Factors to consider include, but are not limited to, hydration status, planned treatment volume, number of treatment sessions, use of nephrotoxic agents including NSAIDs, and expected use of imaging contrast agents. The risk of AKI increases as total treatment volume increases. In patients with compromised pre-procedure renal function, AKI may progress to acute renal failure. Renal risk should be evaluated before treatment, and renal function should be monitored for signs of AKI before, during, and after treatment.
Since sufficient functional liver reserve following treatment is a requirement for any focal liver therapy, patients who are Child-Pugh class C or have decompensated liver cirrhosis prior to treatment should not be considered candidates for histotripsy. Histotripsy of the liver has only been evaluated in patients who are Child-Pugh class A and B, without evidence of decompensated cirrhosis.
Mechanical injury to critical structures (e.g., vascular structures, liver capsule, bile ducts) may occur when these structures are within the PTV. The likelihood of bleeding and/or mechanical injury may increase with additional and/or subsequent treatments within a treatment session or subsequent sessions. In cases where the tumor violates the liver capsule and/or the liver capsule is compromised from prior intervention or therapy, bleeding events may include intraperitoneal hemorrhage, which can be severe and potentially lead to death.

Warning

When any of the following occur, cumulative thermal exposure will increase, elevating the risk of thermal injury to the skin, body wall, or other tissues:

- User-initiated repetition of tasks where energy is delivered, such as re-performing in vivo calibration or establishing voltage settings for any of the seven plan points
- Prolonged energy delivery when establishing voltage settings
- Exceeding the voltage necessary to sustain the bubble cloud
- Anatomical or other structures (e.g., ribs, lung, bowel) located anywhere within the acoustic pathway—including post-focal—with higher absorption and/or reflection
- Anatomy or obstructions (e.g., bowel gas) within the pre-focal acoustic pathway that require higher voltage settings to sustain the bubble cloud
- Multiple treatments within the same procedure when acoustic pathways may intersect and/or pass through previously treated zones

Note the following system behaviors, which further inform energy delivery considerations related to cumulative thermal exposure:

- The system applies a thermally safe protocol to perform automated treatment but does not account for the energy delivered during treatment planning
- While the mechanism of action is non-thermal, localized temperature rise within the acoustic pathway will occur during energy delivery/deposition—particularly in transition zones such as the skin, body wall, or in tissues that absorb/obstruct ultrasound energy, such as bone
- The system enforces a 30-second timeout when establishing a voltage setting but does not limit cumulative energy delivery

While some repetition or extended energy delivery may be required to verify a sustained bubble cloud, procedural goals should be met using the minimum voltage and duration necessary, while limiting or preventing unnecessary repetition. When clinically appropriate, users may consider pausing between energy delivery tasks to allow tissue cooling before proceeding.

Unauthorized modification of the system is strictly prohibited due to the presence of internal components such as lead-acid battery and high-voltage electronics, and may lead to severe adverse consequences including, but not limited to:

- Electric shock
- Fire or explosion
- Chemical burns
- Incomplete or ineffective treatment
- Thermal or cavitation injury

Failure to comply may result in serious harm to the user or patient, as well as damage to the device.

Warning
In the event of a patient emergency where a defibrillator is required, remove any ultrasound gel, coupling oil, or ultrasound medium from the patient's skin if it could prevent the safe and effective use of the defibrillator. Refer to the defibrillator instructions for use.
Do not make any setup changes during the Treat phase. Repositioning the treatment cart, bed, or patient will cause misalignment between the PTV and the targeted tissue. Delivering therapeutic ultrasound when the PTV is misaligned with targeted tissue will result in unwanted tissue destruction or incomplete treatment.
Delivering therapeutic ultrasound when anatomical or other obstructions (bone, cartilage, lung, digestive gas, etc.) are along the acoustic pathway can result in thermal injury to non-targeted tissues. Use imaging and the acoustic field indicator overlay to assess and minimize obstruction prior to finalizing the treatment plan.
Anatomical or other obstructions (bone, cartilage, lung, digestive gas, etc.) as well as acoustic aberration along the acoustic pathway can result in mechanical (cavitation) injury to non-targeted tissues. • Use imaging and the acoustic field indicator overlay to assess and minimize obstructions prior to finalizing the treatment plan • Monitor the location of the bubble cloud throughout the treatment using real-time ultrasound imaging and suspend therapy if the bubble cloud is not within the PTV
Do not use the system outside of the EMC specifications provided in this user guide.
Failure to perform the System Check phase as instructed could result in incomplete or ineffective treatment, tissue destruction outside the PTV, or thermal or cavitation injury.
Failure to confirm that the treatment head properly locks to the treatment arm can result in an impact injury to the patient or user and damage to the treatment head and I/O connection port.
Exceeding the voltage necessary to sustain a bubble cloud in any of the seven plan points and/or failing to calibrate crosshairs that are misaligned with the bubble cloud may result in thermal or cavitational injury to non-targeted tissue.
The bubble cloud must be visible in the live ultrasound to calibrate the crosshairs in vivo.
Muscle layer depth is one of the measurements used by the software to calculate safe treatment parameters. Failure to correctly mark the muscle layer can result in unintended thermal injury.
When establishing voltage settings, immediately stop energy delivery if the patient, bed, or treatment cart move. Movement can cause the PTV to become misaligned with the targeted tissue resulting in unwanted tissue destruction.

Warning
Failure to lock the bed position and lock the treatment cart wheels before energy delivery may result in patient injury.
Failure to inspect the treatment cart and treatment head can result in risk to the patient or user.
Inspect the treatment head for damage before every use. Do not use the treatment head if there are any signs of damage, including, but not limited to, cracks, chips, dents, frayed wires, and compromised wire insulation. Do not use the treatment head if it has been dropped or roughly handled as internal damage may have occurred. Do not connect a damaged treatment head to the treatment cart. Immediately report any damage to HistoSonics.
Do not continue establishing voltage settings if the crosshairs are significantly misaligned with the bubble cloud as it may indicate: • In vivo calibration was not performed correctly • Setup issue (for example, the presence of an air pocket) • System malfunction
Failure to calibrate the crosshairs in vivo as instructed can result in injury to the patient or incomplete treatment.
The imaging transducer must be aligned to -Y and in the home position (fully retracted) when calibrating crosshairs. Calibrating crosshairs when the imaging transducer is not oriented to -Y or is not in the home position can result in injury to the patient or incomplete treatment.
The system is not compatible with an MRI environment.
Inspect the treatment cart power cord for damage before every use. Do not use a damaged power cord as it creates hazardous situations, including fire and electrical shock.
During automated treatment, carefully monitor the patient and the system. Failure to monitor automated treatment can result in unwanted tissue destruction and incomplete treatment. Immediately suspend therapy if the: • Bubble cloud is not confined within the PTV • Patient, bed, or treatment cart move Movement can cause the PTV to become misaligned with the targeted tissue. Do not resume treatment after movement. Evaluate to confirm there are no complications, then begin a new treatment session, if desired.
To meet electromagnetic compatibility requirements (EMC), avoid using the treatment cart adjacent to other equipment. Do not place other equipment on top of the treatment cart.
Use of components such as treatment heads, imaging transducers, and cables other than those specified by HistoSonics may result in increased emissions or decreased system immunity.

Warning
Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the treatment cart. Otherwise, the degradation of system performance could result.
To avoid the risk of electric shock, only power the treatment cart with an earthed, hospital-grade power outlet.
When establishing a voltage setting, always try to minimize energy duration as prolonged energy delivery can result in patient thermal injury.
Delivering energy without consistent bubble cloud visualization increases the risk that a bubble cloud to crosshair misalignment may occur undetected, resulting in cavitational injury to non-targeted tissue. However, once in vivo crosshair calibration is successfully performed, the potential of a bubble cloud being significantly misaligned with the crosshairs is low.
Always verify that the PTV encompasses the target tissue (tumor and desired margin) in multiple planes. Misalignment of the PTV can result in unwanted tissue destruction, incomplete treatment, or both.
Respiration may cause the targeted tissue to move relative to the PTV, causing the treatment zone to be larger than the PTV. The system does not account for respiratory motion. Observe the PTV and targeted tissue throughout the respiratory cycle to assess the relative impact of respiratory motion on the treatment plan. Adjust the plan as necessary to ensure safe treatment.
Before proceeding to the Treat phase, use live ultrasound to verify that the target contour aligns to the tumor in multiple planes. Do not rely on reference images for location verification, even if they are fused with live ultrasound, as they may not be valid or accurate. Failure to use live ultrasound for verification may lead to unwanted tissue destruction and incomplete or ineffective treatment.
After fusing images, always verify that images still align in the Live Fused Images view after making any of these changes: • Swapping the treatment head • Adjusting the patient or bed • Adjusting the treatment cart position • Adding or removing ultrasound medium Repeat the fuse images task if images no longer align.
When cleaning, do not apply liquids directly onto the control panel or let them seep inside the treatment cart. Ingress liquid can result in electric shock or risk of fire.

Warning

Delivering therapeutic ultrasound when lung tissue is located along the acoustic pathway can result in localized pulmonary tissue edema or hemorrhage. Use imaging and the acoustic field indicator overlay to assess if lung is along the acoustic pathway prior to finalizing the treatment plan. Consider using alternate angles to avoid lung tissue.

Precautions

The following precautions apply to the system and its use.

Caution

Avoid exposing the system to flammable liquids or gases, corrosive substances, strong electrical or magnetic fields, and equipment that emits high-frequency waves.

Failure to prepare the patient's skin, apply coupling oil, and remove all bubbles and air pockets as instructed will prevent the membrane from acoustically coupling with the patient's skin, preventing visualization in the live ultrasound view.

Be aware that changes to setup can introduce air pockets and bubbles under the membrane or lift it away from the patient's skin.

Do not deliver energy or begin automated treatment if the membrane is not acoustically coupled to the patient's skin, as the following can occur:

- Surface cavitation resulting in patient skin injury
- Incomplete treatment

Failure to secure the membrane with the membrane cradle may allow the membrane to bulge or sag, which could:

- Lift the membrane off the patient's skin
- Lower the ultrasound medium level and allow air under the treatment head

Bubbles and air pockets between the membrane and patient's skin can prevent visualization and lead to surface cavitation during energy delivery, resulting in patient injury or incomplete treatment.

Do not deliver energy when air pockets or bubbles are trapped under the treatment head, as system damage can occur. Submerge the treatment head and remove all air pockets and bubbles as instructed in this user guide.

Be aware that changes to setup can introduce air pockets and bubbles under the treatment head. For example:

- Ultrasound medium level lowers (inadequate submersion)
- Treatment head is raised too high (inadequate submersion)
- Additional ultrasound medium is poured into the reservoir too quickly or too close to the treatment head

Caution
Before generating a bubble cloud for the System Check, use the live ultrasound view to ensure that the crosshairs are not positioned near the bottom of the system check container. Generating a bubble cloud on its surface could damage the container.
During automated treatment, observe the treatment head's submersion in the ultrasound medium. If the ultrasound medium level falls below the point it was at when setup was verified, immediately stop energy delivery. Delivering energy when the treatment head is not adequately submerged can result in system damage and incomplete treatment.
During automated treatment, do not apply excessive force on the treatment head when using the imaging transducer rotation lever or imaging transducer translation dial. Applying force on the treatment head can cause a fault that can abort automated treatment and require a repeat of the workflow.
Do not turn off the main power switch or unplug the treatment cart until the sequenced shutdown has completed.
Do not use the coupling kit beyond its use-by date. An expired use-by date may indicate that the coupling kit accessories have physically degraded and are not safe to use. • Membrane may form holes or rupture when filled with ultrasound medium • Membrane cradle may fail to secure the membrane during the procedure • Coupling oil may be rancid and cause skin irritation
All coupling kit accessories are single-use only. Do not reuse, as cross-contamination may occur.
Coupling oil (castor oil) may cause skin irritation, and patients with an allergy to castor oil may develop hives or rash.
Never attempt to move or shift the patient using the membrane cradle as it could result in patient injury and damage to the membrane cradle.
The use of cleaning agents or use of cleaning products other than those specified may damage equipment and void the warranty.
To clean the touchscreen, use a soft, non-abrasive cloth with a small amount of water. Do not use paper towels as they may cause light scratches.
Use a soft cloth to clean the treatment head. Do not use a brush.
Never use sterilization methods (autoclave, ultraviolet, gamma radiation, gas, steam, or heat sterilization) on the treatment head. Sterilization methods may severely damage treatment head components.
Selecting the wrong room setup button will result in inverted images and prevent successful completion of the fuse images task.

Caution
Do not drop or roughly handle the treatment head as it may damage the therapy transducer or imaging transducer components. Take care when handling the treatment head, especially during setup and transport. Before removing or attaching the treatment head, ensure the imaging transducer is in the home position (fully retracted) to protect it against physical damage. Keep the imaging transducer in the home position during storage.
Do not allow connectors or electrical contacts to come into contact with cleaning solutions.
Do not apply, spray, or spill liquids on the control panel or treatment cable connection points.
Do not use chemicals (cleaning agents) to clean the touchscreen, as they may cause damage.
HistoSonics cannot guarantee the performance of the system if stored or used outside of the specified environmental conditions.
Delivering energy through ultrasound medium that is insufficiently degassed can: • Prevent the bubble cloud from generating and/or prevent a sustained bubble cloud • Cause damage to the treatment head
Failure to prepare a sufficient volume of ultrasound medium will delay the procedure. A histotripsy procedure typically requires 13–15 liters of ultrasound medium.
To prevent damage during transportation, ensure that the: • Treatment head is removed and stored in the provided case • Treatment arm is in the storage position • Monitor arm secures the monitor within the treatment cart handrail
When transporting the treatment cart, use care and move slowly to avoid damage. The treatment cart wheels are designed for smooth surfaces; rough surfaces can damage the wheels. Because the treatment cart is heavy, it is recommended that two people transport it over inclines to prevent injury or damage.
Only use the handrail to move the treatment cart. Do not attempt to move the treatment cart using any other component, such as the treatment arm or monitor.
Ensure that the area around the treatment arm is clear before moving the treatment arm. Do not touch the treatment arm when in use. Touching and/or pushing on the treatment arm when it is moving could result in a pinch injury and cause a fault, which could delay the procedure.
Do not attempt to remove or disassemble treatment head components.
Never submerge the treatment head beyond the bottom of the notch on the imaging transducer rotation lever. Submersion beyond this point could allow ingress that could damage the treatment head.

Caution
Failure to perform the survey can lead to excessive force on the patient's abdomen and an aborted procedure if the system detects excessive resistance during treatment.
Leaks from holes in the membrane or from an improper seal between the frame and the membrane may introduce air into the ultrasound medium. If a leak is detected, immediately stop energy delivery and address the leak. Never assemble the frame without the membrane as doing so can damage the frame gasket.
The weight of the ultrasound medium can cause the end of the frame to sag slightly, placing pressure on the patient which could lead to a medical device related pressure injury if the frame rests against the patient for an extended period. Before transferring ultrasound medium into the reservoir, verify that there is at least 6 cm (2.5 inches) between the frame and the patient to allow for sagging. For patients with compromised skin integrity, consider cushioning or protecting the skin with dressings in high-risk areas.
Do not overfill the reservoir as it adds additional weight on the patient and may cause the ultrasound medium to overflow when the treatment head is introduced.
Allow for slack when attaching the membrane cradle to the frame; do not stretch or pull the membrane cradle taut as it will place unnecessary pressure on the patient's skin which could lead to a medical device related pressure injury if pressed against the patient for an extended period. It is normal for the patient to have some temporary red marks on their skin as a result of lying on the membrane cradle during the procedure.
Federal law (USA) restricts this device to sale by or on the order of a physician.
Performance of procedures, adjustments, or use of controls other than as specified in this user guide may result in hazardous exposure to ultrasonic energy.
Preventive maintenance and system service can be performed only by HistoSonics service or an authorized service provider.
Do not attempt to use the system with components other than those provided or specified by HistoSonics.
Connect the treatment cart power cord directly to a power outlet (mains connection). Do not use extension cords or power strips.
To prevent the risk of electric shock, do not touch the patient while simultaneously touching a USB port or video output port.
Follow local governing ordinances and recycling plans regarding disposal or recycling of device components.

Caution
With the exception of temporarily removing the splash guard to allow attaching/detaching the treatment cable, do not remove panels or covers from the treatment cart.
Before moving the treatment arm, verify that the treatment cable and imaging transducer cable are routed and have sufficient slack to allow the full range of motion required for the procedure. A snagged or tightly pulled cable can cause a fault that could delay the procedure.
Accessory equipment connected to the analog and digital interfaces must be certified according to the respective IEC standards (IEC 60950 for data processing equipment and IEC 60601-1 for medical equipment). Furthermore, all configurations shall comply with the system standard IEC 60601-1. Any person who connects additional equipment to the signal input part or signal output part configures a medical system and is therefore responsible for ensuring that the system complies with the requirements of the system standard IEC 60601-1. For more information, contact HistoSonics or an authorized service provider.
Use the patient data protection precautions and procedures required by your institution's protected health information data management policies to protect created and stored patient data.
Do not exceed the voltage necessary to verify bubble cloud formation during the system check. Raising the voltage beyond what is required may cause the system to emit audible acoustic energy that exceeds 80 dBA, which could cause user discomfort or hearing damage.
Connecting medical devices to a local area network (LAN) via Ethernet or Wi-Fi, or connecting removable storage (e.g., USB drives) to these devices, can introduce unidentified risks to patients, operators, or third parties in the event of a cybersecurity breach.
To maintain cybersecurity measures, do not modify hardware components or install unauthorized software.
Failure to calibrate resistance detection as instructed may prevent the procedure from proceeding due to resistance limit detection.
Resistance detection must be recalibrated if changes to the setup are made after calibrating resistance detection. Failing to recalibrate may prolong or prevent the completion of the procedure. Setup changes include: • Adjusting bed height • Adding or removing ultrasound medium • Repositioning the frame
When calibrating resistance detection, verify that nothing is pushing or pulling on the treatment head.
Do not submerge the treatment head when calibrating resistance detection; the treatment head should just touch the surface of the ultrasound medium.

Caution
Take extra precautions when moving the treatment head when its imaging transducer is extended to prevent the imaging transducer from colliding with the frame or patient, as it could cause a fault that could delay the procedure.
Take care to prevent the inspection mirror from introducing bubbles or air pockets under the treatment head.
The ultrasound system provided with the system has been configured for use with the treatment cart. Do not service or reconfigure the ultrasound system settings. If service is needed, contact HistoSonics or an authorized service provider. Reconfiguring does not include making adjustments to optimize visualization. For example, adjusting gain, depth, width, etc.
The system is only compatible with the B-mode ultrasound setting on the ultrasound system. Selecting other ultrasound modes (for example, Doppler, C-mode) during use may suspend progress and result in the loss of live ultrasound displayed on the system.
During the fuse images task, the sweep (recording) must capture the region of interest. Using a different region to fuse images will result in inaccurate imaging.
Failure to use the electromagnetic interference (EMI) shield may result in EMI, which could cause malfunction in this system or surrounding equipment, potentially delaying the procedure.

Therapeutic Ultrasound Safety Information

HistoSonics has implemented histotripsy to enable the mechanical destruction of tissue within a defined treatment volume, while mitigating the risk of thermal or mechanical (cavitation) injury to tissue along the acoustic pathway. This section documents the design mitigations in place as well as the residual risks of thermal or mechanical damage to non-targeted tissue.

Caution

Performance of procedures, adjustments, or use of controls other than as specified in this user guide may result in hazardous exposure to ultrasonic energy.

Unintended Thermal Injury

Although histotripsy's mechanism of action is inherently mechanical, the delivery of therapeutic ultrasound includes the potential for local tissue heating. Depending on the patient's anatomy, a percentage of therapeutic ultrasound may be obstructed (reflected and/or absorbed) when bone, cartilage, lung, or digestive gas are along the acoustic pathway. These obstructions can result in thermal injury to non-targeted tissues.

The system is designed to mitigate the risk of thermal injury by the design of the therapy transducers and energy delivery parameters utilized in combination with a treatment protocol that imposes, when necessary, cooling time and average voltage limits based on treatment head, target depth, PTV size, and voltage settings. It is important to strictly follow instructions provided when marking the muscle layer and establishing the voltage settings during the procedure workflow, as these parameters serve as inputs used by the system to determine the treatment protocol.

The system is designed to account for the presence of minor to moderate levels of anatomical obstruction without impacting safety and effectiveness. However, more excessive obstruction combined with a larger PTV does present an increased risk of thermal injury. Use imaging and the acoustic field indicator overlay to assess and minimize anatomical obstructions along the acoustic pathway prior to finalizing the treatment plan. Consider that some target locations will not be treatable due to excessive anatomical obstruction.

Warning

Delivering therapeutic ultrasound when anatomical or other obstructions (bone, cartilage, lung, digestive gas, etc.) are along the acoustic pathway can result in thermal injury to non-targeted tissues. Use imaging and the acoustic field indicator overlay to assess and minimize obstruction prior to finalizing the treatment plan.

Warning

When any of the following occur, cumulative thermal exposure will increase, elevating the risk of thermal injury to the skin, body wall, or other tissues:

- User-initiated repetition of tasks where energy is delivered, such as re-performing in vivo calibration or establishing voltage settings for any of the seven plan points
- Prolonged energy delivery when establishing voltage settings
- Exceeding the voltage necessary to sustain the bubble cloud
- Anatomical or other structures (e.g., ribs, lung, bowel) located anywhere within the acoustic pathway—including post-focal—with higher absorption and/or reflection
- Anatomy or obstructions (e.g., bowel gas) within the pre-focal acoustic pathway that require higher voltage settings to sustain the bubble cloud
- Multiple treatments within the same procedure when acoustic pathways may intersect and/or pass through previously treated zones

Note the following system behaviors, which further inform energy delivery considerations related to cumulative thermal exposure:

- The system applies a thermally safe protocol to perform automated treatment but does not account for the energy delivered during treatment planning
- While the mechanism of action is non-thermal, localized temperature rise within the acoustic pathway will occur during energy delivery/deposition—particularly in transition zones such as the skin, body wall, or in tissues that absorb/obstruct ultrasound energy, such as bone
- The system enforces a 30-second timeout when establishing a voltage setting but does not limit cumulative energy delivery

While some repetition or extended energy delivery may be required to verify a sustained bubble cloud, procedural goals should be met using the minimum voltage and duration necessary, while limiting or preventing unnecessary repetition. When clinically appropriate, users may consider pausing between energy delivery tasks to allow tissue cooling before proceeding.

Unintended Mechanical (Cavitation) Injury

Obstruction and Aberration

Depending on the patient's anatomy, a percentage of therapeutic ultrasound may be obstructed (reflected and/or absorbed) when bone, cartilage, lung, or digestive gas are along the acoustic pathway. The presence of these anatomical obstructions along with acoustic aberration – caused by sound speed variation along the acoustic pathway – may cause a shift in the location of the focal zone/bubble cloud.

The system is designed to account for the expected in vivo shift of focal zone/bubble cloud location with the calibration of the crosshairs at the beginning of the Establish Voltage Settings task of the workflow. The risk of off-target cavitation injury is mitigated by the design of the therapy transducers and energy delivery parameters utilized in combination with operating near the minimum voltage required to generate a sustained bubble cloud throughout treatment.

If it is suspected that anatomical obstructions and/or acoustic aberration is excessive consider re-planning the procedure after repositioning the treatment head or manipulating the patient anatomy to improve the acoustic pathway to the targeted tumor. Note that some locations will not be treatable due to excessive anatomical obstruction and/or acoustic aberration.

Warning

Anatomical or other obstructions (bone, cartilage, lung, digestive gas, etc.) as well as acoustic aberration along the acoustic pathway can result in mechanical (cavitation) injury to non-targeted tissues.

- Use imaging and the acoustic field indicator overlay to assess and minimize obstructions prior to finalizing the treatment plan
- Monitor the location of the bubble cloud throughout the treatment using real-time ultrasound imaging and suspend therapy if the bubble cloud is not within the PTV

Critical Structures and Bleeding Risk

Cavitation from histotripsy tends to preserve collagen-rich structures such as larger luminal vessels, ducts, and organ capsules due to their higher mechanical strength compared to surrounding parenchymal liver tissue.[1] However, the mechanical strength of collagen-rich structures varies with structure size, patient comorbidities and/or prior therapies, which may reduce mechanical strength and increase susceptibility to mechanical injury. Mechanical injury to collagen-rich structures within the PTV may occur even when the minimum voltage required to generate a sustained bubble cloud is used. The potential for injury may increase as voltage is raised beyond this threshold and/or when treatments overlap, either within the same treatment session or subsequent sessions. Bleeding may occur due to mechanical injury to vascular structures. Mechanical injury to critical structures is a risk of histotripsy and should be considered when evaluating patient anatomy and planning treatments.

Warning

Mechanical injury to critical structures (e.g., vascular structures, liver capsule, bile ducts) may occur when these structures are within the PTV. The likelihood of bleeding and/or mechanical injury may increase with additional and/or subsequent treatments within a treatment session or subsequent sessions. In cases where the tumor violates the liver capsule and/or the liver capsule is compromised from prior intervention or therapy, bleeding events may include intraperitoneal hemorrhage, which can be severe and potentially lead to death.

[1] Vlaisavljevich et al. Phys. Med. Biol. 2014;59(2): 253–270

Unintended Lung Injury

Warning

Delivering therapeutic ultrasound when lung tissue is located along the acoustic pathway can result in localized pulmonary tissue edema or hemorrhage. Use imaging and the acoustic field indicator overlay to assess if lung is along the acoustic pathway prior to finalizing the treatment plan. Consider using alternate angles to avoid lung tissue.

Safety Features

Resistance Detection

Prevents the treatment arm and treatment head from applying excessive force on the patient. Utilizing real-time data from a sensor in the treatment arm, the system initiates a stop if the resistance limit is reached.

When the system initiates the stop, the system:

- Displays an error message
- Stops treatment (energy delivery)
- Stops movement of the treatment arm to prevent additional force from being applied
- Enables the use of the freedrive feature to allow the physician to move the treatment arm/ treatment head away from the patient
- Returns the user to the plan phase

To continue the procedure, the physician must correct setup to allow full treatment arm/treatment head range of motion during automated treatment without applying excess pressure.

Important

During the Plan phase, the physician calibrates resistance detection.

Energy Delivery Safeguards

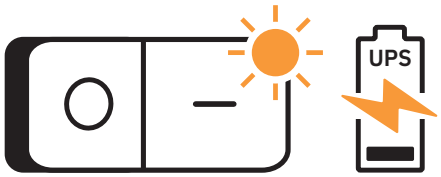
The system is designed with these safeguards to mitigate the risk of accidental energy delivery:

- Software only permits energy delivery when it is required to perform a task that is actively displayed in the workflow
- To enable energy delivery, the physician must select the Enable Voltage toggle displayed in the workflow, then press the voltage knob
- The default voltage setting is always 0%, requiring the physician to rotate the voltage knob to establish a voltage setting
- When energy is being delivered, pressing the voltage knob immediately de-energizes the therapy transducer

Uninterruptible Power Supply (UPS)

The system is automatically powered by a UPS in the event of a power loss. The UPS provides approximately 60 seconds of backup power. This short duration is designed to give the user enough time to shut down the system during extended power outages (protects equipment), or to plug the system back in, should it be accidentally unplugged.

Whenever the treatment cart is plugged into a power outlet, it is recommended that the main power switch remain in the "on" position, allowing the UPS to charge its battery when necessary. A diagram adjacent to the main power switch indicates that battery charging can only occur when the switch is in the "on" position.



Important
When the UPS powers the system, energy delivery is immediately suspended and energy cannot be initiated.
The UPS is only to be used as a safety measure to provide temporary power to the system in the event of an unexpected power outage. If the system is powered on without being plugged into a power outlet, an error message will display during initialization.
Adhere to the preventive maintenance schedule to maintain the UPS battery health, ensuring that the system will have sufficient power in the event of a power outage.

Emergency Stop Button

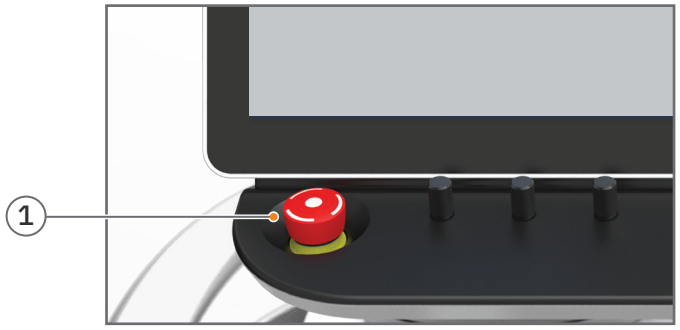
Pressing during automated treatment will de-energize and prevent the use of the therapy transducer and immediately stop and prevent treatment arm motion.

To deactivate the emergency stop condition, twist the emergency stop clockwise until it releases.

Important

When the emergency stop condition is active, the treatment arm cannot be moved using freedrive or the space mouse, and live ultrasound does not display.

Use the emergency stop only in an emergency. Under normal conditions, use the voltage knob to pause therapy.



① Emergency stop button

Patient Emergency

In the event of a patient emergency during use of the system, the following steps provide guidance and example methods on how to rapidly access the patient.

Warning

In the event of a patient emergency where a defibrillator is required, remove any ultrasound gel, coupling oil, or ultrasound medium from the patient's skin if it could prevent the safe and effective use of the defibrillator. Refer to the defibrillator instructions for use.

Important

With help from an assistant, this patient emergency procedure can be performed more efficiently and with fewer difficulties.

1. If the space mouse or freedrive is available, use it to move the treatment head away from the patient. If the space mouse or freedrive is unavailable (for example, during automated treatment), the following methods may be used to enable movement of the treatment head:

   Abort Automated Treatment

   a. Use the voltage knob to pause treatment.
   b. Select **Abort Automated Treatment**. The Review Treatment screen displays.
   c. Use the space mouse to move the treatment head away from the patient.

   E-Stop Method

   a. Activate the E-stop.
   b. Rotate the E-stop knob clockwise reset the E-stop. Freedrive will be available after several seconds.
   c. Use freedrive to move the treatment head away from the patient.
2. Disconnect the imaging transducer cable from the ultrasound system.
3. Move the system carts away from the bed as needed to treat the patient emergency.
4. Disconnect Ethernet cable(s) if they prevent system movement.
5. Position the emergency evacuation container (EEC) as close to the bed as possible—either on the floor or on a raised surface—based on container height and fastest access for disposal.

   Important

   Place the EEC on the side of the bed with the rail clamp to help prevent the reservoir frame from contacting the patient during the disposal step.

   The EEC should be adequately sized to accommodate the ultrasound medium present in the reservoir. The HistoSonics fluidics cart waste basin can function as an EEC.

6. Detach the membrane cradle from the frame.
7. Choose the disposal method that provides the fastest access to the patient and minimizes spilling or splashing during disposal. Two common methods are described; use clinical judgment based on the type and height of the EEC:

Pour Method

Important

This method is best when there is an EEC that is tall or elevated enough to allow direct tipping and disposal without significant risk of spillage on the patient.

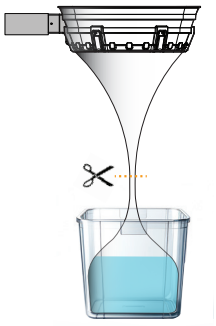
With help from an assistant, use the support arm to move the reservoir away from the patient and tip and pour out the reservoir contents directly into the EEC.

Sever Method

Important

This method is best when using a low or shallow EEC where the reservoir cannot be tipped directly into the EEC.

a. With help from an assistant, use the support arm to move the reservoir off the patient allowing access to the patient. Moving the reservoir off the side with the bed rail clamp helps prevent the frame from contacting the patient. Avoid sharp objects that could rupture the membrane.
b. Use the support arm to lower the membrane into the EEC. The weight of the ultrasound medium will cause the membrane to stretch down significantly.
c. Gather and hold the material above the ultrasound medium.
d. Use a scissors or other cutting tool to sever the membrane above the gathered area.



Emergency Treatment Arm Movement

In the unlikely event of an emergency where treatment arm power is either unavailable or unwanted, force can be used to move each treatment arm joint as necessary to move the treatment head away from the patient. Each joint brake has a friction clutch that enables movement when sufficient manual force is applied.

Important

If emergency treatment arm movement is performed, tag the treatment cart out-of-service and contact HistoSonics or an authorized service provider. If the treatment cart is powered on, the system will display an initialization error, and its use will be prevented.

Reporting of Incidents

Please report any serious incidents occurring during or as a result of using this device to HistoSonics at complaints@histosonics.com and your national authority.

Patient Privacy

Caution

Use the patient data protection precautions and procedures required by your institution's protected health information data management policies to protect created and stored patient data.

The privacy and security of certain protected health information is protected by state/province, federal, international, and foreign laws that regulate and restrict how such information may be used, disclosed, stored, and transmitted. Prohibitions exist regarding disclosure of, or access to, such information without prior written authorization from the affected individual.

The system is compliant with existing patient data protection regulations. However, it is the user's responsibility to understand local patient data protection regulations and properly safeguard against the unauthorized disclosure of protected health information.

If you are not able to comply with laws or restrictions that apply to the use and disclosure of protected health information, you should not enter or save such information.

The system does not require the entry of protected health information to function. Records can be stored and recalled using an arbitrarily assigned identifier (de-identified). If a user chooses to enter protected health information, all risks, responsibilities, and liabilities associated with those actions are assumed by the user.

Cybersecurity

This section provides information about cybersecurity features and how to help protect patient health information, how to help prevent unauthorized physical and electronic access, and what to do in the event of a cybersecurity breach.

Caution

To maintain cybersecurity measures, do not modify hardware components or install unauthorized software.

With the exception of temporarily removing the splash guard to allow attaching/detaching the treatment cable, do not remove panels or covers from the treatment cart.

Connecting medical devices to a local area network (LAN) via Ethernet or Wi-Fi, or connecting removable storage (e.g., USB drives) to these devices, can introduce unidentified risks to patients, operators, or third parties in the event of a cybersecurity breach.

Important

If a USB drive will be used to import a study and/or export a treatment report, it is recommended to use a new, dedicated USB drive and to secure it in a safe place when not in use.

Upon request, HistoSonics will assist a PACS administrator to configure the system so that it can retrieve reference images from a picture archiving communication system (PACS). This configuration requires a change to firewall settings to allow PACS traffic.

Additionally, upon request, HistoSonics will assist with enabling Wi-Fi on the Samsung R20 Ultrasound System, allowing it to push ultrasound images to PACS.

It is the responsibility of hospital information technology administrators to ensure that the LAN and PACS is secure against cybersecurity threats.

Windows operating system credentials are provided directly to the user. Upon request, HistoSonics will help an Active Directory administrator connect the system to Windows Active Directory.

If the system is added to a Microsoft Active Directory, the Active Directory administrator must limit access to authorized users.

Following the successful configuration of PACS or Active Directory, the customer's administrators will be responsible for resolving communication issues, as such issues typically result from subsequent changes to the local network settings.

Cybersecurity Features

The treatment cart software runs on the Microsoft Windows® IoT operating system with Windows® Firewall and Windows® Defender Antivirus enabled to protect against unauthorized access, viruses, and malicious software. Additional operating system settings have been configured to harden against unauthorized access.

PHI and user authentication data is encrypted.

Contact HistoSonics if more information is required about the safeguards that have been designed into the treatment cart or to verify that you have the latest operating system and software available for the treatment cart.

Protection from Unauthorized Electronic Access

Operating system and application credentials (user name and password) are required to access the treatment cart software. To help prevent unauthorized electronic access, HistoSonics personnel provides credentials directly to users.

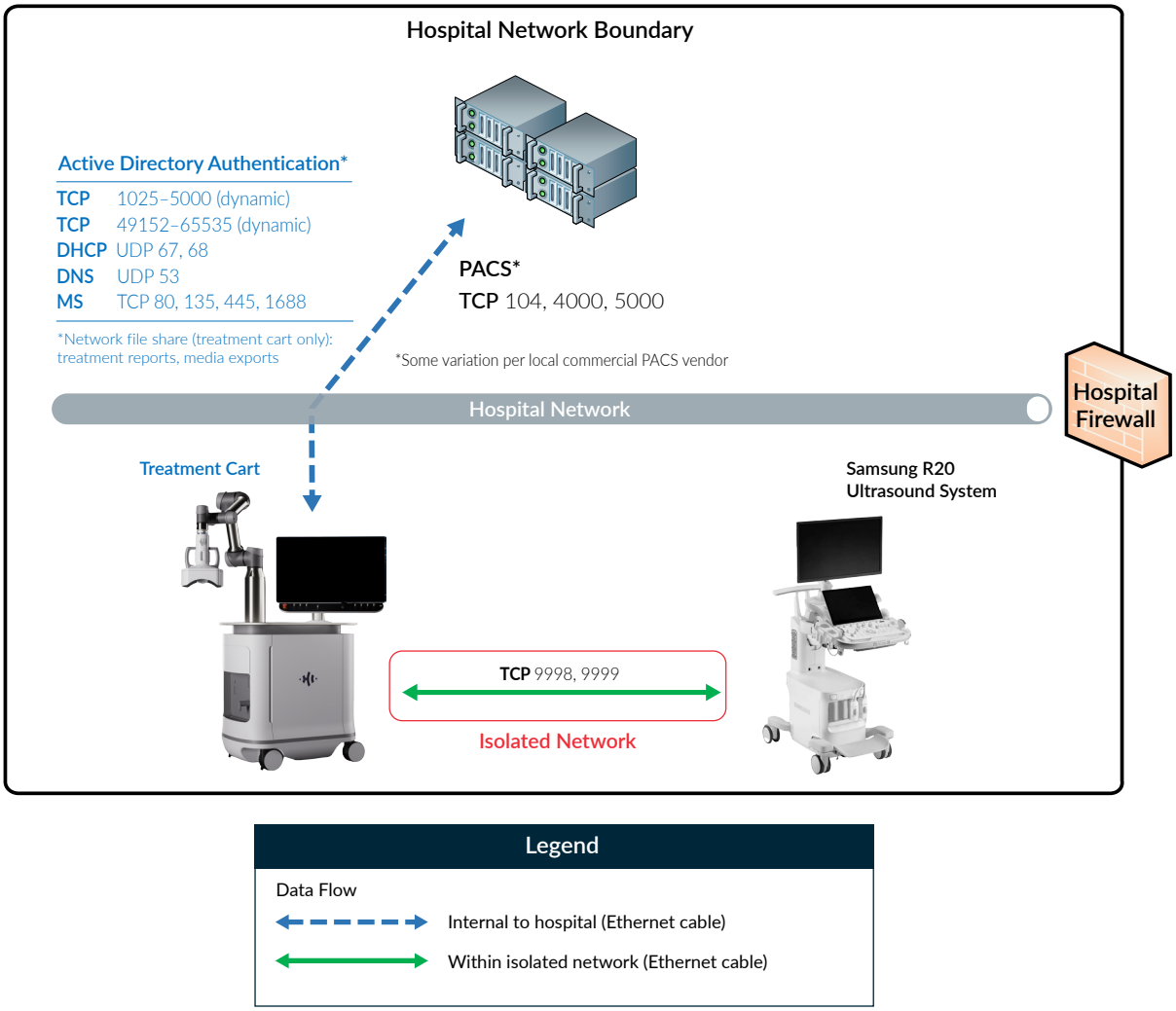
Users can make a request for HistoSonics to:

- Create a new operating system account
- Disable an existing operating system account

Users should:

- Create new application credentials
- Keep their credentials in a safe location

System Network Diagram



Protection from Unauthorized Physical Access

To help prevent unauthorized physical access:

- Shutdown the treatment cart when not in use
- Do not leave the treatment cart in locations that are accessible to the public

Responding to a Cybersecurity Breach

If you are aware of a cybersecurity breach, or if you suspect a cybersecurity breach may have occurred, perform the following steps:

1. Shut down the treatment cart.
2. Disconnect the power cord from the power outlet.
3. Disconnect Ethernet cables from the connection panel.
4. Provide specific details to your information technology administrator and to HistoSonics.

Medical Electrical Equipment—International Standard

Caution

Accessory equipment connected to the analog and digital interfaces must be certified according to the respective IEC standards (IEC 60950 for data processing equipment and IEC 60601-1 for medical equipment). Furthermore, all configurations shall comply with the system standard IEC 60601-1. Any person who connects additional equipment to the signal input part or signal output part configures a medical system and is therefore responsible for ensuring that the system complies with the requirements of the system standard IEC 60601-1. For more information, contact HistoSonics or an authorized service provider.

The system is classified and certified in accordance with IEC 60601-1 Medical Electrical Equipment for basic safety and essential performance by a credentialed third-party medical device testing facility as follows:

Type	Classification/Certification
Medical electric equipment standard	IEC 60601-1 Edition 3.2
Type of protection against electrical shock	Class I
Degree of protection against electrical shock	Type B
System degree of protection against ingress (excludes treatment head)	IP20

3 Pre-Planning Considerations

Use the following imaging requirements and recommendations to prepare for a histotripsy procedure.

Recommended Study Protocols

- Studies used for planning should not be older than 30 days
- Use of contrast is recommended
- MR imaging is recommended for optimal 3D model construction and when performing the fusion workflow on the Histotripsy System
- For efficiency, it is recommended to only import the series that provides the optimal visualization of the targeted tumor and vascular structures (e.g., portal venous phase, 60–75 second delay post contrast injection)

Format Requirements

Important

Do not include non-DICOM files in the import directory (for example, read-me files, software applications, hospital logos, etc.).

Format	Modality	Data Compression	Maximum Slice Thickness	Spacing/Gap
DICOM	MR, CT	No compression	2 mm	0 mm

Recommended MRI Protocol

T1	T2	Diffusion Weighted Imaging (DWI)	Post-Contrast Sequences T1 2D or 3D Gradient-echo Sequences (VIBE, LAVA)
Plane Axial	**Plane** Axial and coronal	**Plane** Axial	**Arterial Phase** 20–30 seconds
Sequence Examples In-phase and out-of-phase (DIXON), T1 fat-saturated	**Sequence Examples** T2 HASTE, T2 fat-saturated (TSE)	**Sequence** Fat-saturated single-shot diffusion-weighted EPI	**Portal Venous Phase** 60–70 seconds **Equilibrium Phase** 3–5 minutes

Recommended CT Scan Parameters

Scan Type	Image Resolution	Scan Delay
Contrast study	512 x 512	Portal venous (additional phases based on tumor type)

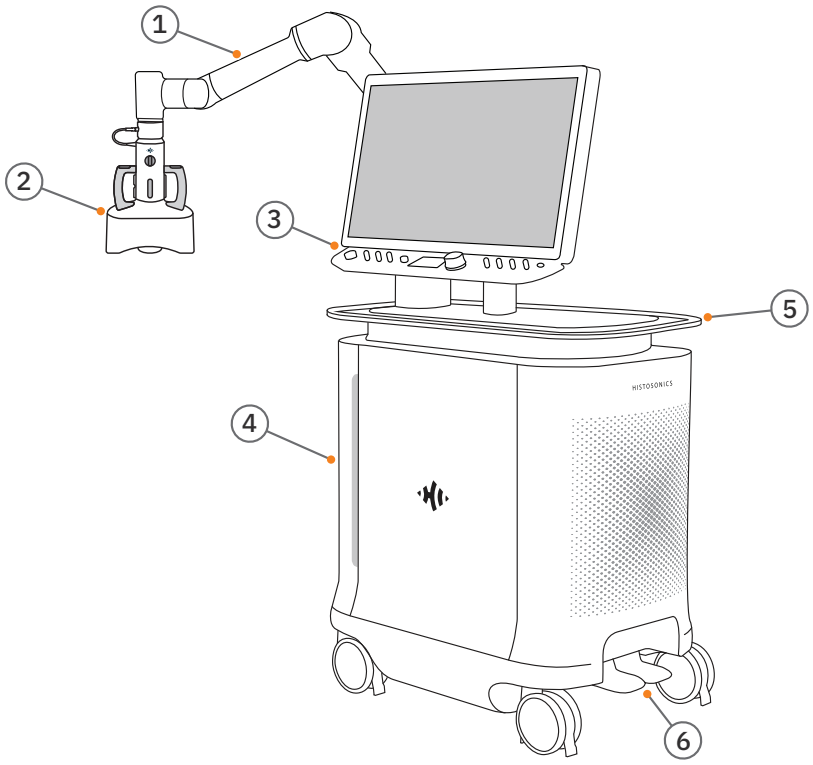
4 Equipment & Accessories

Important

For a complete list of the equipment, accessories, and materials required to perform a procedure, refer to *Gather Equipment, Accessories, and Supplies on page 6-4*.

Treatment Cart

The treatment cart is a mobile, therapeutic ultrasound medical device. Its main components include a high voltage power supply, integrated amplifier circuitry, waveform generator boards, computer, and treatment arm with micropositioning system.



1. Treatment arm
2. Treatment head
3. User interface (touchscreen monitor and control panel)
4. Connection panel
5. Handrail
6. Wheel controls

Touchscreen Monitor

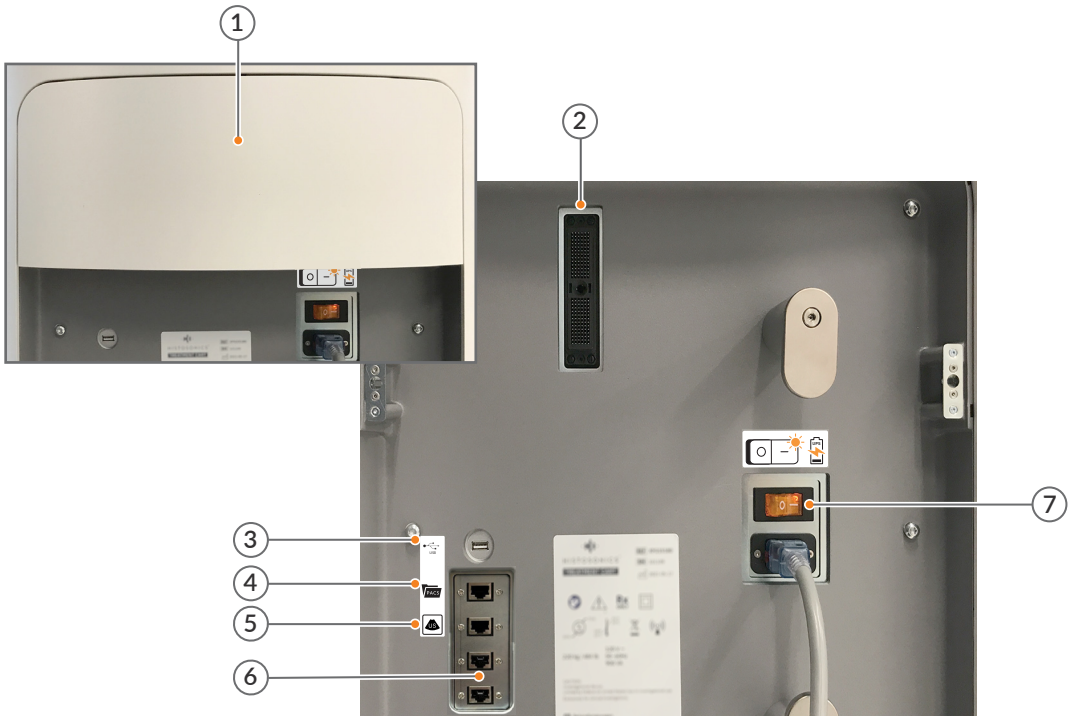
A 32-inch touchscreen display with a 16:9 aspect ratio and 4K resolution. Features anti-reflective glass that helps prevent scratching. Mounted on an adjustable arm.

Control Panel

Location of E-stop, power button, status bar, planning knobs, voltage knob, trackpad and space mouse. Details are provided in *Primary Controls on page 5-5*.

Connection Panel

Located on the side of the treatment cart, has the following components.



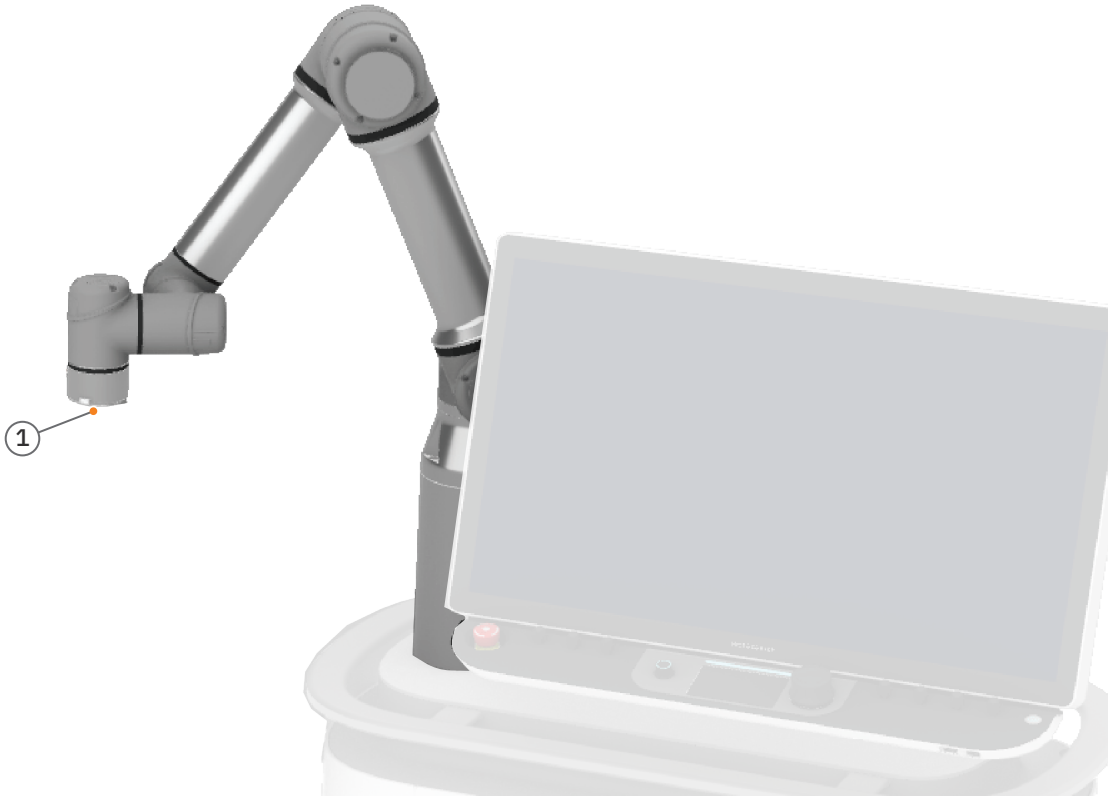
① **Splash guard**	Protects the treatment cable and treatment cable port from accidental splashes or spills. Temporarily remove the splash guard to gain access to the treatment cable port when attaching or detaching the treatment cable.
② **Treatment cable port**	Connection point for the treatment cable, which powers the therapy transducer.
③ **USB port** 	Supports the use of a USB drive to import a study and export a treatment report.
④ **PACS port** 	Used to connect to a local network (LAN) via Ethernet cable for importing studies from a picture archiving and communication system (PACS).
⑤ **Ultrasound port** 	Used to connect to the ultrasound system via Ethernet cable.
⑥ **Unused ports**	Unused Ethernet ports are capped to prevent attempted use and are intended for features that may be introduced in a future version.
⑦ **Main power switch**	I = Power-on 0 = Power-off

Treatment Arm

Provides mechanical support to the treatment head. The treatment arm has multiple joints and is capable of:

- Gross or fine positioning
- Simultaneous movement in multiple axes
- Rotating the treatment head around all axes (Rx, Ry, and Rz)

During certain tasks, such as localization, the physician manually positions the treatment head. During other tasks or phases, such as automated treatment, the system automatically moves the treatment head.



1 Treatment arm/treatment head interface

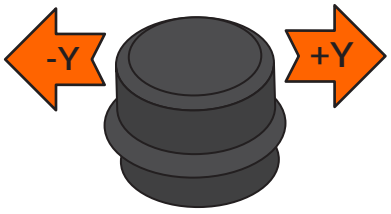
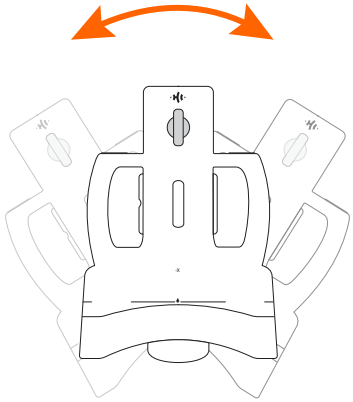
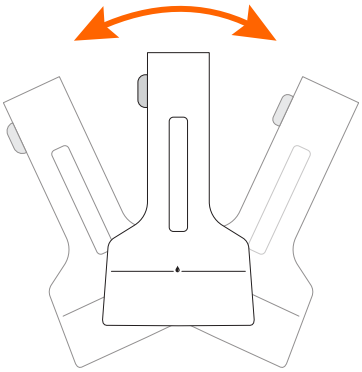
Space Mouse

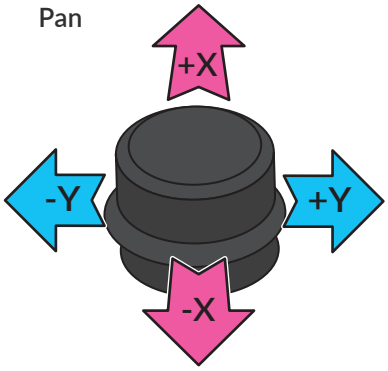
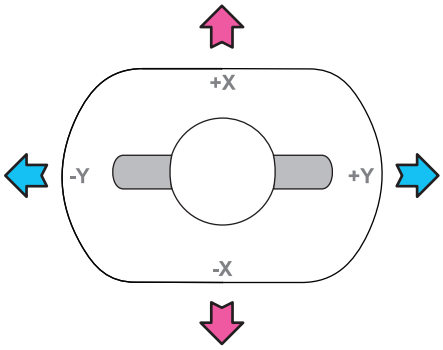
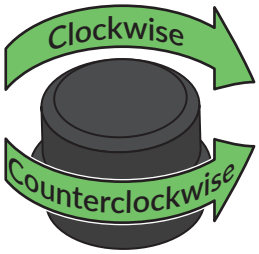
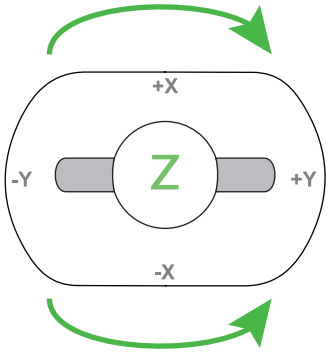
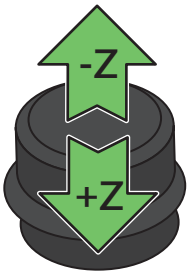
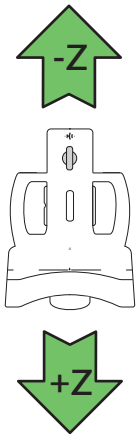
Provides manual control (movement) of the treatment arm. The space mouse:

- Moves the treatment head along the operational axes (X, Y, Z)
- Provides full, 360-degree rotational control of the treatment head around all three axes (Rx, Ry, and Rz)
- Allows the user to control the speed of treatment arm movement. The more force applied to the space mouse, the faster the movement

Important

When the space mouse tile is grayed out, including during automated treatment, or when the system or user suspends energy delivery, the space mouse cannot be used to control the treatment arm.

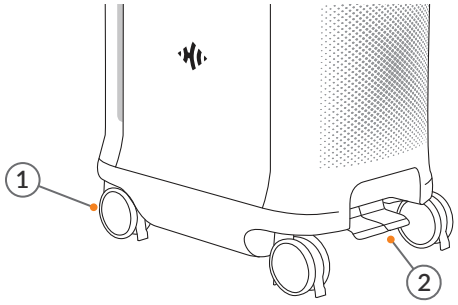
Space Mouse Action	Corresponding Treatment Head Movement
Tilt 	
Tilt 	

Space Mouse Action	Corresponding Treatment Head Movement
Pan 	Top-down view 
Rotation 	Top-down view 
Pull up  Depress	

Wheel Controls

Use the pedals to:

- Lock all four wheels in their current orientation (lock mode)
- Prevent the drive wheels from swiveling during transportation (drive mode)
- Enable all wheels to roll and swivel (full mobility mode)



① Drive wheel ② Pedals

Desired Operation	Left Pedal Position	Right Pedal Position	Mode Icon
Full mobility mode • All wheels roll • All wheels swivel	Neutral	Neutral	Full mobility mode is engaged when the mobility icons align (both pedals are in neutral position).
Drive mode • All wheels roll • Drive wheels prevented from swiveling	Up	Down	Drive mode is engaged when the pedal with the arrow icon is down.
Lock mode • All wheels prevented from rolling and swiveling	Down	Up	Wheel locks are engaged when the pedal with the lock icon is down.

Treatment Heads

Two treatment heads are available. Select the treatment head based on depth of treatment. The labeling for, and marking on, each treatment head indicate their maximum treatment depth.

Treatment Head	Recommended Treatment Range (Approximate)	Maximum Treatment Depth
REF EDNTH12	2 cm*–12 cm	12 cm†
REF EDNTH14	8 cm–14 cm	14 cm†

*Treatment at 2 cm is dependent on the patient's body wall thickness.
†Only achievable when the treatment head can be fit to the patient's abdomen.

Important

Maximum treatment depth is the deepest possible treatment depth as measured from the skin to the furthest extent of the PTV.



1. I/O cable with push-pull connector
2. Imaging transducer translation dial
3. Freedrive buttons
4. Imaging transducer rotation lever
5. Lock release button

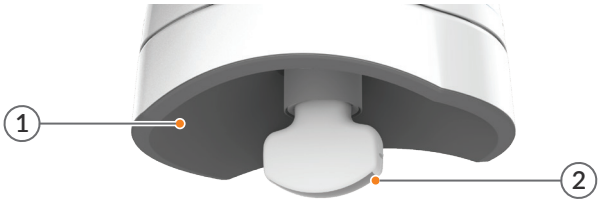
Therapy Transducer

Piezoelectric elements in the therapy transducer convert high-voltage signals to high-pressure ultrasonic waves to generate a bubble cloud.

Imaging Transducer

A curvilinear ultrasound transducer that connects directly to the ultrasound system. The imaging transducer is integrated in the treatment head to provide the physician with real-time, continuous visualization of the region of interest and bubble cloud.

The imaging transducer can extend (translate) to improve visualization of the region of interest, and rotate to plan and monitor treatment in multiple planes. The user interface displays the orientation and position of the imaging transducer using encoders in the treatment head.



1 Therapy transducer 2 Imaging transducer

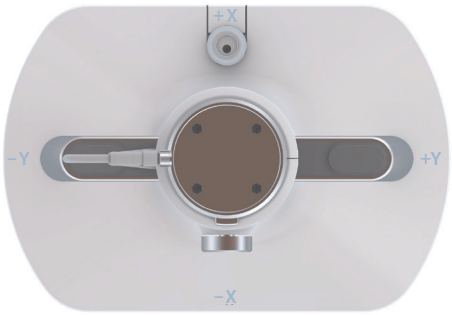
I/O Cable

Communicates the freedrive button signal and allows the system to detect the state of the imaging transducer (orientation and translation).

The I/O cable features a push-pull connector. To connect the I/O cable to the treatment head, simply align the connector's keyway with the corresponding slot on the receptacle, and then gently push the connector in until it clicks into place. To disconnect, pull back the outer sleeve of the connector, and then gently pull the connector out from the receptacle.

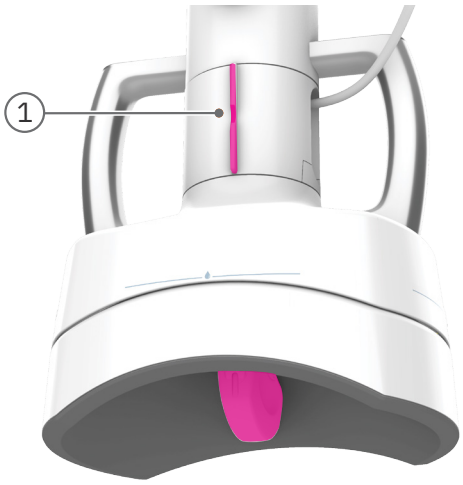
Axis Markings

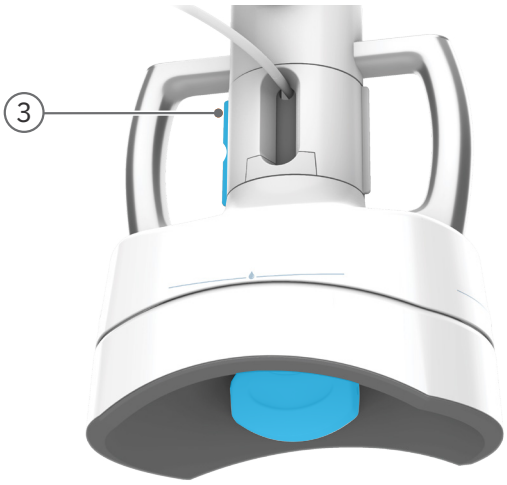
Axis marks (-X, +X, -Y, +Y) are located on top of the treatment head. Refer to the axis marks when rotating or verifying the position of the imaging transducer rotation lever.

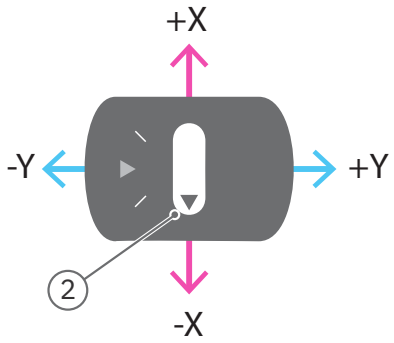


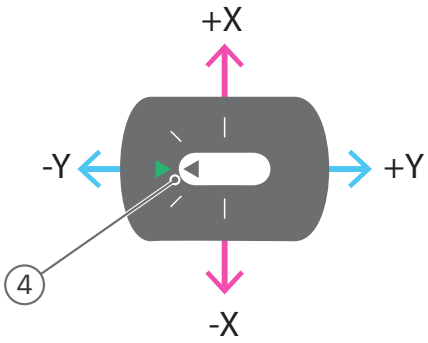
Imaging Transducer Rotation Lever

To rotate the imaging transducer, rotate the treatment head column. The two protruding tabs on the treatment head column provide grip. The notched tab, referred to as the imaging transducer rotation lever, aligns with the orientation of the imaging transducer. The user interface also shows the orientation of the imaging transducer.









① Imaging transducer rotation lever: Oriented to -X

② User interface: Imaging transducer oriented to -X

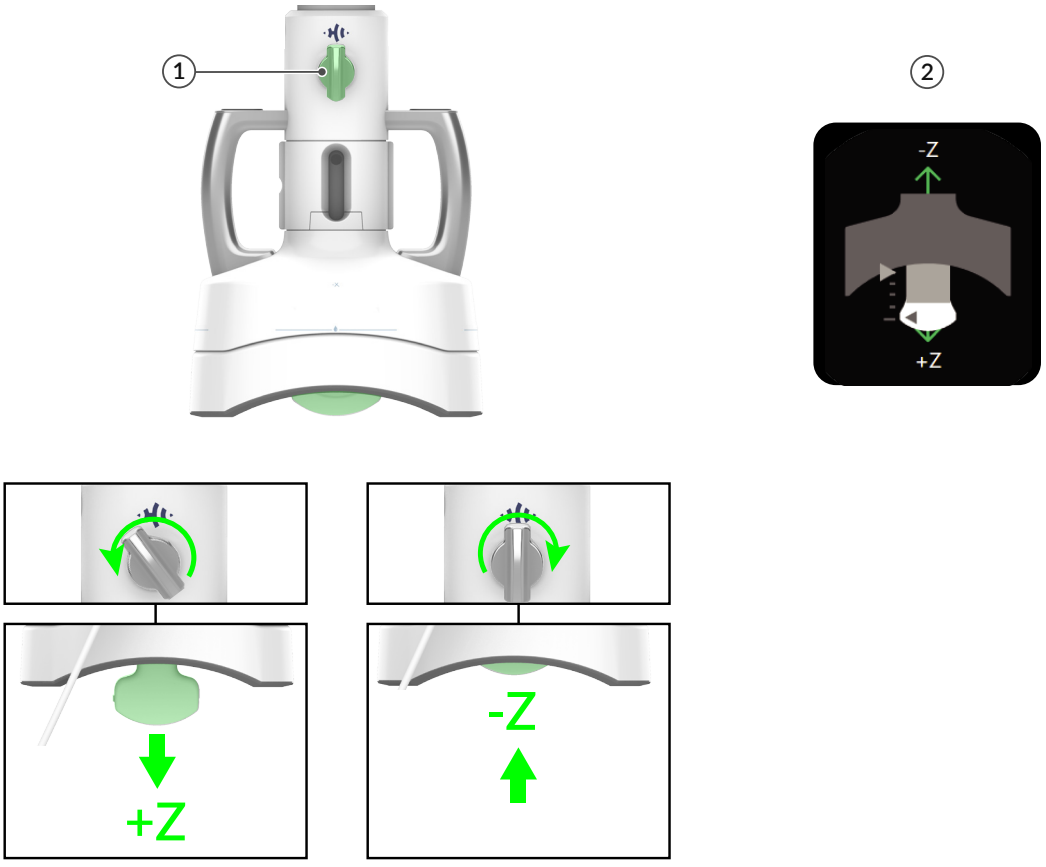
③ Imaging transducer rotation lever: Oriented to -Y

④ User interface: Imaging transducer oriented to -Y

Imaging Transducer Translation Dial

Rotate to extend or retract the imaging transducer along the Z-axis. The user interface displays the current position of the imaging transducer.

- Rotate the dial counterclockwise to extend the imaging transducer (towards +Z).
- Rotate the dial clockwise to retract the imaging transducer (towards -Z).



① Imaging transducer translation dial ② User interface: Extended imaging transducer

Maximum Submersion

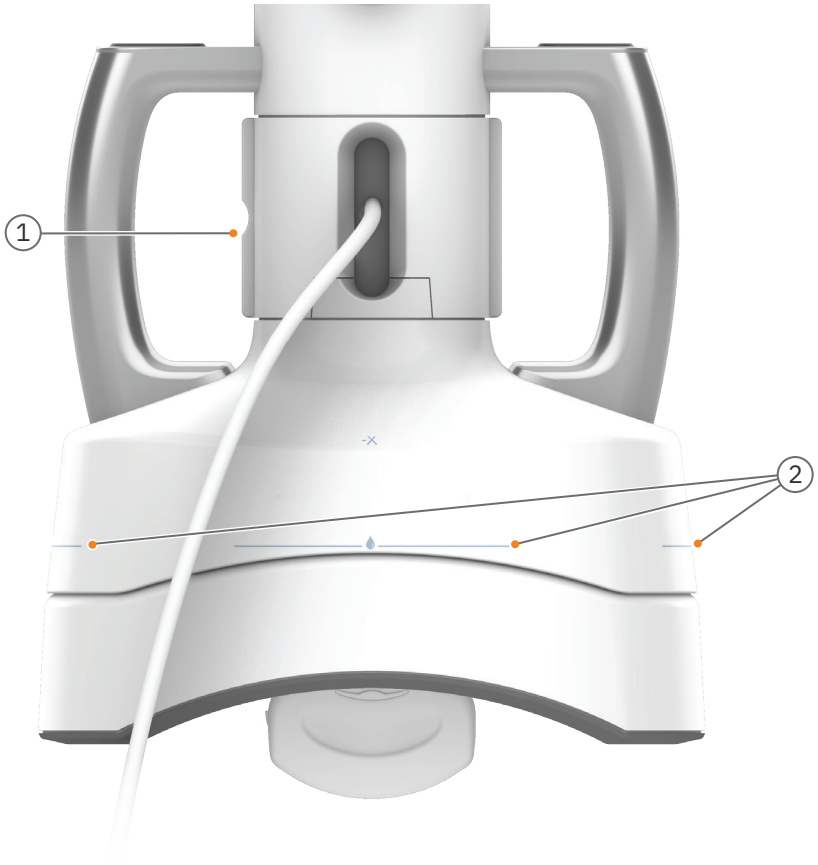
The bottom of the notch on the imaging transducer rotation lever is the highest point on the treatment head that can be safely submerged without ingress causing damage to internal treatment head components. While it is important to be aware of this limitation, this point is located far above where the treatment head needs to submerge during a system check or during a procedure.

Submersion Reference Lines

Indicates the approximate depth that the treatment head should be submerged to safely deliver energy. The lines are located on all four sides of the treatment head.

Important

It is acceptable to deliver energy when one or more submersion reference lines are not submerged, provided that there are no air pockets or bubbles trapped under the treatment head.



1. Bottom of the notch is maximum submersion point
2. Submersion reference lines

Freedrive Buttons

Activating enables load-assisted gross positioning of the treatment head.

Important

The treatment arm is capable of simultaneous movement in multiple axes.

Freedrive of the treatment arm is not available when:

- PTV is locked
- Emergency stop condition is active (E-stop button is engaged)

Use the following steps to freedrive the treatment arm:

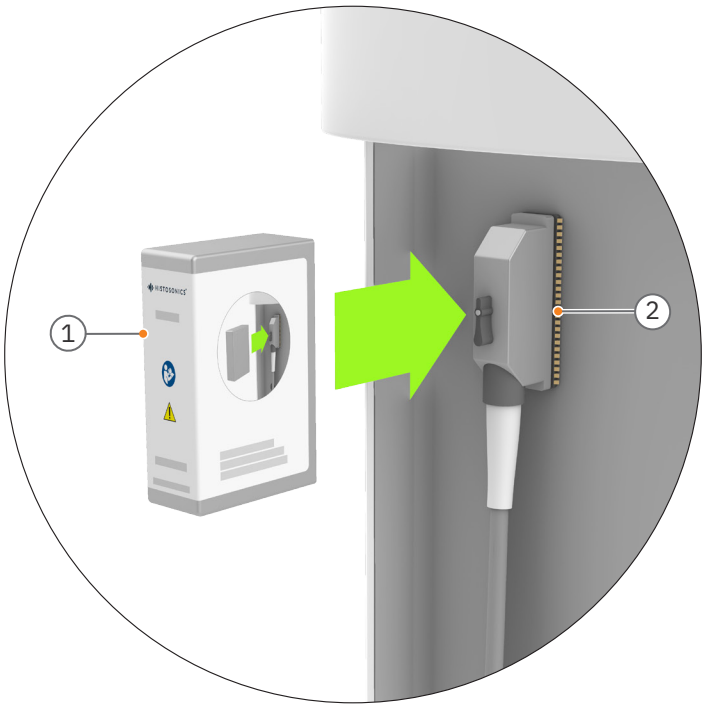
1. Grab both treatment head handles, then use a thumb to depress one of the freedrive buttons.
2. Physically move the treatment head into the desired position. The treatment arm provides load assistance.
3. Release the freedrive buttons to fix position.



Electromagnetic Interference (EMI) Shield

Each treatment head is packaged with an EMI shield used to reduce electromagnetic interference, protecting the treatment cart from external interference and preventing it from emitting interference that could affect other equipment.

After connecting the treatment cable to the treatment cart, the EMI shield slides over the connection and secures around the port when pushed into place.



1 EMI Shield 2 Treatment cable connected to port

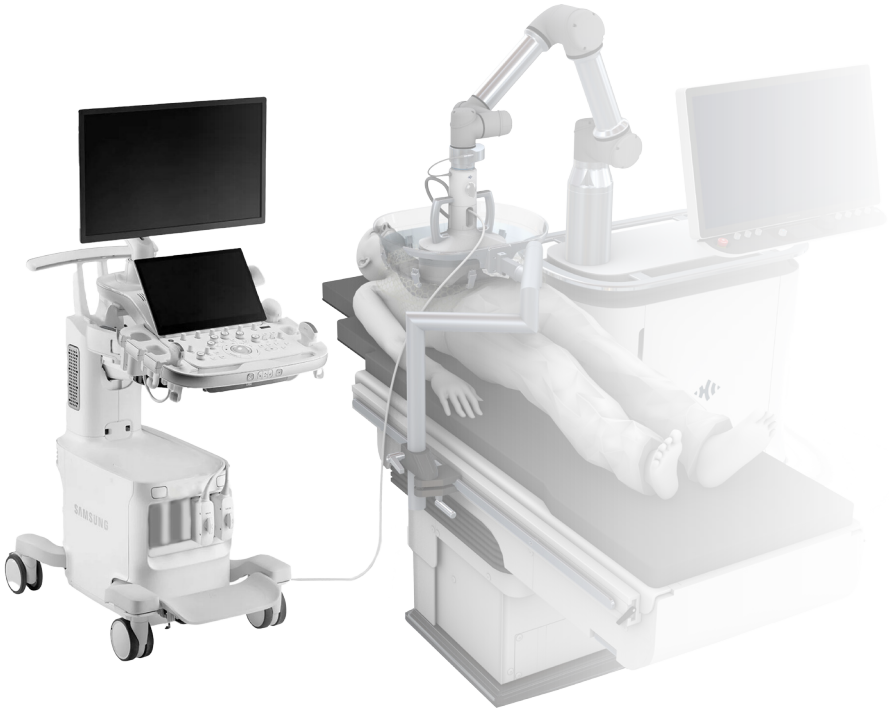
Samsung R20 Ultrasound System

Provides the live ultrasound image displayed on the treatment cart. Two imaging presets (Histotripsy and Abdomen) are preconfigured to support the procedure. For the task, use the appropriate preset.

Important

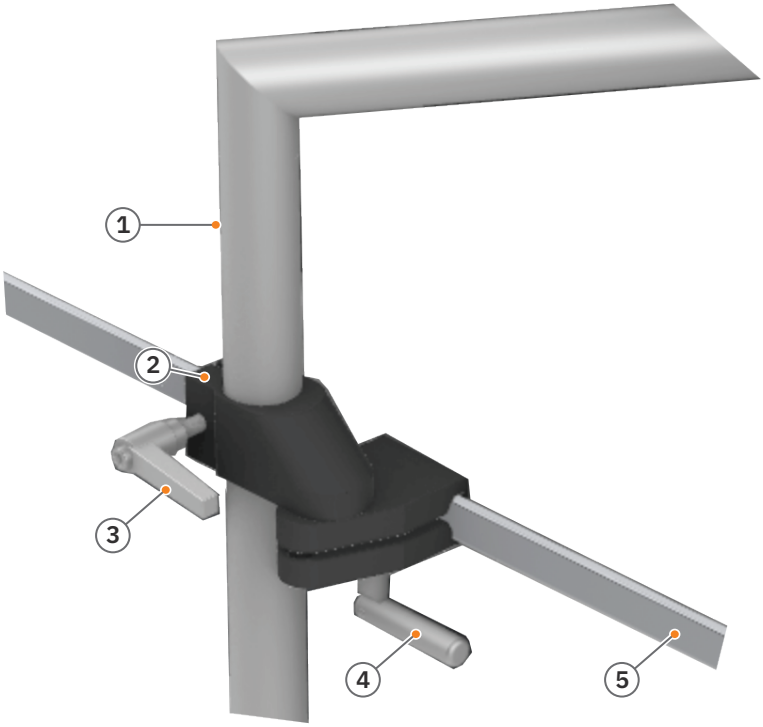
Using the appropriate preset provides optimal imaging performance and maintains the ultrasound system settings required for live streaming to the treatment cart. If the live image becomes unavailable, confirm that one of the preconfigured presets (Histotripsy or Abdomen) is selected.

Imaging Presets	Description	Used During Phase
Histotripsy	Optimizes the view of the bubble cloud. Use whenever bubble cloud visualization is required.	System Check, Treat
Abdomen	Best image quality for abdominal imaging. Required setting when fusing images.	Localize, Plan



Bed Rail Clamp

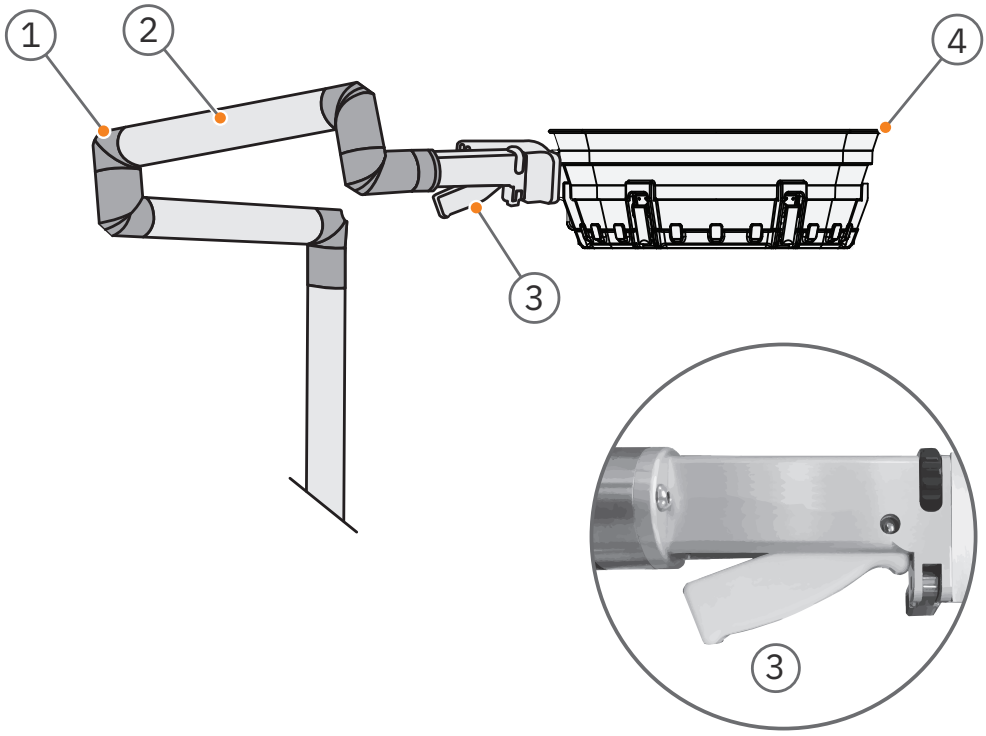
Secures the support arm to a 2.5 cm (1-inch) bed rail. The friction ring lever allows vertical adjustment of the support arm.



1. Support arm
2. Friction ring
3. Friction ring lever
4. Bed rail clamp lever
5. Bed rail

Support Arm

A multi-joint articulating arm that holds the frame and membrane in the desired position above the patient. Squeezing the adjustment trigger releases the locking mechanisms in all joints allowing for full adjustment, including rotation of the frame.



1	Joint	3	Adjustment trigger
2	Link	4	Frame

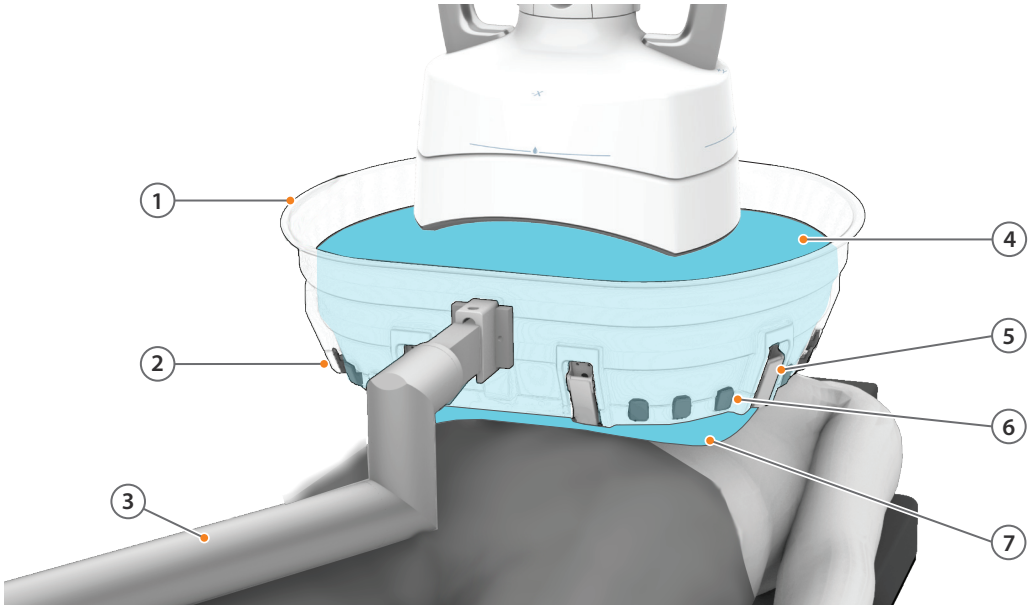
Frame

Together, the frame and membrane form a reservoir to hold ultrasound medium.

- Frame is transparent for visibility
- Upper half of the frame is permanently affixed to the support arm
- Lower half of the frame is removable for insertion and removal of the single-use membrane
- Eight latches secure the lower half of the frame to the upper half of the frame
- Hooks around the frame perimeter secure the membrane cradle (cradle not shown)

Important

Depending on the frame model, hooks to secure the membrane cradle may be located around the lower half of the frame (as shown) or around the upper half.



1. Frame (upper half)
2. Frame (removable lower half)
3. Support arm
4. Ultrasound medium in reservoir
5. Latch
6. Membrane cradle hook
7. Membrane

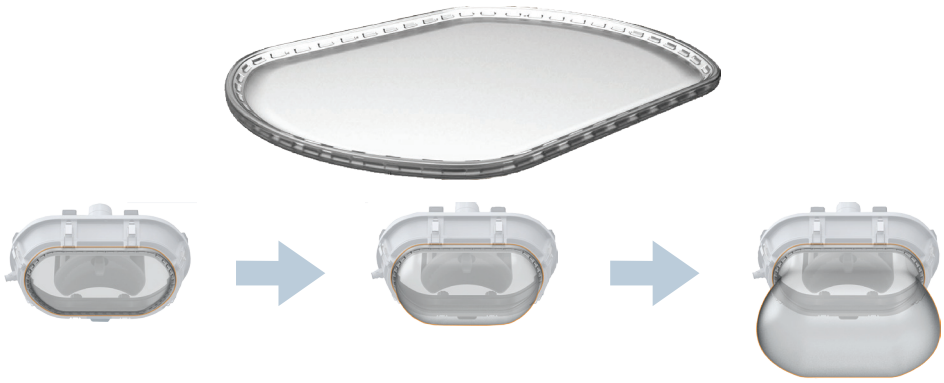
Coupling Kit

Includes the single-use accessories required for a histotripsy procedure:

- Membrane
- Membrane cradle
- Inspection mirror
- Bubble removal tool
- Coupling oil (2 bottles)
- Coupling band

Membrane

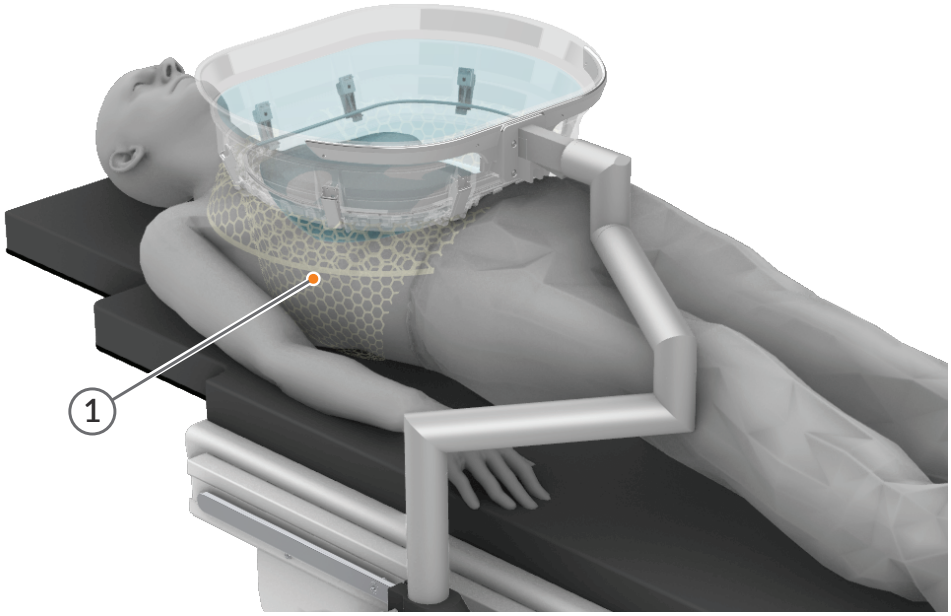
- The membrane inserts between the upper and lower halves of the frame
- It conforms to the patient as the reservoir is filled with ultrasound medium
- It is transparent for checking for air bubbles and air pockets
- It is acoustically transparent to ultrasound



Membrane Cradle

Silicone webbing that helps prevent the membrane from excessively bulging or shifting on the patient. The membrane cradle and frame have multiple connection points (open cells and hooks, respectively) to distribute load and ease setup and adjustment.

- Placed on the mattress before the patient is transferred to the bed
- Secured to the frame hooks



① Membrane cradle

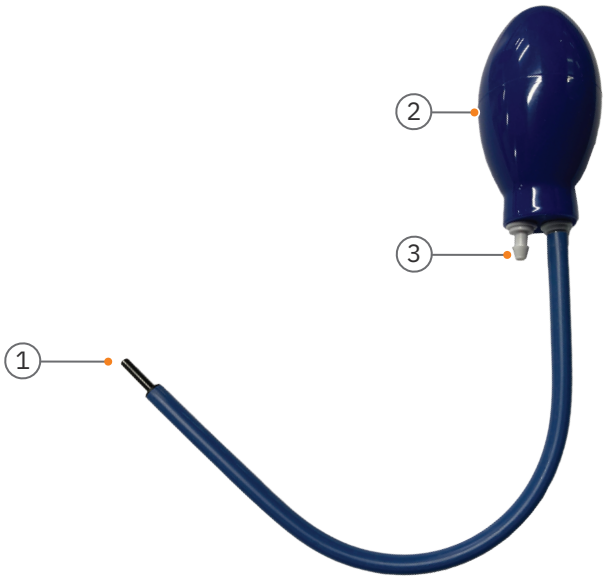
Inspection Mirror

Used to inspect for bubbles and air pockets on the face of the therapy transducer.



Bubble Removal Tool

The inlet tube is placed under the face of the therapy transducer to remove (suction) bubbles and air pockets.



1. Inlet tube
2. Squeeze bulb
3. Release valve

Coupling Oil

Castor oil is applied to the patient's abdomen to acoustically couple the membrane with the patient's skin. Helps fill in air pockets and prevent their formation.



Coupling Band

Flexible tube with handles that is slowly pulled between the membrane and patient to evenly spread coupling oil and remove any micro-bubbles.



5 User Interface

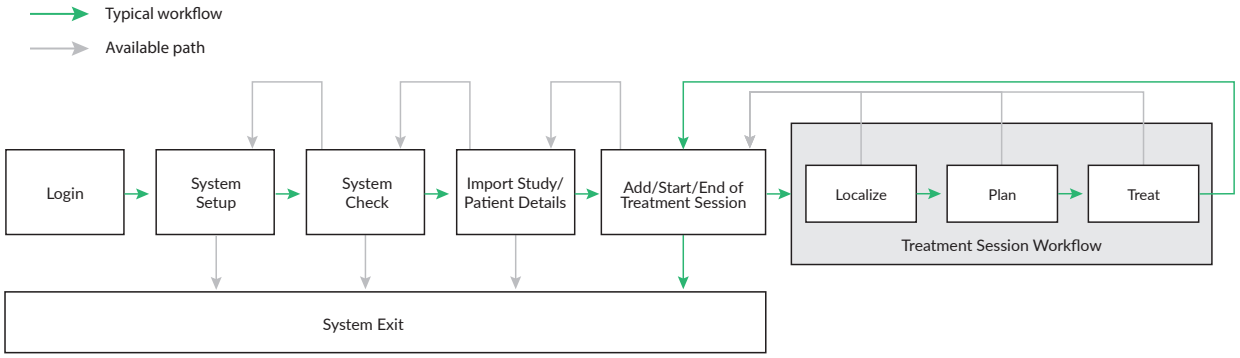
Workflow overview, primary controls, and common elements.

Application Description

The application guides the physician through the histotripsy procedure from setup to exit. All histotripsy procedure parameters are set in the application.

Application Architecture

The flow chart shows the typical workflow and the ability to go back or exit from various points.



Exit & Shutdown

Access the System Exit phase to shut down the system. This section provides information on how to access the System Exit phase from anywhere in the workflow. For details on shutting down the system in a typical workflow, refer to Chapter 5 (Operation).

Prior to the Treatment Session Workflow:

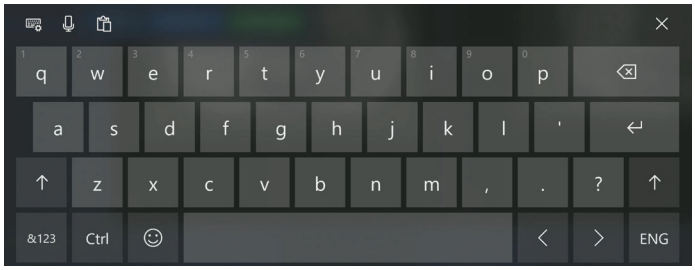
1. Select **Exit** from the main menu to navigate to the System Exit phase.
2. Perform the tasks displayed, then select the **Shutdown** button.

Within the Treatment Session Workflow:

1. Select **End Treatment Session** from the main menu.
2. Confirm selection to return to the Treatment Session screen.
3. Select **Exit** from the main menu to navigate to the System Exit phase.
4. Perform the tasks displayed, then select the **Shutdown** button.

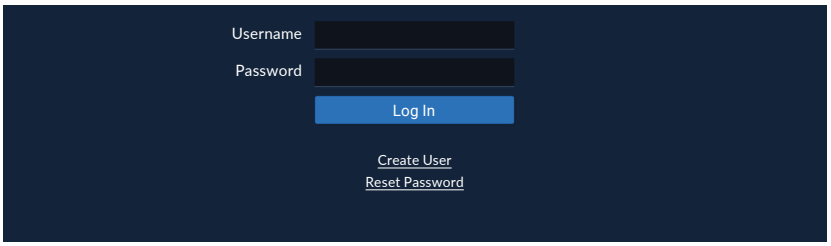
Virtual Keyboard

Automatically displays on-screen when selecting a text field.



Create User and Reset Password Links

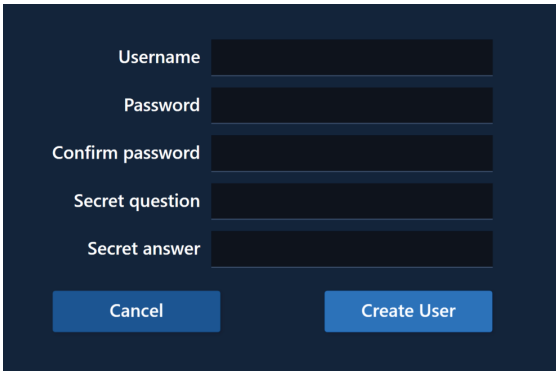
Create User and Reset Password links display at the bottom of the login screen.



Create User

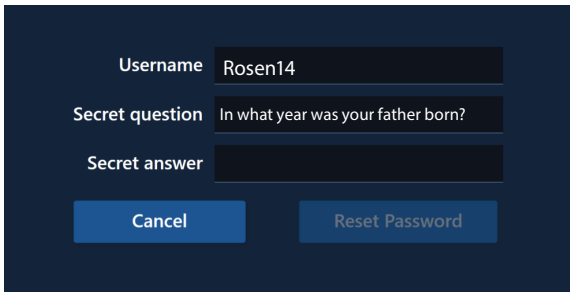
Selecting the **Create User** link displays a pop-up window.

Important
Do not use a secret question used for other logins.
Answers to secret questions are not case-sensitive.
Password requirements: • Lower-case letter, upper-case letter, and number or symbol • Eight characters or more • Not previously used
Passwords are valid for six months.



Reset Password

Selecting the **Reset Password** link displays a pop-up window. After a valid username is entered, the secret question displays.



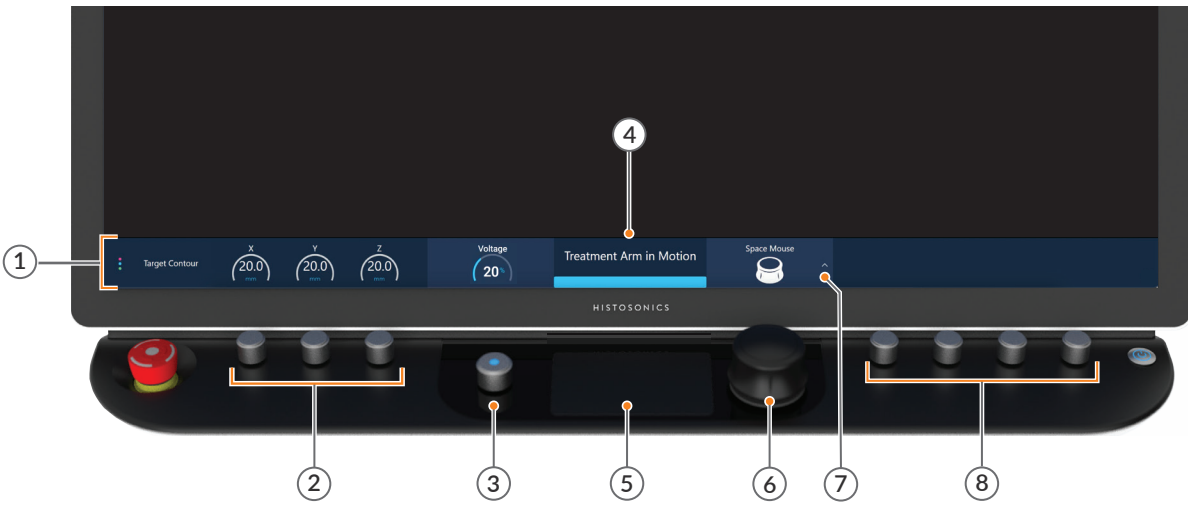
Primary Controls

Control panel and associated settings in the control panel display.

Important

Trackpad performance may be affected by the presence of water on its surface. Dry off any water before use.

Controls are shown in their active state for demonstration purposes.



① Control panel display

Located at the bottom of the screen during the procedure workflow, the control panel displays:

- Settings that are actively controlled by the corresponding physical knob just below the screen
- Treatment arm information
- Notification/system status information

② Planning knobs

Adjusts the plan parameters actively displayed in the control panel display. Knobs are used to adjust:

- Target contour diameters (X, Y, Z)
- Size of margin contour
- Plan location (fine adjustment)

③ Voltage knob

- Pressing the voltage knob toggles between its enabled and disabled state
- The voltage knob illuminates when enabled
- Rotating the voltage knob adjusts the voltage setting
- Pressing the voltage knob during energy delivery deactivates the therapy transducer

④ Status notification display

Displays status notifications with color bar:

- Resistance notifications:
  Low Resistance (yellow bar)
  Medium Resistance (orange bar)
  Limit Reached (red bar)
- **Treatment Arm in Motion** (blue bar)
- **Delivering Energy** (orange bar)
- **Automated Treatment** (green bar)
- **Treatment Paused** (orange bar)

⑤ Trackpad

Provided as an alternative to using the touchscreen. Functions like a trackpad on a laptop computer:

- Slide your finger to move the cursor
- Tap to make a selection
- Tap on the right side of the trackpad (right-click) on length measurements and annotations to display the delete button
- Slide finger while pressing down (click and drag) to drag and scroll elements

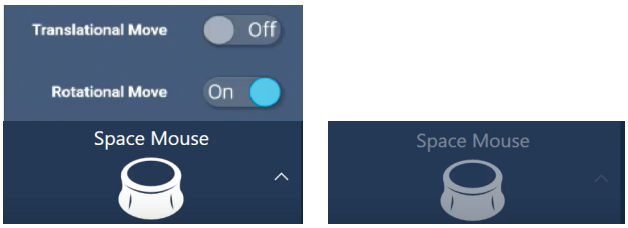
⑥ Space mouse

Moves the treatment head in six degrees of freedom (X, Y, Z, pitch, roll, and yaw) at the desired speed and allows precise, fine tune positioning of the treatment head.

⑦ Space mouse tile

Selecting the space mouse tile displays toggles that can be activated to restrict translational and rotational movement of the treatment arm while using the space mouse.

- Newer users may prefer to enable these restrictions as needed to prevent unwanted movement of the treatment arm
- The toggles have no effect when using freedrive or on automated movement
- When the space mouse tile is grayed-out, space mouse control is disabled and space mouse settings cannot be accessed



⑧ Non-functional knobs

Four knobs reserved for features that may be introduced in a future version.

Common Elements

Main Menu

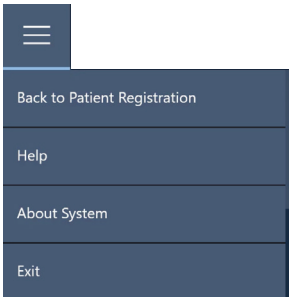
Displays at the top of the screen and is used to access the content described in this section.



① Main Menu

Selecting displays a drop-down menu with selections that vary by phase:

- Help (opens user guide)
- About System
- Back to Patient Registration
- End Treatment Session
- Exit



② Patient Information Area

Displays the patient's initials and ID number. Selecting the drop-down displays the patient's name, birth, age, and gender (if entered during patient registration).



③ Treatment Head Status Icon

Displays the current status of the treatment head. Selecting the icon opens the Treatment Head panel.

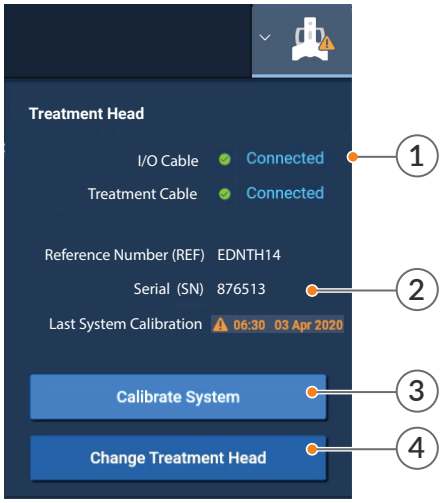
- Green check mark displays when treatment head is ready for use
- Orange notification symbol displays when there is a connection issue or when too much time has passed since the system was calibrated with the treatment head





Treatment Head Panel

To display, select the treatment head icon in the main menu.



① Connection status

- I/O Cable
- Treatment Cable (connects therapy transducer)

② Treatment head information

- Reference Number (REF)
- Serial Number
- Date and time of last system calibration

③ Calibrate System button

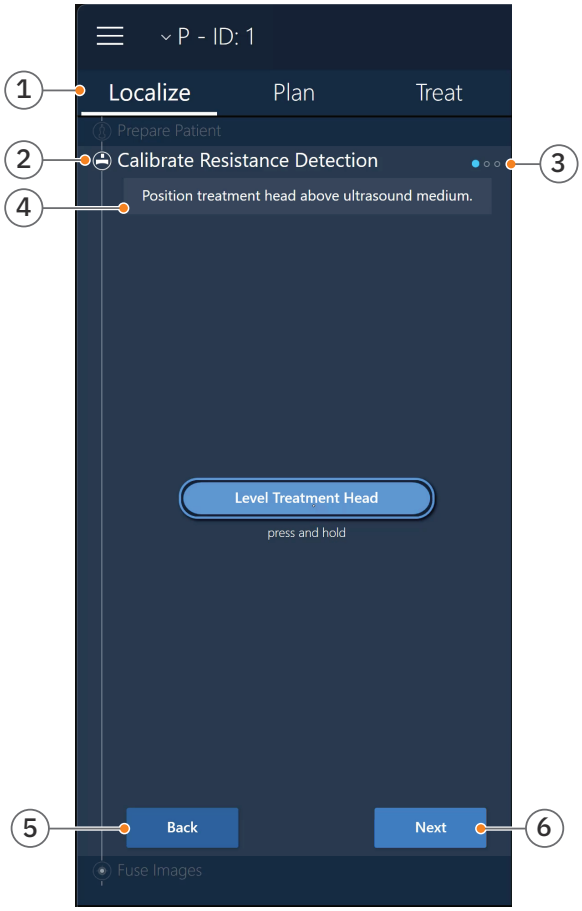
Select to go to the beginning of the System Check phase.

④ Change Treatment Head button

Select to open a panel that displays the tasks and buttons required to change the treatment head. Button availability and tasks are dependent on the current progress in the workflow. Refer to *Changing the Treatment Head on page 5-35*.

Workflow Panel

Displayed on the left of the screen, the workflow panel guides you through the procedure, providing instructions, results, and unique controls (buttons) to complete the current task.



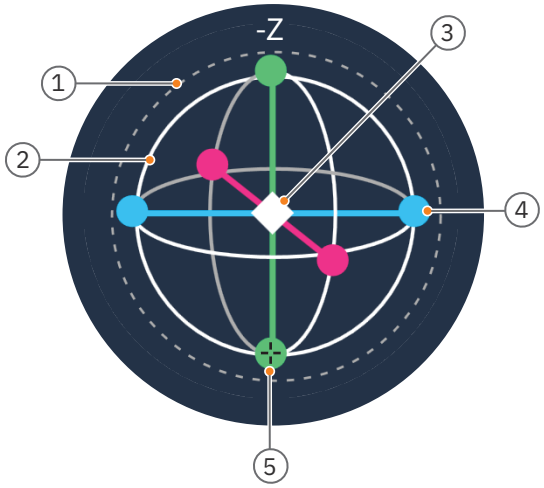
① **Phase**	Displays at the top of the workflow panel. During the treatment session, its three phases display (Localize, Plan, Treat) and the white bar underlines the active phase.
② **Current task**	Brief description of the current task. Each task has a unique icon that displays on a timeline. Previous and upcoming tasks are grayed-out.
③ **Task progression indicator**	When a task requires more than one screen, this indicator displays to show progression. In the example, the first of three screens is displayed.
④ **Steps**	The steps required to perform the current task.
⑤ **Back button**	Select to return to the previous task or phase.
⑥ **Next screen/Task complete button**	Select to confirm all steps were performed and to progress to the next task or phase.

PTV Tool

Displays in the workflow panel during various tasks as a reference and a tool for selecting plan points.

Important

The PTV tool is always a perfect sphere, it does not conform to the actual shape of the PTV.



①	**Margin contour**	Dashed line represents the outer boundary of the PTV.
②	**Target contour**	Solid white lines represent the target contour.
③	**Center**	White diamond represents the center of the PTV and the center plan point. Selectable during the plan survey.
④	**Plan points**	Colored circles represent six plan points. Selectable during the plan survey. Each color relates to an axis: X-axis, Y-axis, Z-axis
⑤	**Survey location**	Black crosshairs in a plan point indicate the current location of the survey.

Treatment Session Screen

Used to create a new treatment session, enter and edit treatment session details, launch the Treatment Session, and export treatment reports.

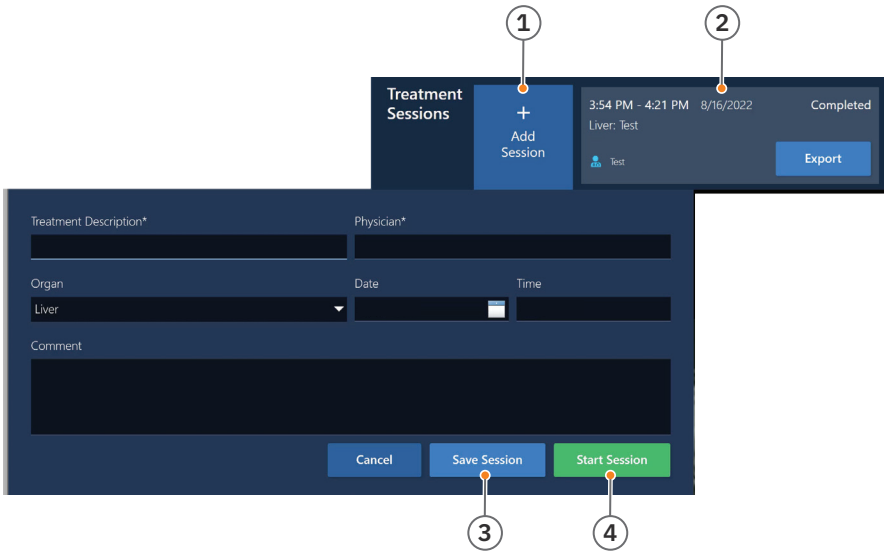
Add Session tile: Selecting opens a drop-down window with blank fields and buttons.

Save Session button: Saves details and closes the window. This button is typically used when pre-registering a patient in advance of the procedure. After a treatment session is saved, changes to details can be made by selecting the treatment session tile, which reopens the drop-down window.

Start Session button: Saves the treatment session details and launches the Localize phase of the Treatment Session.

Important

After starting a treatment session, only comments can be added or modified.



1. Add Session tile (button)
2. Treatment session tile
3. Save Session button
4. Start Session button

Treatment Session Tiles

Saved treatment sessions display along the top of the Treatment Session screen. The status of the treatment session displays in the tile. Buttons display in the tile according to the treatment session status.

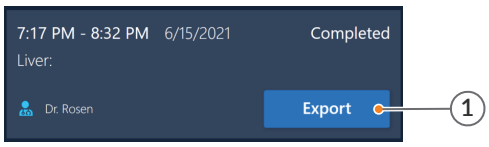
Treatment Session Status	Text Displayed in Tile	Button Displayed in Tile
Not started	Blank	Start Session
Stopped before completion	Incomplete	Export (Treatment Report)
Completed	Complete	Export (Treatment Report)

Exporting a Treatment Report

The system generates a treatment report with a summary of treatment details. The report includes comments added by the user and screen/pane captures taken during the procedure.

Treatment reports can be exported as a PDF to a location preconfigured for the site. The default export location is a USB drive. Upon request, the system can be configured to export reports to another location, such as a hospital network location.

1. Select the **Export** button from the treatment session tile. The report displays.
2. If the configured export location is a USB drive, insert a USB drive into the USB port on the connection panel.
3. Select the **Save** button.





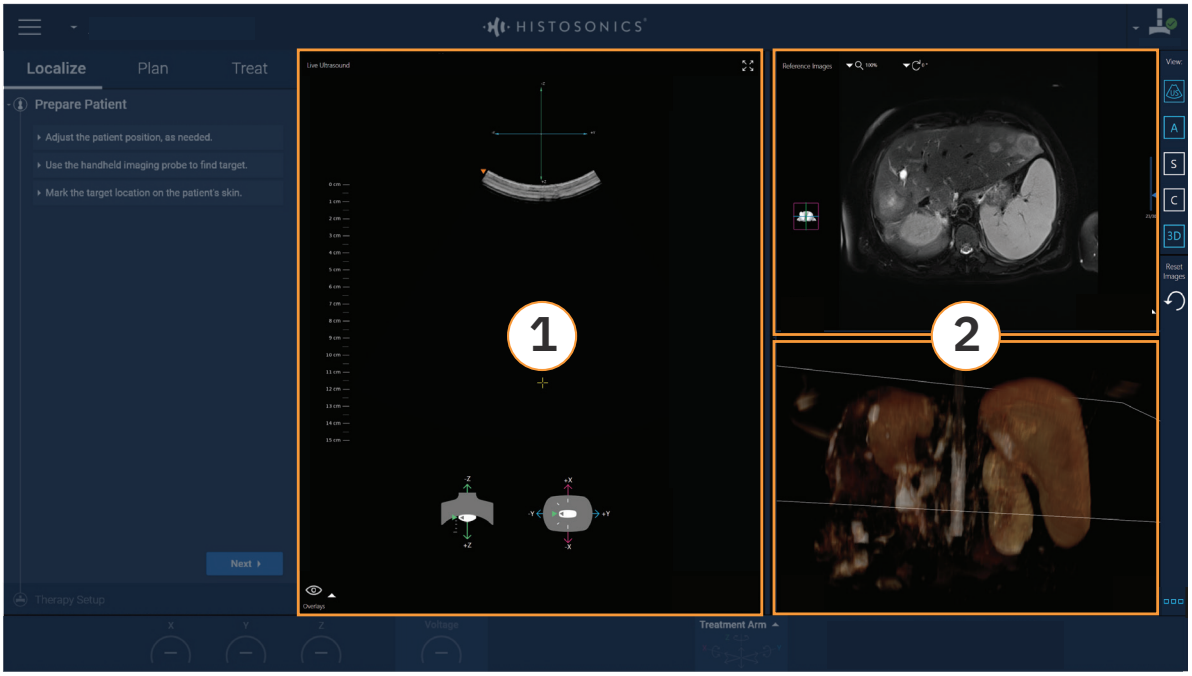
① **Export button**

② **Treatment report**

Image Panes

Automatically display the recommended view(s) for a given task. Image panes can also be configured by the user. The following image types can be displayed.

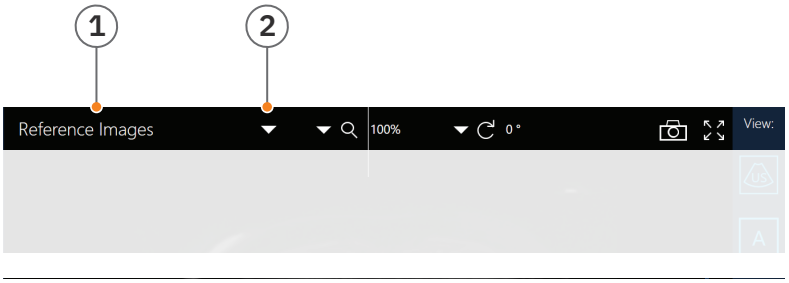
- Live ultrasound
- Reference images (DICOM)
- 3D
- Static fused images
- Live fused images



① **Primary image pane**
Typically displays live ultrasound.

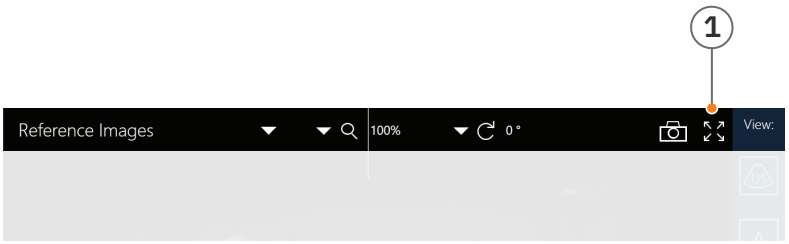
② **Secondary image panes**
Display reference images and 3D view.

Image Type and Selection Menu



① **Image type**	Identifies the image type currently displayed in the image pane.
② **Image Type Menu**	Selecting the white arrow opens a drop-down menu used to select other image types. Options are phase and task-dependent.

Image Pane Expansion



① **Expand to full screen**	Select to expand the image pane to cover the entire image pane area and hide all others.

View Tools



① View buttons

Select a view type to display it in an image pane. A blue icon indicates that the view is displayed; a white icon indicates that the view is not displayed.

Ultrasound	Axial	Sagittal	Coronal	3D
				

② Reset images

Select to reset all reference images to their default view settings:

- 100% zoom
- 0° rotation
- Default orientation (3D view only)



③ Axes buttons

Used only for the Static Fused Images view that displays within the Fuse Images task.

Ultrasound Recording

Active by default. When active, the axes are based on the plane of the ultrasound image in the recording.



Reference Image

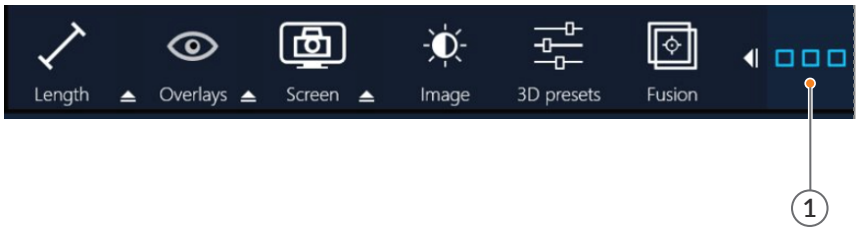
Select to base the axes on the reference images.



Toolbar

Select the toolbar icon (three squares) to display/hide the toolbar. On the toolbar:

- Activated tools are blue; inactive tools are white
- White arrows indicate that a drop-down menu is available with additional tools or settings
- The Length, Overlays and Screen tools can be activated from the toolbar
- After choosing the Annotation tool from the Length/Annotation drop-down menu, it can also be activated via the toolbar
- Selecting the Image tool displays image adjustment sliders/settings
- Selecting 3D Presets displays the available 3D presets



① **Toolbar icon** Displays/hides the toolbar.

Length and Annotation Tools

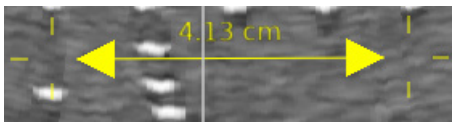


Length

The length tool displays the distance (in cm) between two points placed in a view. More than one measurement can be taken.

With the length tool active (blue):

1. Select a location on the image as the starting point.
2. Drag to the desired location, then release to complete the measurement.
3. A line connecting the two points displays with the measurement.
4. To delete a measurement, select it, then select the **Delete** button that displays.





Annotate

The length tool is the default selection in the toolbar. To toggle to the annotation tool, select the white arrow, then select the annotation tool.

With the annotate tool active (blue):

1. Select a location for the text annotation. The virtual keyboard automatically displays.
2. Use the virtual keyboard to enter text.
3. Select **Enter**.
4. To delete a text annotation, select it, then select the **Delete** button that displays.

Screen Capture Tools

The pane capture tool displays at the top of every image pane. The screen capture tool is located in the toolbar.

Important

Pane and screen captures are automatically added to the treatment report, which can be reviewed and exported at the end of the procedure.



Pane

Select to capture just the image in the pane.



Screen

Select to capture the entire screen.

Image Settings



Image

Select the Image button in the toolbar to display image settings, then use the sliders as needed to adjust the brightness and contrast of axial, sagittal, and coronal images to improve visualization in the region of interest.

- **Level** adjusts the center of the grayscale range (**affects brightness**).
- **Width** limits the dark and light extremes (**affects contrast**).
  A larger window means the transition from black to white takes longer.



3D Presets



3D Presets

Select to display a menu with settings that adjust the window level for the 3D view.
Available 3D presets:

- Default
- Bone
- Skin/Soft Tissue/Bone
- MRI Muscle
- PET

Fusion



Fusion

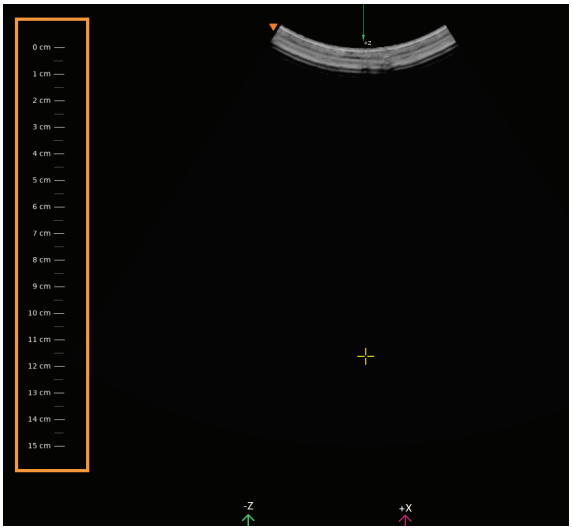
After a Fusion is performed, you can select the Fusion button to display and change blending settings (color mode or grayscale mode) and the ultrasound opacity setting (default is 50%).

Live Ultrasound Image Pane

The following sections cover tools and elements unique to the live ultrasound image pane.

Depth Gauge

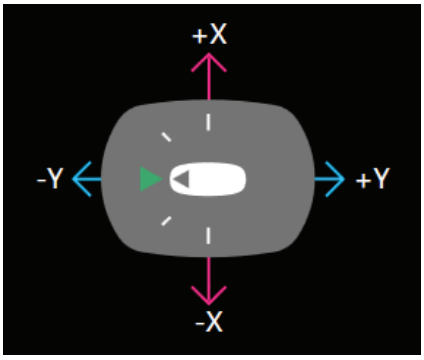
A visual aid that shows the approximate distance from the imaging transducer (0 cm to 15 cm).

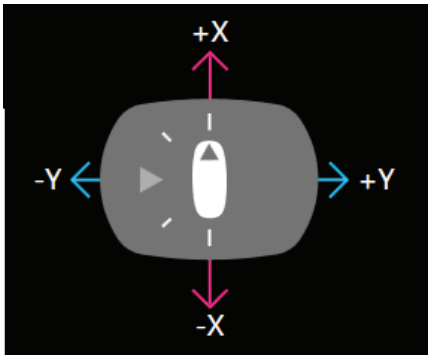


Imaging Transducer Orientation

A top-down representation of the treatment head and imaging transducer. Displays the current orientation of the imaging transducer in relation to the X-axis and Y-axis of the treatment head.

- Dark gray triangle indicates the imaging transducer orientation
- Green triangle displays when the imaging transducer is oriented to -Y and is in the home position (fully retracted)

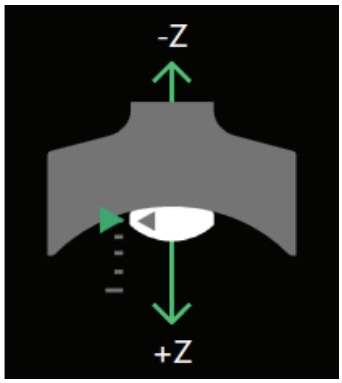


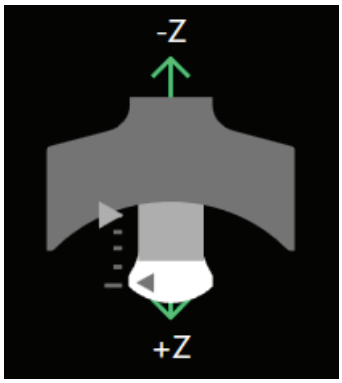


Imaging Transducer Translation

A side profile of the treatment head that displays the current position of the imaging transducer along the Z-axis.

- Short graduation marks indicate incremental translation between the home position and fully extended
- Long graduation mark is the fully extended position
- Dark gray arrow indicates the current position of the imaging transducer
- Green triangle displays when the imaging transducer is oriented to -Y and is in the home position (fully retracted)

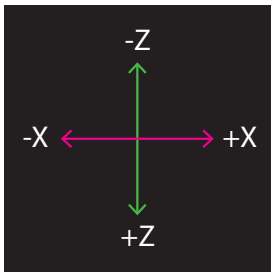


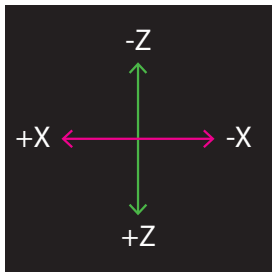


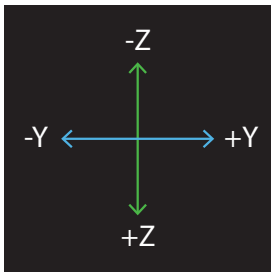
Ultrasound Axes

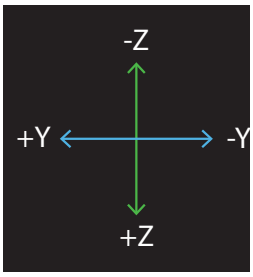
Indicate the orientation of the live ultrasound image in relation to the treatment head axes.

- A horizontal line with axis letters displays when the imaging transducer is oriented to (or within 30 degrees of) the X-axis or Y-axis of the treatment head. X-axis is magenta, Y-axis is cyan
- The vertical green line is static and correlates to the Z-axis of the treatment head



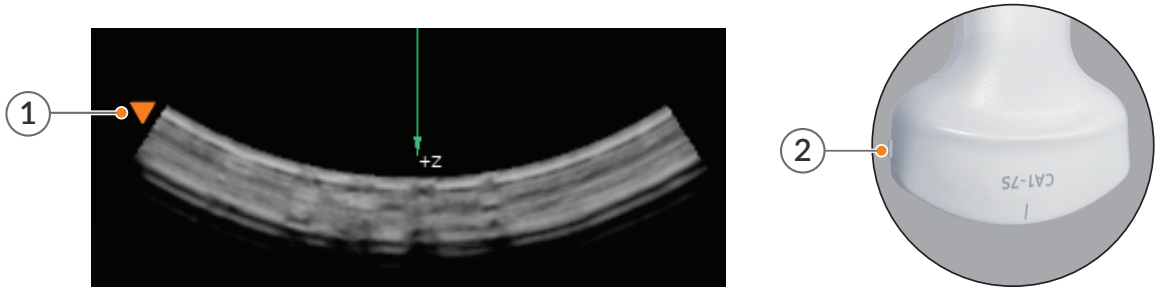






Ultrasound Orientation Reference Marker

An orange triangular marker displayed in the live ultrasound view that corresponds to the physical orientation indicator on the imaging transducer housing. The marker is always displayed on the left side of the ultrasound image.



① Ultrasound orientation reference marker ② Imaging transducer orientation indicator

Overlays

Superimposed elements that display over the Live Ultrasound view and Live Fused Images view. All overlays display by default and include:

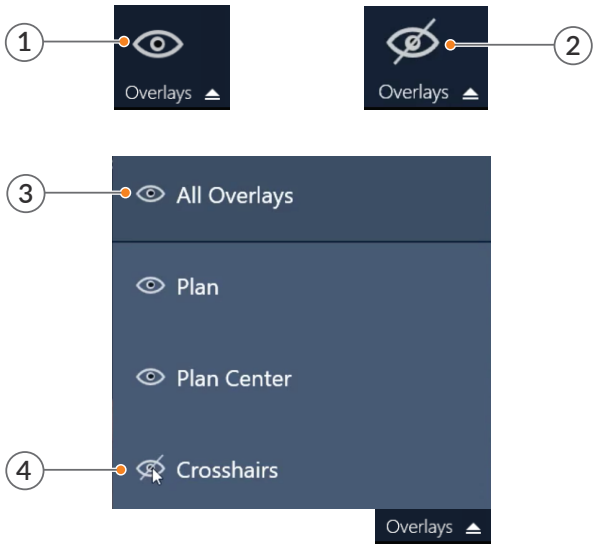
- Plan (target contour and margin contour)
- Plan Center
- Crosshairs
- Major Axes
- Annotations (length measurements and text annotations)
- Acoustic Field Indicator (displays in Live Ultrasound and Live Fused Images)
- Ultrasound Recording Outline (recorded during the Fuse Images task)

Hide All Overlays

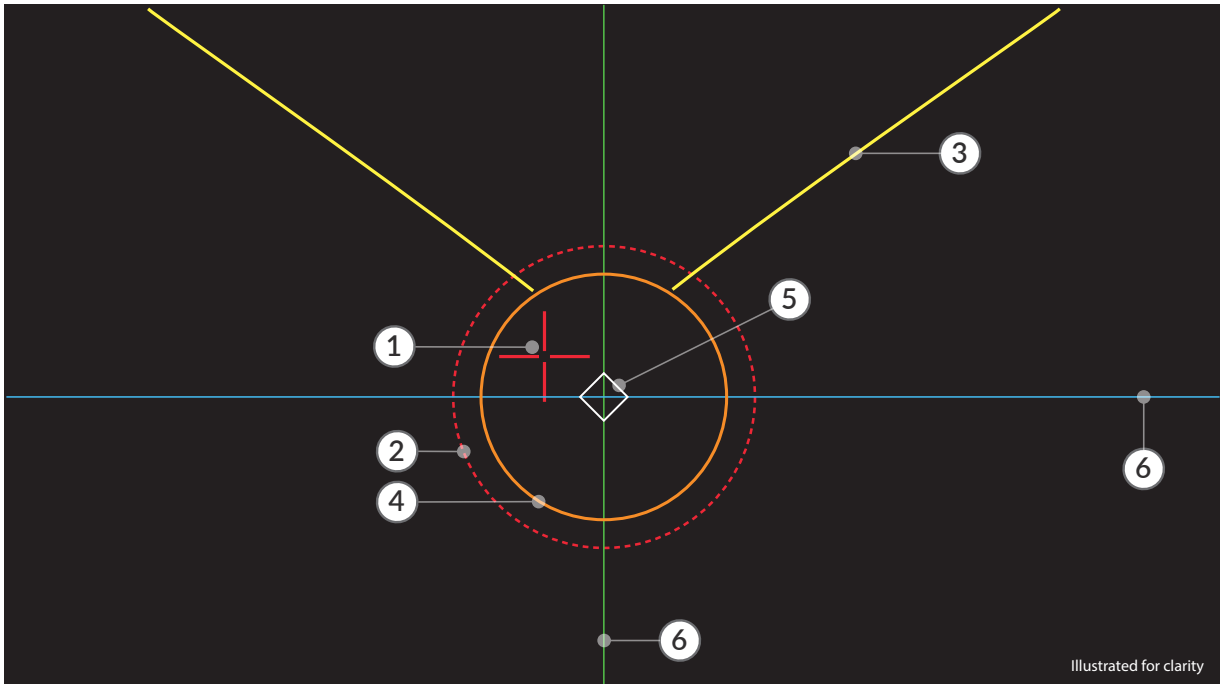
To hide all overlays, select the toolbar eye icon; select again to redisplay all overlays. You can also use the **All Overlays** selection in the Overlays menu.

Hide Specific Overlay(s)

Open the Overlays menu, then select the eye next to the specific overlay(s); select again to redisplay.



1. Toolbar eye icon: Default state
2. Toolbar eye icon: All overlays hidden
3. All overlays
4. Crosshairs overlay hidden

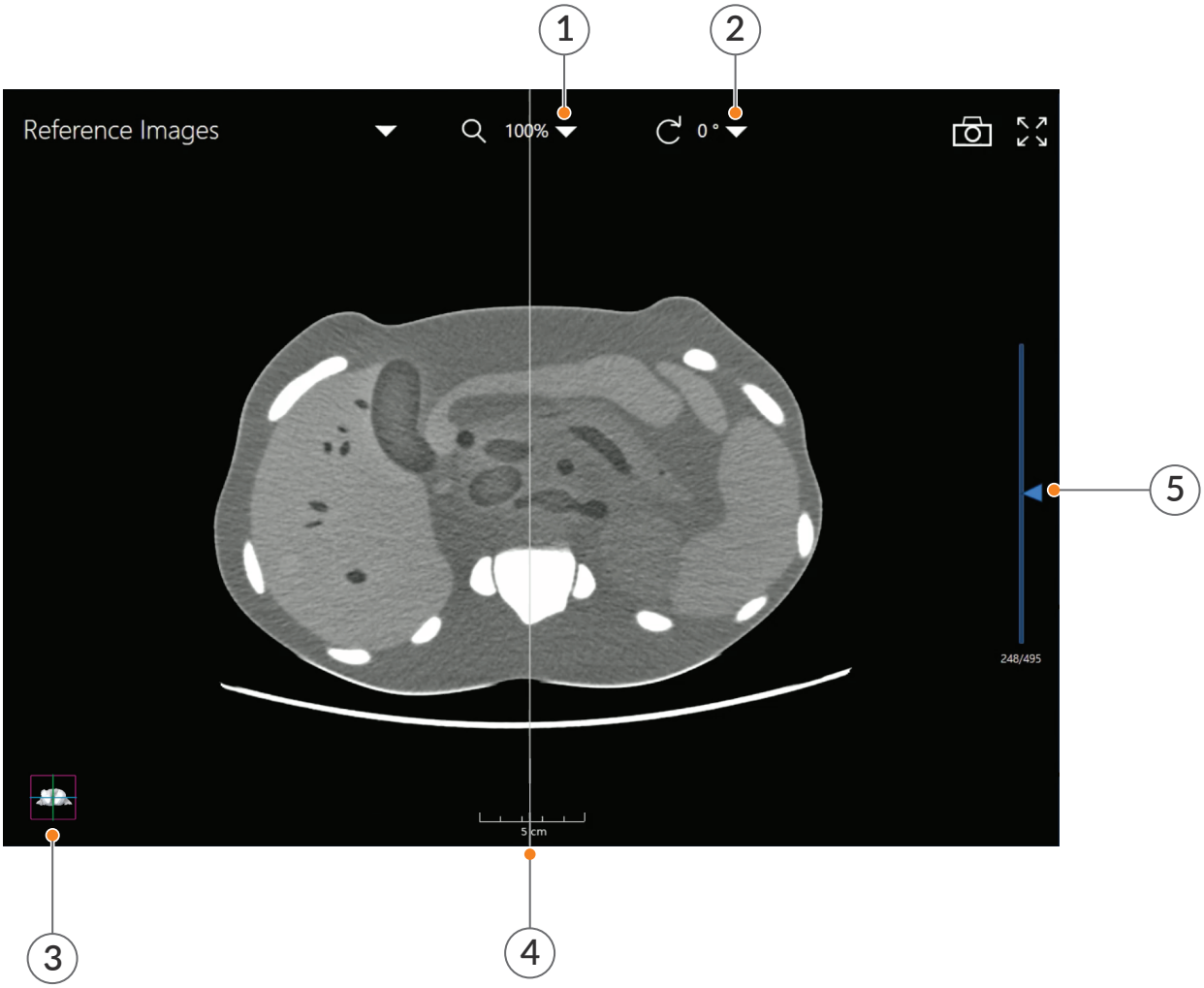


① **Crosshairs**	Expected location of the bubble cloud center.
② **Margin contour**	Outer boundary of the PTV.
③ **Acoustic field indicator**	Represents the ultrasonic energy boundaries from the therapy transducer to its focal point. • The shape of the acoustic field indicator updates with the orientation of the imaging transducer • Use the acoustic field indicator to help optimize the acoustic pathway and to avoid excessive blockage
④ **Target contour**	Used by the physician to outline the tumor intended for destruction.
⑤ **Plan center**	The center of the PTV.
⑥ **Major axes**	Indicate the orientation of the live ultrasound image. • The vertical green line is static and correlates to the Z-axis of the treatment head • The horizontal line displays when the imaging transducer is oriented to (or within 30 degrees of) the X-axis or Y-axis of the treatment head (magenta = X-axis, cyan = Y-axis)

Reference Images

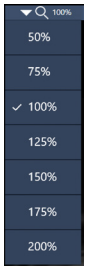
A study with MR or CT images can be displayed throughout the workflow in the axial, sagittal, and coronal views to help the physician localize the region of interest which includes the targeted tumor, critical anatomy, and relevant structures and landmarks.

The user interface automatically displays the recommended views for a given task, but the views can also be toggled on or off by the user. Views can be scrolled, zoomed, and rotated. An axial view is shown as an example.



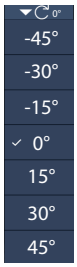
① Zoom

The current zoom setting displays in the image pane. To change the zoom level, select the white arrow to open the drop-down menu, then select the desired zoom setting.



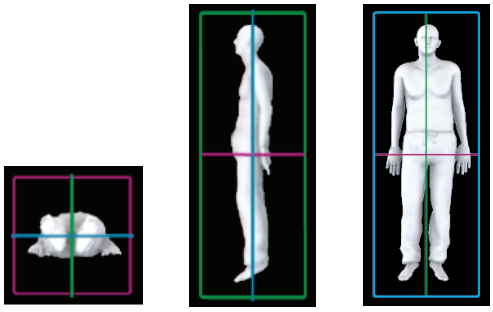
② Rotation

The current rotation setting displays at the top of the image pane.
To change the rotation setting, select it, then select the desired rotation setting in the menu that displays.



③ Image orientation

Human model that indicates the planar view of the reference image.



④ Multiplanar reconstruction line

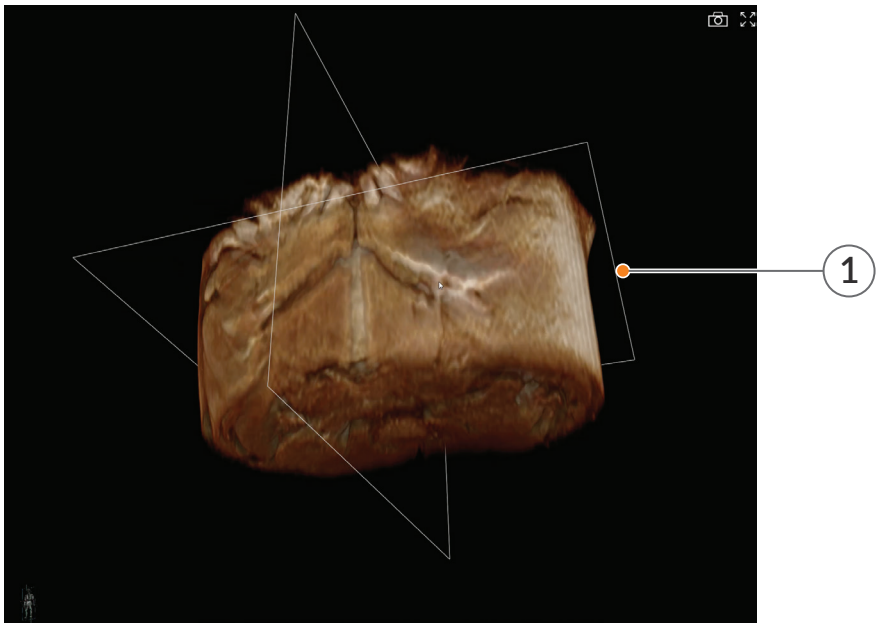
Displays the location of the displayed slice in other planes. Can be selected to scroll views.

⑤ Slice scroll bar

Drag the arrow to scroll through the slices in the reference image. The displayed slice and the total number of slices display at the bottom of the scroll bar.

3D View

The three-dimensional image is automatically constructed from an imported study and helps the physician localize and align the treatment head to the region of interest which includes the targeted tumor, critical anatomy, and relevant structures and landmarks.



① **3D view planes** Indicates the orientation of the three-dimensional image.

Touch Gestures

Use touch gestures on the touch screen or trackpad to interact with reference and 3D images.

Reference Image Control	Touch Gesture
Zoom out	Pinch 
Zoom in	Spread 
Pan	Two-finger swipe 
Rotate (3D only)	Two-finger rotate 
Orientation (3D only)	One-finger drag 

Fuse Images

An optional task within the Localize phase that aligns and conforms reference images with live ultrasound.

Important

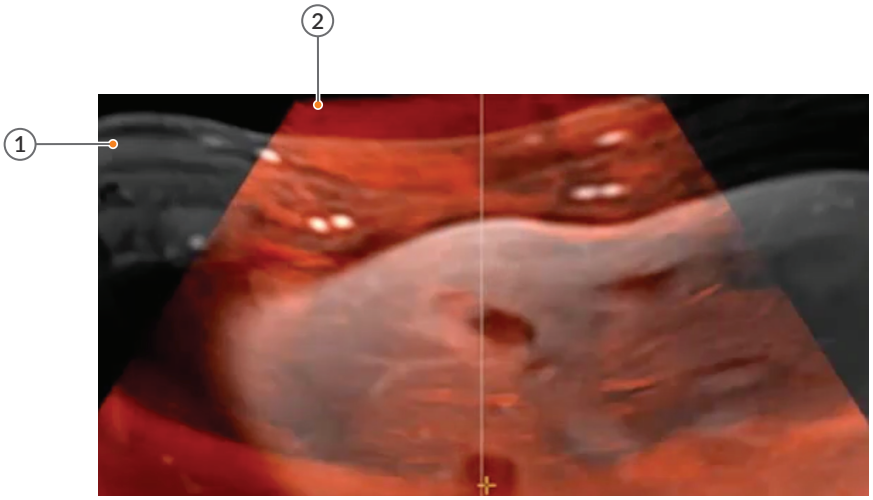
Fusing images conforms reference images to account for changes that can occur between the study and the histotripsy procedure. For example:

- The weight of the ultrasound medium on the patient's abdomen can cause displacement
- Anatomy can shift from the passing of time or change in patient position between the study and histotripsy procedure

Additional information and step-by-step instructions are provided in *Fuse Images on page 6-44*.

Overview of Steps

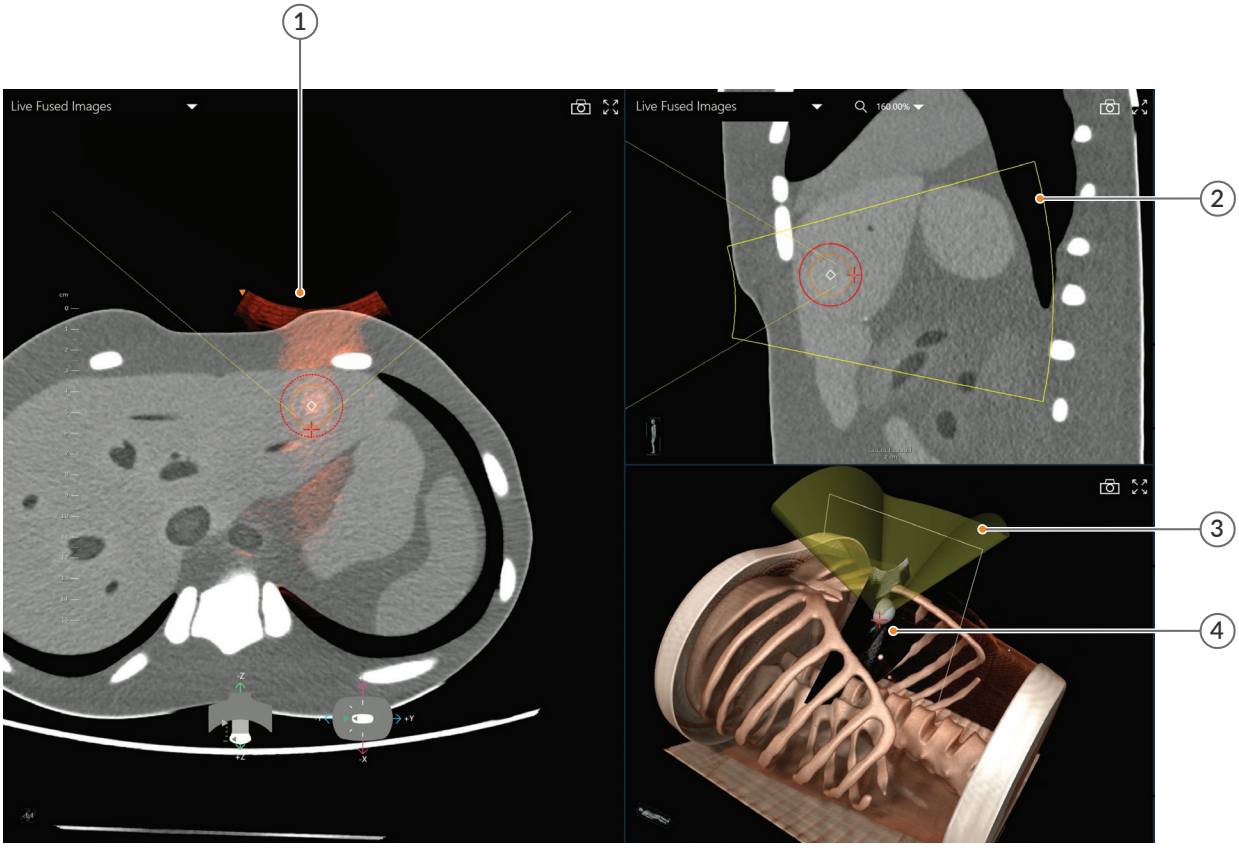
1. The physician imports a study (MR or CT images).
2. After the physician performs the necessary steps, the system performs an automated sweep of the treatment head over the region of interest while it records ultrasound imaging. The system creates an interactive, three-dimensional image from the ultrasound recording.
3. The physician places registration points on easily identifiable landmarks in the ultrasound recording and reference images.
4. The system fuses the images using the registration points and an image-based algorithm.
5. The physician reviews and accepts the results (or makes necessary adjustments).
6. The fused images display in the Live Fused Images view.



1 Reference image (fused) 2 Live ultrasound (fused)

Live Fused Images

After fusing images, the Live Fused Image views display. The table and accompanying callouts provide details on key elements within these views.



① **Live ultrasound fused with reference images**	Live ultrasound is colorized and blended with reference images to help the user identify the targeted tumor and other critical anatomy in the region of interest.
② **Ultrasound recording outline (sagittal view)**	Shows the region captured by the automated sweep.
③ **Acoustic field indicator (3D view)**	3D representation of the ultrasonic energy boundaries from the therapy transducer to its focal point. • The shape of the acoustic field indicator updates with the orientation of the imaging transducer • Use the acoustic field indicator to help optimize the acoustic pathway and to avoid excessive blockage
④ **Live Ultrasound and PTV (3D view)**	Live ultrasound plane that dynamically displays the orientation and angle of the imaging transducer in a 3D view. A cross-section representation of the PTV (including shape, size, and location) displays in the live ultrasound plane.

Resistance Detection

Real-time resistance detection monitors and prevents the treatment arm from applying excessive force on the patient or against an object, such as the frame.

Caution

Failure to calibrate resistance detection as instructed may prevent the procedure from proceeding due to resistance limit detection.

Important

Resistance detection is not active when using freedrive to move the treatment arm.

Resistance detection thresholds are predefined and cannot be adjusted by the user.

Calibrating resistance accounts for the buoyant force present when the treatment head is submerged in the ultrasound medium.

Resistance Indicators

When resistance is detected:

- Message and color bar display
- Live ultrasound view is bordered with the resistance color (during certain tasks)
- Resistance indicator (arc) displays in the treatment head graphic (during certain tasks)
- Axis arrow(s) changes from their default color (green, magenta, cyan) to the resistance color

Level of Resistance

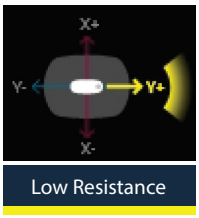
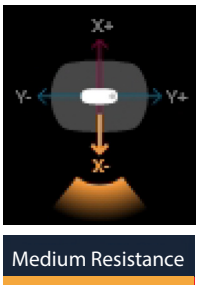
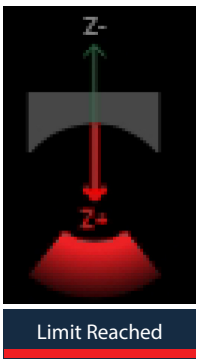
- The color of the resistance indicators relates to the level of physical resistance detected

Direction of Resistance

- The position of the arc(s) correlates to the direction of resistance from the perspective of the treatment head
- The axis arrow changes color to indicate the direction and level of resistance
- Top-down representation of the treatment head displays when resistance is detected to one of the sides of the treatment head (displayed as X-axis or Y-axis)
- Side view representation of the treatment head displays when resistance is detected above or below the treatment head (displayed as Z-axis)

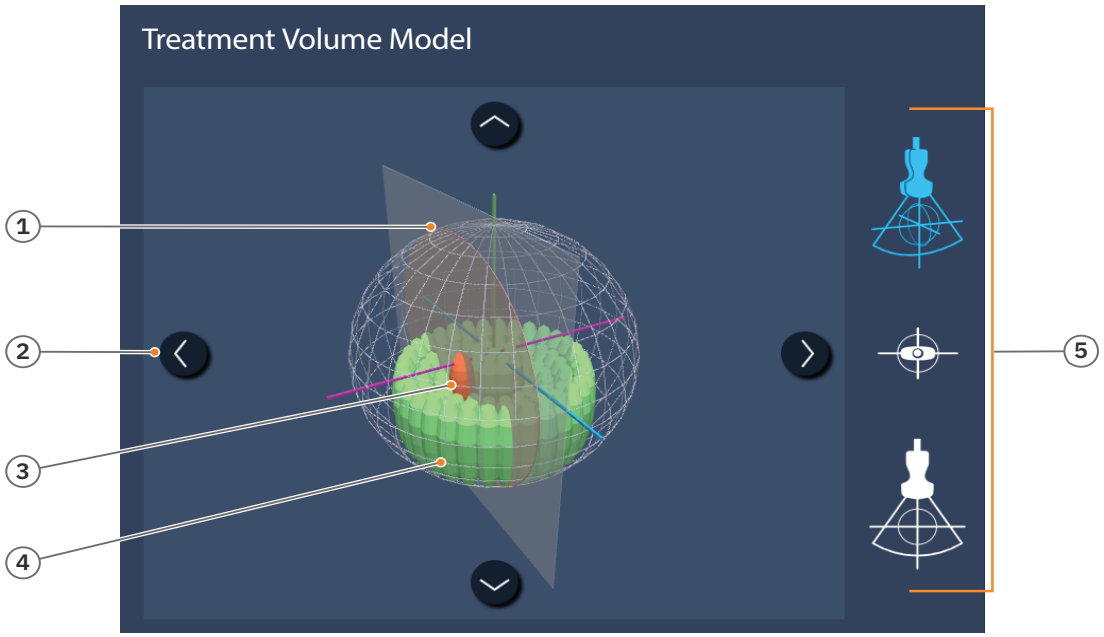
System Behavior and User Action

System behavior and user action are dependent on the level of force applied by the treatment head and the phase in which it occurs.

Resistance Indicator and Message	Resistance	System Behavior
Yellow  	**Low**	• Significantly slows treatment arm movement in the direction of physical resistance during user-commanded actions (e.g., space mouse, move to point) • Does not slow the treatment arm during automated treatment
Orange  	**Medium**	• Further slows treatment arm movement in the direction of physical resistance during user-commanded actions (e.g., space mouse, move to point) • Does not slow the treatment arm during automated treatment
Red  	**Limit Reached**	• Limit can be reached in any phase; response depends on phase and current task • Stops automated treatment • Prevents further movement towards physical resistance during user-commanded actions (e.g., space mouse, move to point) • Stops automated movement after completing the current move; if the 50-newton limit is reached, the system initiates a soft emergency stop • Displays corrective action message when corrective action is required

Treatment Volume Model

A visual representation of automated treatment progress. Controls are available to orient the view.

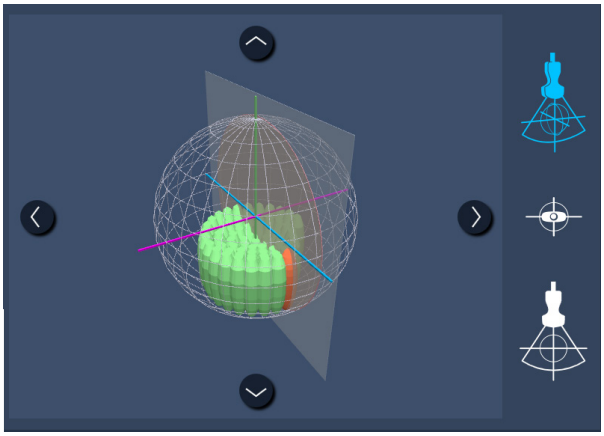


①	**Ultrasound imaging plane**	Shows the position and orientation of the live ultrasound plane.
②	**Rotation arrow**	Left/right arrows rotate the model around the Z-axis. Up/down arrows rotate the model around the X-axis and Y-axis.
③	**Bubble cloud location**	The orange ellipsoid shows the current location of the bubble cloud as it moves in an overlapping spiral pattern.
④	**Focal zones**	Green ellipsoids represent focal zones that received treatment.
⑤	**View buttons**	Select to display a view (off-axis, top-down, front).

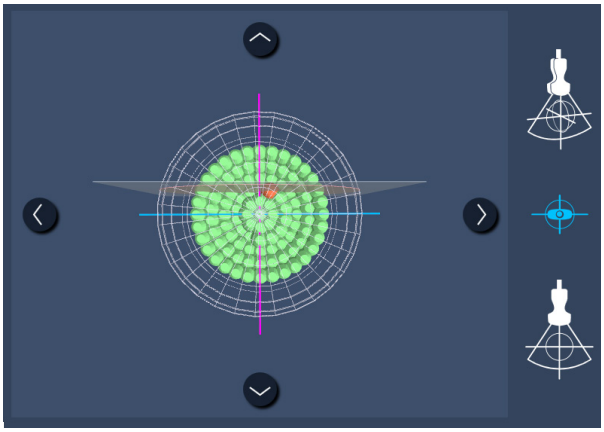
Views

The blue icon indicates the active view.

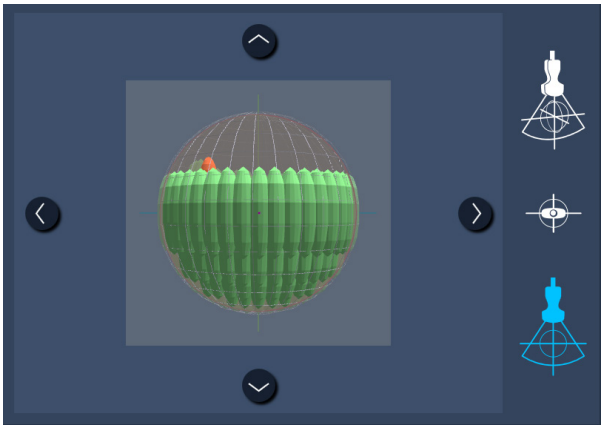
Off-axis view



Top-down view



Front view



Changing the Treatment Head

Ideally, the treatment head used for the procedure is connected before or during the System Setup phase. However, the system does allow swapping to a different treatment head after completing the System Setup phase. The required steps to swap the treatment head depend on where the user is in the workflow.

During	Steps Required in User Interface
System Check	Use the **Back** button to navigate to the beginning of the System Setup phase. Remove the treatment head, then perform the System Setup workflow as usual.
Patient Registration	From the main menu, select **Return to System Setup**. Remove the treatment head, then perform the System Setup workflow as usual.
Treatment Report	
Treatment Session Workflow (Localize/Plan/Treat)	Select the **Change Treatment Head** button from the treatment head panel. See *page 5-8*. A panel displays on the right side of the screen with instructions and a treatment arm pose button to facilitate changing the treatment head. • If the system was not calibrated with the new treatment head within the last 24 hours, the system will return to the System Check phase and you will need to create a new treatment session to continue. • The treatment head cannot be changed when the automated treatment task is active.

Pausing Automated Treatment

Press the voltage knob to pause automated treatment. When automated treatment is paused, a panel displays on the right side of the screen with a cooling timer and the following buttons:

- Abort Automated Treatment
- Resume Automated Treatment

Important

The Resume Automated Treatment button will not be selectable until the displayed cooling timer completes its countdown.

Reasons for pausing automated treatment:

- To inspect and remove trapped air or bubbles from the underside of the treatment head or from patient's skin
- Adjust image settings to enhance quality
- Adjust voltage
- Rotate the imaging transducer to view and evaluate the targeted tumor in other planes (this can also be performed while automated treatment is active)
- Adjust the ultrasound medium level

Resuming Automated Treatment

Caution

Resistance detection must be recalibrated if changes to the setup are made after calibrating resistance detection. Failing to recalibrate may prolong or prevent the completion of the procedure. Setup changes include:

- Adjusting bed height
- Adding or removing ultrasound medium
- Repositioning the frame

1. Before resuming, verify that setup has not changed and that the PTV still aligns to the targeted tumor.
2. Select the **Resume Automated Treatment** button
3. Select the **Enable Voltage Knob** toggle.
4. Press the voltage knob.

Important

To ensure adequate therapy coverage, automated treatment continues in a focal zone that was treated just prior to pausing.

Aborting Automated Treatment

1. If not already paused, press the voltage knob to pause automated treatment.
2. Select the **Abort Automated Treatment** button. The Review Treatment screen displays.

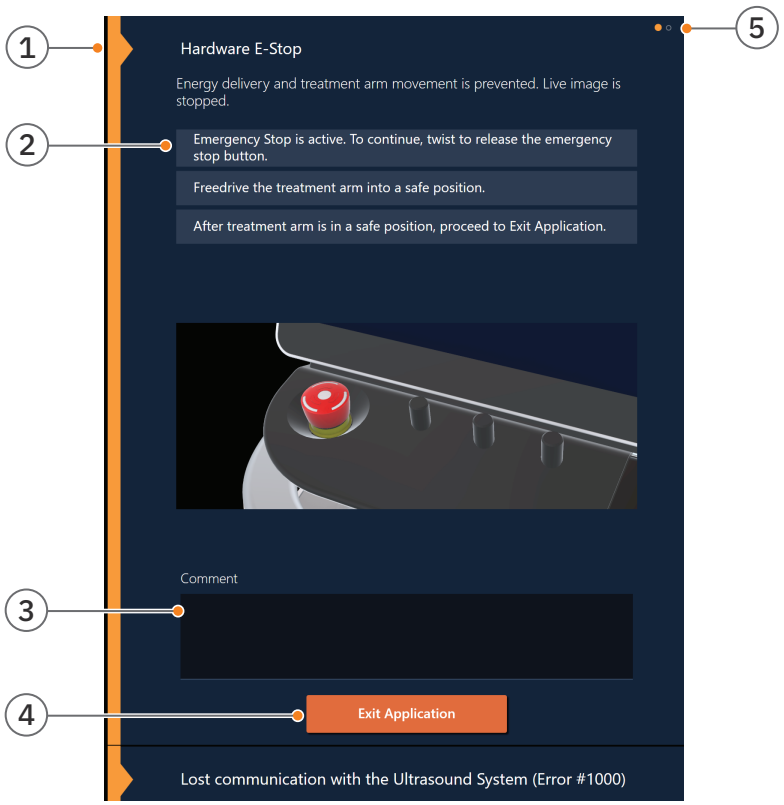
Important

Certain situations require aborting automated treatment. Reasons include:

- Patient emergency (refer to *Patient Emergency on page 2-26*)
- Need to adjust the treatment head angle
- Need to reposition the patient

Error Notifications

Display in a panel on the right side of the screen. If there are multiple errors, the highest priority error presents first.



①	**Error notification**	Brief description of the error.
②	**Instruction steps**	Instructs how to resolve the error to continue or what action to take before exiting the procedure.
③	**Comment field**	Comments can be added to the treatment report.
④	**Button(s)**	Used for actions such as navigating to a previous task in the workflow to make necessary adjustments, confirming steps were performed, or exiting the application.
⑤	**Fault progression indicator**	When there is more than one error notification, this indicator shows progression through the errors.

6 Operation

Step-by-step instructions for operating the system from setup to storage.

Inspect Before Use

Warning

Failure to inspect the treatment cart and treatment head can result in risk to the patient or user.

Inspect the treatment head for damage before every use. Do not use the treatment head if there are any signs of damage, including, but not limited to, cracks, chips, dents, frayed wires, and compromised wire insulation. Do not use the treatment head if it has been dropped or roughly handled as internal damage may have occurred. Do not connect a damaged treatment head to the treatment cart. Immediately report any damage to HistoSonics.

Inspect the treatment cart power cord for damage before every use. Do not use a damaged power cord as it creates hazardous situations, including fire and electrical shock.

Use of components such as treatment heads, imaging transducers, and cables other than those specified by HistoSonics may result in increased emissions or decreased system immunity.

Caution

Do not use the coupling kit beyond its use-by date. An expired use-by date may indicate that the coupling kit accessories have physically degraded and are not safe to use.

- Membrane may form holes or rupture when filled with ultrasound medium
- Membrane cradle may fail to secure the membrane during the procedure
- Coupling oil may be rancid and cause skin irritation

All coupling kit accessories are single-use only. Do not reuse, as cross-contamination may occur.

Do not drop or roughly handle the treatment head as it may damage the therapy transducer or imaging transducer components. Take care when handling the treatment head, especially during setup and transport. Before removing or attaching the treatment head, ensure the imaging transducer is in the home position (fully retracted) to protect it against physical damage. Keep the imaging transducer in the home position during storage.

Failure to prepare a sufficient volume of ultrasound medium will delay the procedure.
A histotripsy procedure typically requires 13–15 liters of ultrasound medium.

Delivering energy through ultrasound medium that is insufficiently degassed can:

- Prevent the bubble cloud from generating and/or prevent a sustained bubble cloud
- Cause damage to the treatment head

Do not attempt to use the system with components other than those provided or specified by HistoSonics.

Caution

To prevent the risk of electric shock, do not touch the patient while simultaneously touching a USB port or video output port.

1. Verify that the coupling kit use-by date has not passed. Do not use any of its contents if the use-by date has passed.

2. Remove the membrane from its packaging and inspect for holes or other damage. Do not use if damaged.

3. Inspect the support arm for damage. Inspect the latches on the support arm frame. Do not use if damaged.

4. Verify that the system is clean. If there is visual contamination, clean before use. Refer to *Cleaning Protocol on page 8-3*.

5. Inspect the treatment head for cracks, bent or dented surfaces, and other physical defects indicative of damage. Do not use if damaged.

6. Inspect the treatment cart wheels for damage or excessive tread wear that could affect stability. Verify the wheel lock function. Do not use if the wheels are damaged to the point that stability could be impacted, and do not use if the wheels do not lock.

7. Inspect for loose fasteners on the treatment head and treatment arm mount. Do not use if the fasteners are loose.

8. Inspect all cables for signs of damage. For example, look for bent connection pins, broken or missing Ethernet cable retaining tabs, wire crimps, evidence of being crushed, fraying, damaged wiring insulation, or similar physical damage. Do not use damaged cables. Do not use a cable if you suspect it may be damaged internally. Inspection includes:

   - Treatment cart power cord
   - Treatment cable
   - I/O cable
   - Imaging transducer cables (handheld and treatment head imaging transducer)
   - Ethernet cables

Gather Equipment, Accessories, and Supplies

Equipment	REF
Treatment Cart	EDNTC1001
12 cm Treatment Head	EDNTH12
14 cm Treatment Head	EDNTH14
Fluidics System	HISFL1001 (Fluidics Cart) HISFK2001 (Fluidics Disposable Kit)
Ultrasound System	Samsung R20 (displays a HistoSonics label for identification)
Support Arm (includes Frame and Bed Rail Clamp)	EDNSA1001

Histotripsy Procedure Kit Contains the following kits	REF HISKT2000
Coupling Kit Included single-use accessories: • Membrane • Membrane Cradle • Inspection Mirror • Bubble Removal Tool • Coupling Band • Coupling Oil	REF EDNCK2001
Fluidics Disposable Kit Included single-use accessories: • Fill Cartridge • Waste Cartridge	REF HISFK2001

Equipment & Supplies (Not Supplied by HistoSonics)	Requirements
Procedure Bed	2.5 cm (1-inch) bed rail
Emergency Evacuation Container (EEC)	• Minimum volume: 18 liters • Shatter-resistant plastic
Scissors or similar tool	Able to cut the membrane
Ultrasound Gel	
Skin Marker	
Towel	
Absorbent Underpad	Approximately 43 x 61 cm (17 x 24 inches)

Substituting Fluidics Equipment

While the use of HistoSonics' Fluidics System is recommended, it is not mandatory if a site has a clinical water source that meets the required specifications. In lieu of HistoSonics' Fluidics System, the following equipment is required.

Equipment & Supplies (Not Supplied by HistoSonics)	Requirements
Dissolved Oxygen Meter	• Calibrated
Container	• Transparent • Shatter-resistant plastic • Graduated • Minimum volume: 18 liters • Minimum dimensions (height, width, length): 10.5 inches (27 cm) • Handles
Mobile Cart	• Minimum dimensions: Safely accommodates width and length of ultrasound medium container • Minimum support weight: 23 kg (51 lbs) • Casters
Transfer Cup	• Shatter-resistant plastic

Caution

Delivering energy through ultrasound medium that is insufficiently degassed can:

- Prevent the bubble cloud from generating and/or prevent a sustained bubble cloud
- Cause damage to the treatment head

Important

If HistoSonics' Fluidics System is not used, a dissolved oxygen meter is required to verify that the ultrasound medium is degassed to the required specification and is within the specified temperature range. Perform this verification before the system check and once more before the procedure. Refer to *Ultrasound Medium Specifications on page 10-2*.

Prepare Ultrasound Medium

Prepare ultrasound medium as instructed in the Fluidics System User Guide. The ultrasound medium must be prepared to the required specifications. Refer to *Ultrasound Medium Specifications on page 10-2*.

Position Equipment

Important

Position the treatment cart and ultrasound system equipment to allow Ethernet cable and imaging transducer connections.

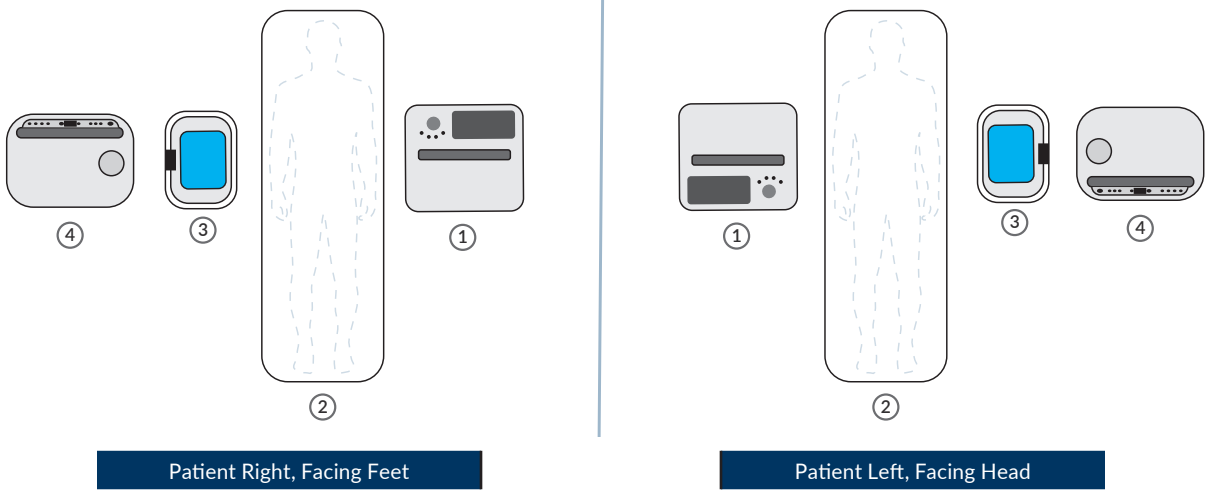
The system check can be skipped if one has been performed within 24 hours with the treatment head that will be used for the procedure.

1. Position the treatment cart near the bed. Orient the treatment cart for the preferred room setup (patient left or patient right).
2. Position the ultrasound system on the opposite side of the bed.
3. If a system check will be performed, position the fluidics cart between the bed and the treatment cart.

   Important

   The fluidics cart is only required to be next to the treatment cart when performing the system check.

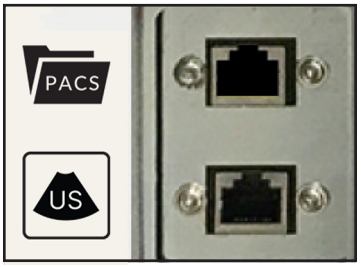
   The fluidics cart is only required to be next to the bed when filling or emptying the reservoir.



1. Ultrasound system
2. Bed
3. Fluidics cart
4. Treatment cart

Connect Systems

1. Using an Ethernet cable, connect the ultrasound system to the ultrasound port (US) port on the treatment cart.
2. If PACS will be used to import a study, use an Ethernet cable to connect the local network to the PACS port on the treatment cart.



3. Plug in the treatment cart and ultrasound system into dedicated power outlets. Do not power on the treatment cart yet.

Warning

To avoid the risk of electric shock, only power the treatment cart with an earthed, hospital-grade power outlet.

Caution

Connect the treatment cart power cord directly to a power outlet (mains connection). Do not use extension cords or power strips.

Important

Verify that you will be able to position the treatment cart and ultrasound system as required for the procedure before you plug them in and turn them on. Refer to *System Setup on page 6-14* for setup requirements.

Do not power the ultrasound system using its internal battery, as ultrasound imaging could be lost during the procedure.

Ready Ultrasound System

1. Connect the handheld imaging transducer and/or treatment head imaging transducer. For the systems to communicate, a live ultrasound image must be transmitted.

   Important

   Connect the treatment head imaging transducer to the far-right port to maximize available cord length.



2. Power on the ultrasound system.
3. Use your credentials to log in to the ultrasound system.
4. Enter patient information (or other unique procedure-related information). This information must be entered in order for the systems to save images and/or cine.
5. Set the ultrasound system to display from the imaging transducer in the treatment head.
6. Enable the **Histotripsy** imaging preset to improve visualization of the bubble cloud during the System Check.

Important

Failure to connect and power on the ultrasound system, as well as to connect an imaging transducer (handheld or treatment head) and transmit a live ultrasound image before powering on the treatment cart, will prevent system communication and cause an initialization error on the treatment cart.

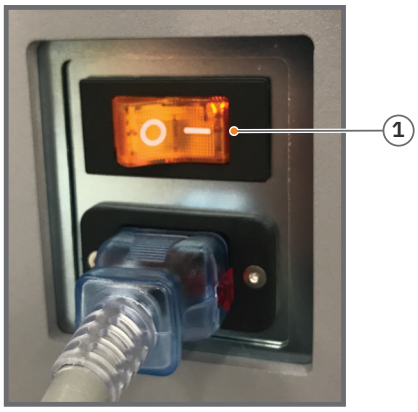
Important

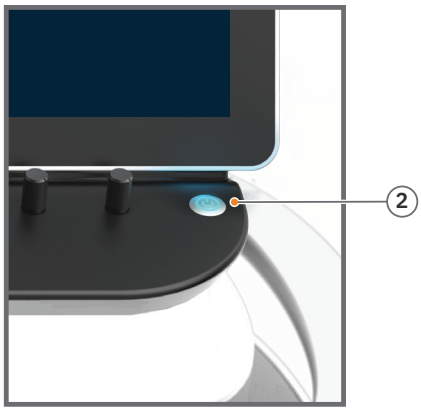
If the connection of the treatment head imaging transducer interferes with system positioning, it is recommended to initially connect only the handheld imaging transducer. This approach allows more flexibility for system positioning. The treatment head imaging transducer can be connected later in the setup process.

For Samsung R20 Ultrasound System safety and use information, refer to the manufacturer's instructions for use.

Ready Treatment Cart

1. Power on the treatment cart:
   a. Locate the main power switch on the connection panel. If it isn't already, move the switch to the on position.
   b. Press the power button on the control panel.





① Main power switch in the on position

② Power on (illuminated) on control panel

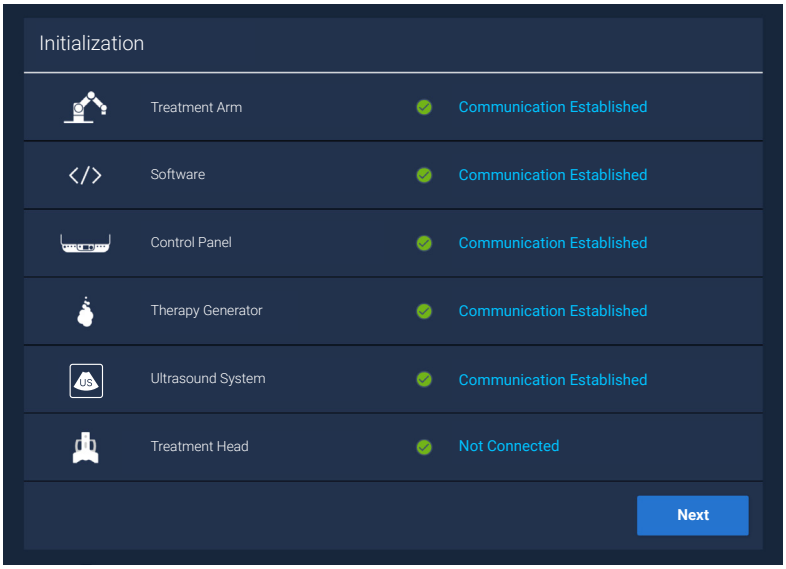
Log In

1. After startup, the Microsoft Windows™ login screen displays. Enter the virtual keyboard to enter your Microsoft Windows™ credentials. This waiting period allows the treatment arm to complete initialization.

Important
Credentials are provided at time of purchase or during training.
If the system is added to a Microsoft Active Directory, the Active Directory administrator controls what users will be able to access the system.

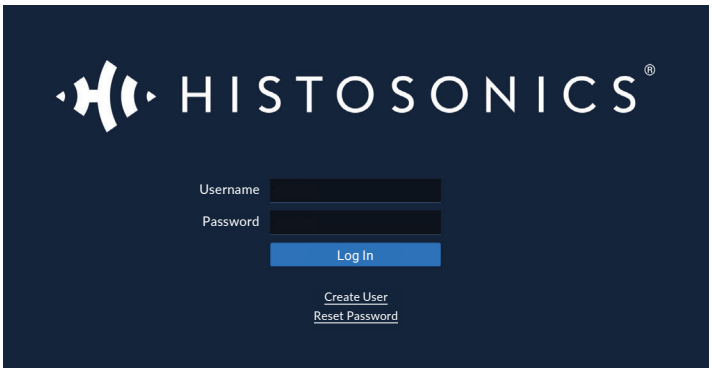
2. The application loads, the system performs an initialization check, and the results display.

Important
A treatment head is not required during initialization. The treatment head is typically connected during System Setup, so a Not Connected status is expected.
If an initialization error occurs, an error message will display with a resolution.



3. Select **Next**.

4. Enter your application credentials, then select **Log In**.



Important

Enter application credentials carefully. The system will impose a time-out after multiple unsuccessful login attempts.

For information about creating a user or resetting a password, refer to *Create User and Reset Password on page 5-4*.

System Setup

Important

The following sections include the corresponding task icon and task progression indicator (when they appear in the user interface). For example, this icon and progression indicator display on the first of three screens for the Prepare Treatment Head task.



Position Treatment Arm

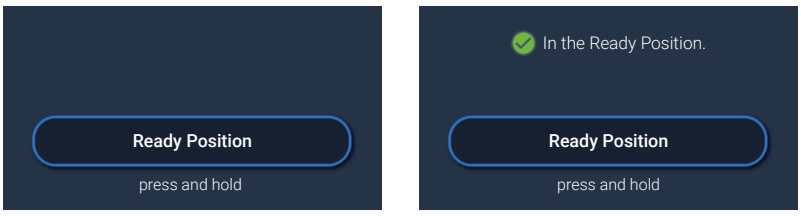
Caution

Before moving the treatment arm, verify that the treatment cable and imaging transducer cable are routed and have sufficient slack to allow the full range of motion required for the procedure. A snagged or tightly pulled cable can cause a fault that could delay the procedure.

Important

If a treatment head is already connected to the treatment arm, ensure that no external forces are being applied to it before selecting the **Ready Position** button. Any pushing or pulling on the treatment head may influence force monitoring and potentially extend the duration of the procedure.

1. Press and hold the **Ready Position** button until the treatment arm stops moving and the **In the Ready Position** message displays.
2. Select the **Next** button.



Prepare Treatment Head

Warning

Failure to confirm that the treatment head properly locks to the treatment arm can result in an impact injury to the patient or user and damage to the treatment head and I/O connection port.

Caution

Ensure that the area around the treatment arm is clear before moving the treatment arm. Do not touch the treatment arm when in use. Touching and/or pushing on the treatment arm when it is moving could result in a pinch injury and cause a fault, which could delay the procedure.

Important

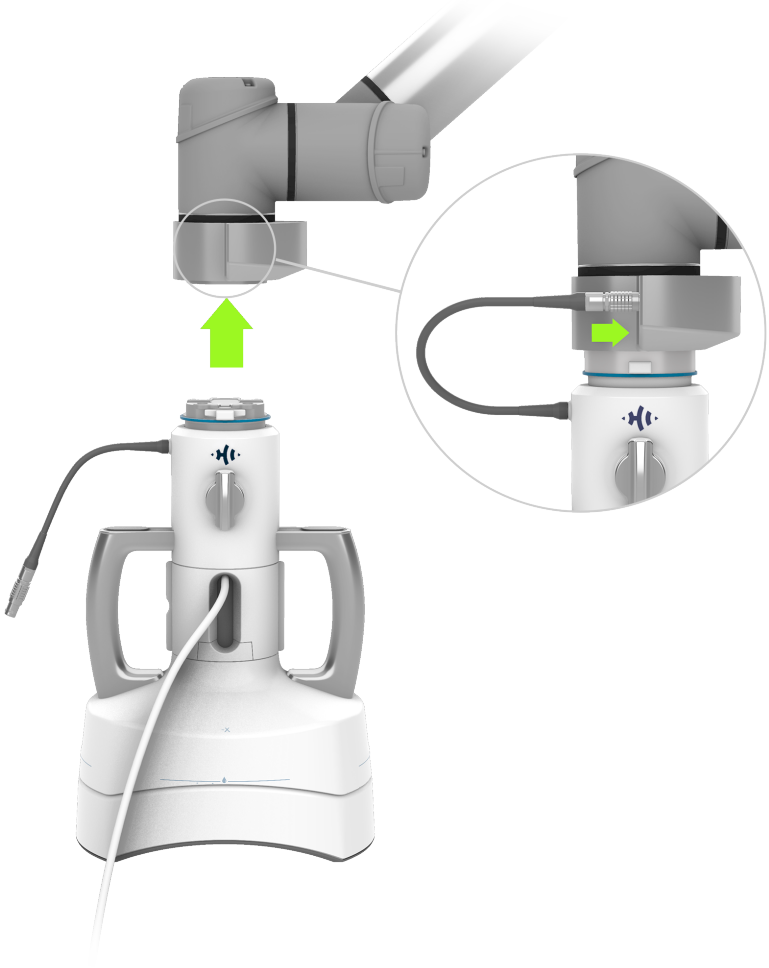
For information on which treatment head to use, refer to *Treatment Heads on page 4-8*.

It is recommended to perform the system check with both treatment heads. Performing the system check with both treatment heads helps prevent delaying the procedure should there be an unexpected need to switch treatment heads. To streamline setup, use the treatment head that is expected to be used for the procedure for the last (second) system check.

1. Attach treatment head:
   a. Angle the treatment head so the tab on the treatment head inserts into the groove on the treatment arm.
   b. Lift up on the opposite side of the treatment head to lock it into the treatment arm.
   c. Before releasing, confirm that the treatment head is locked to the treatment arm. An audible and haptic click occurs when it locks.

2. Connect the I/O cable to the receptacle on the treatment arm. To connect the I/O cable to the treatment head, align the connector's keyway with the corresponding slot on the receptacle, and then gently push the connector in until it clicks into place.

3. Select the **Next** button.



Prepare Treatment Head

Caution

Failure to use the electromagnetic interference (EMI) shield may result in EMI, which could cause malfunction in this system or surrounding equipment, potentially delaying the procedure.

1. Remove the splash guard panel from the treatment cart. To remove, pull on the bottom of the splash guard panel.
2. Connect the treatment cable to the treatment cart. Ensure that the connector is fully inserted, then turn the lever to lock.

   Important

   Before connecting, note the treatment head serial number on the connector label. The serial number is located after the SN symbol.

3. Place the EMI shield over the treatment cable connection, then push it into place to secure it around the port.



4. Route the treatment cable in the cable channel on the treatment arm.
5. If not already connected, ensure that both the treatment head imaging transducer and the handheld imaging transducer are attached to the ultrasound system.
6. Route the treatment head imaging transducer cable to avoid snags and allow for movement of the treatment arm.

7. Using the dropdown menu, select the serial number (SN) of the attached treatment head.



8. Replace the splash guard panel. Tilt the top of the panel in so the two tabs slide behind the frame, then press on the bottom of the panel.



1 Splash panel tab

9. If a study will be imported using a USB drive, insert the USB drive into the port on the side of the treatment cart.

10. Select the checkbox to confirm the EMI shield is attached.

11. Select the **Next** button.

Prepare Treatment Head

Caution

The system is only compatible with the B-mode ultrasound setting on the ultrasound system. Selecting other ultrasound modes (for example, Doppler, C-mode) during use may suspend progress and result in the loss of live ultrasound displayed on the system.

1. Configure the ultrasound system to display from the imaging transducer in the treatment head.
2. Enable the **Histotripsy** imaging preset on the ultrasound system to improve visualization of the bubble cloud during the System Check.

System Check

Warning

Failure to perform the System Check phase as instructed could result in incomplete or ineffective treatment, tissue destruction outside the PTV, or thermal or cavitation injury.

Important

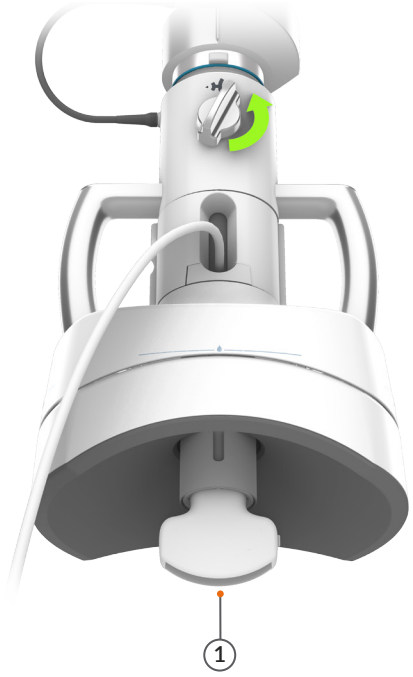
You can skip the System Check phase if it has been performed within the last 24 hours with the treatment head that will be used for the procedure. Selecting the **Skip System Check** link brings you directly to Patient Registration.

Position Imaging Transducer

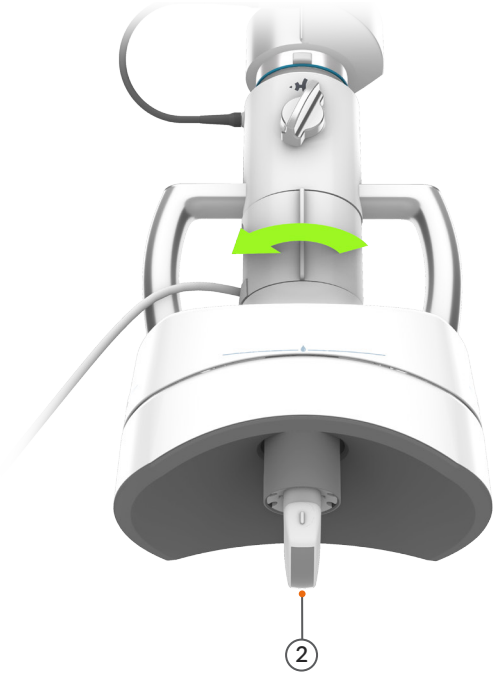
Important

Performing this task verifies that the system is correctly detecting and displaying imaging transducer extension and orientation. If the system detects an error, it will display a message and prevent progress.

1. Fully extend the imaging transducer. To fully extend, rotate the dial counter-clockwise until resistance is felt.
2. Rotate the imaging transducer to the +X position.
   - A detent can be felt when orienting the imaging transducer rotation lever to +X
   - Verify that the imaging transducer rotation lever is aligned to the +X mark on the top of the treatment head; do not verify by the orientation displayed on-screen
3. Select the **Confirm** button.



① Extended imaging transducer



② Imaging transducer aligned to +X

Position Imaging Transducer

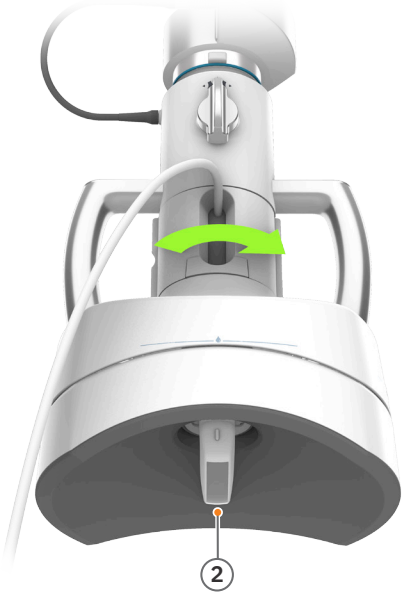
1. Fully retract the imaging transducer to its home position. To fully retract, rotate the dial clockwise until resistance is felt.

2. Rotate the imaging transducer to -Y.
   - A detent can be felt when orienting the imaging transducer rotation lever to -Y
   - Verify that the imaging transducer rotation lever is aligned to the -Y mark on the top of the treatment head; do not verify by the orientation displayed on-screen

3. Select the **Confirm** button.



① Retracted imaging transducer



② Imaging transducer aligned to -Y

Introduce Treatment Head

Caution

Do not deliver energy when air pockets or bubbles are trapped under the treatment head, as system damage can occur. Submerge the treatment head and remove all air pockets and bubbles as instructed in this user guide.

Be aware that changes to setup can introduce air pockets and bubbles under the treatment head. For example:

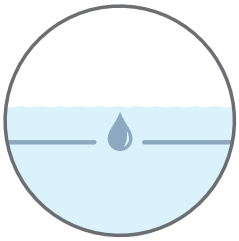
- Ultrasound medium level lowers (inadequate submersion)
- Treatment head is raised too high (inadequate submersion)
- Additional ultrasound medium is poured into the reservoir too quickly or too close to the treatment head

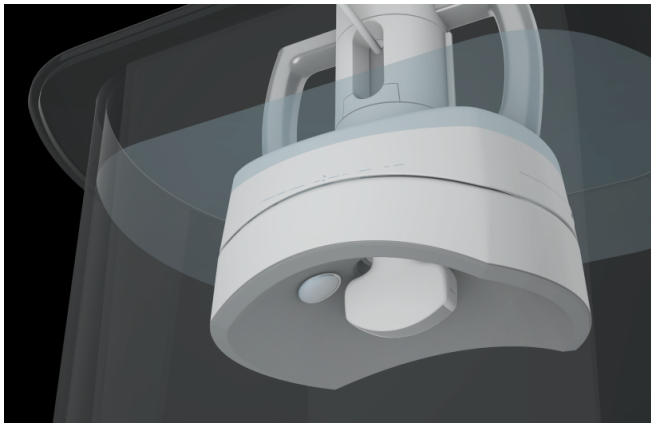
Never submerge the treatment head beyond the bottom of the notch on the imaging transducer rotation lever. Submersion beyond this point could allow ingress that could damage the treatment head.

Take care to prevent the inspection mirror from introducing bubbles or air pockets under the treatment head.

1. Position the treatment head over the system check container on the fluidics cart. The system check container must be filled with ultrasound medium that has been prepared to the required specifications. Refer to *Ultrasound Medium Specifications on page 10-2* and the Fluidics System User Guide.

2. Using freedrive or the space mouse, lower the treatment head in the ultrasound medium until **all four** submersion reference lines are at or under the surface of the ultrasound medium.





3. Using the mirror at the bottom of the system check container and the hand-held inspection mirror, inspect for air bubbles and air pockets under the treatment head. If air bubbles or air pockets are present, remove them with the bubble removal tool.

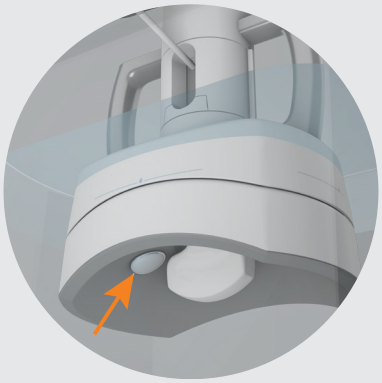
4. Select the **Next** button.

Important

Take care not to introduce air bubbles with the inspection mirror.

Avoid submerging the release valve on the bubble removal tool.

Air pockets typically form around the base of the imaging transducer and have a reflective, metallic appearance against the dark therapy transducer.



Calibrate Crosshairs

Warning

The imaging transducer must be aligned to -Y and in the home position (fully retracted) when calibrating crosshairs. Calibrating crosshairs when the imaging transducer is not oriented to -Y or is not in the home position can result in injury to the patient or incomplete treatment.

Caution

Before generating a bubble cloud for the System Check, use the live ultrasound view to ensure that the crosshairs are not positioned near the bottom of the system check container. Generating a bubble cloud on its surface could damage the container.

Do not exceed the voltage necessary to verify bubble cloud formation during the system check. Raising the voltage beyond what is required may cause the system to emit audible acoustic energy that exceeds 80 dBA, which could cause user discomfort or hearing damage.

Important

During the system check, the bubble cloud should form with a voltage setting between 19%–27%. The system will not allow you to continue with the voltage set lower than 19%, or higher than 27%.

The voltage setting is established when voltage is deactivated.

If the bubble cloud does not form near these voltage levels, it may indicate that the ultrasound medium is not adequately degassed or that the system is not performing to specifications.

When the toggle is selected (on), it simply permits utilization of the voltage knob on the control panel to activate/deactivate energy and adjust voltage. The toggle cannot be selected again to disable the voltage knob or stop energy delivery.

There is a 30-second time limit to initiate energy. If the time lapses, select the **Enable Voltage Knob** toggle again to reset the time limit, then continue.

1. Select the **Enable Voltage Knob** toggle.



① Default toggle position (off position)

② Toggle selected (on position)

2. Press the voltage knob to activate it. The voltage is set to 0% by default.
3. Rotate the voltage knob to increase voltage until you can visualize a sustained bubble cloud.
4. Use the trackpad to mark the center of the bubble cloud.

Important
The crosshairs move to the location marked by the physician. Marking the center of the bubble cloud corrects for any offset (calibrates the crosshairs).
The trackpad provides better accuracy than the touchscreen.
If needed, use the fine adjustment arrows (up, down, left, right) to refine the position of the crosshairs over the center of the bubble cloud.

5. Press the voltage knob to deactivate the knob and stop energy delivery.
6. The calibration results display:

Offset	Y ± mm Z ± mm	Distance that the crosshairs moved for calibration.
Offset Limit	Within range/ Out-of-range	Indicates if the offset is within the acceptable range. Out-of-range indicates that the distance is too great to allow calibration, which may indicate that there is an issue with setup or equipment.
Voltage	Within range/ Out-of-range	Indicates if the voltage used to form the bubble cloud was within the typical range. Out-of-range indicates that the voltage was too high or too low to allow calibration, which may indicate that there is an issue with setup or equipment.

7. If the results are within the typical voltage range and the bubble cloud was sustained, select the **Accept** button.

Important

If the results are out of range, or if the results are not acceptable to you, check setup and repeat the steps in this section. If the problem persists, contact HistoSonics.

Calibrate Crosshairs

1. Press and hold the **Raise Treatment Head** button to remove the treatment head from the system check container.



2. Select **Accept**. The Patient Registration screen displays.

Important

To perform the system check with the other treatment head, go to the Patient Registration screen, select **Return to System Setup** from the main menu, remove the attached treatment head, and repeat the System Setup workflow.

Patient Registration

Caution

Use the patient data protection precautions and procedures required by your institution's protected health information data management policies to protect created and stored patient data.

Import or Skip Study, Then Add and Start Session

This section explains how to import a study or proceed without import, then add and start a treatment session.

Important

Importing a study is at the physician's discretion. When importing, patient details are automatically pulled from the imported study.

Study requirements:

- DICOM format
- MR or CT images
- 2 mm maximum slice spacing
- A study must be imported before fusing images; if slice spacing exceeds 2 mm, images may not fuse correctly

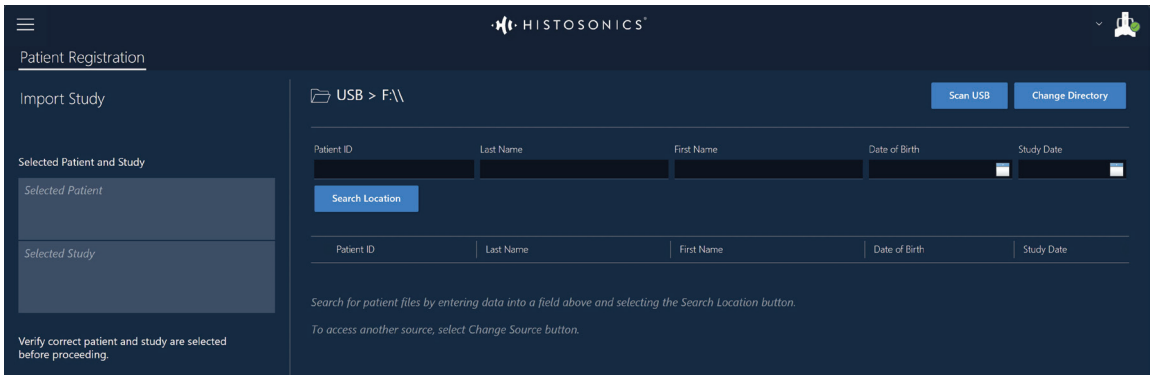
Studies can be imported from either a USB drive or PACS. Follow the steps based on the source:

- **USB Drive**: If the USB drive was not inserted during setup, insert it now, then select the Scan USB button
- **PACS**: Select the Change Directory button, then use the menu to select the PACS directory

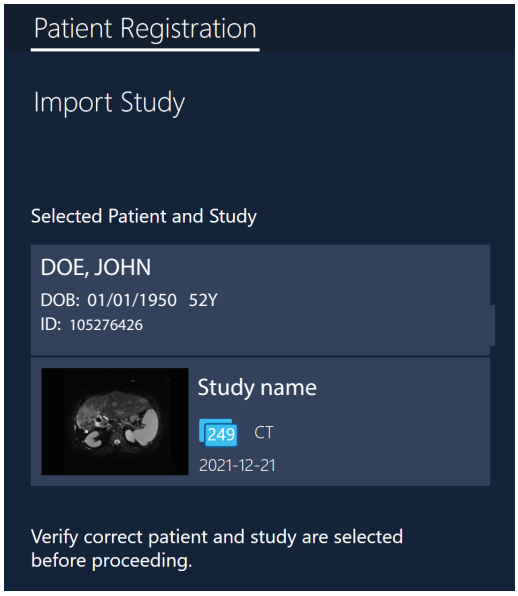
To bypass study import, select Skip Import. The Enter Patient Details will display for manual entry.

Skipping patient detail entry using the Skip Patient Details link prevents the Treatment Session Record from being retrieved after exiting the application.

1. Enter search criteria in fields. For example, enter the patient ID.



2. Select the **Search Location** button. Available results display.
3. Select the desired study. The study details thumbnail display.



4. Select the **Next** button.
5. Select the study, then scroll through the reference images to verify the study.
6. Select the **Add Session** button.
7. Enter the treatment session details.

Important

Use DD/MM/YYYY format when entering the procedure date.

8. Select the **Start Session** button to proceed to the treatment session.

Important

If you are pre-registering a patient before a procedure, select the **Save Session** button, then exit the application.

If you are starting the session, there is no need to first select **Save Session**, as it will be saved automatically.

Localize

Prepare Patient

Caution

Selecting the wrong room setup button will result in inverted images and prevent successful completion of the fuse images task.

To prevent the risk of electric shock, do not touch the patient while simultaneously touching a USB port or video output port.

1. Select the room setup button that indicates how the patient will be oriented in relation to the treatment cart.
2. Select the **Next** button.



① Patient Left, Facing Head

② Patient Right, Facing Feet

Prepare Patient

Caution

Never attempt to move or shift the patient using the membrane cradle as it could result in patient injury and damage to the membrane cradle.

1. Lay the membrane cradle across the bed as shown. Position it so it will be centered under the patient when they are on the bed.

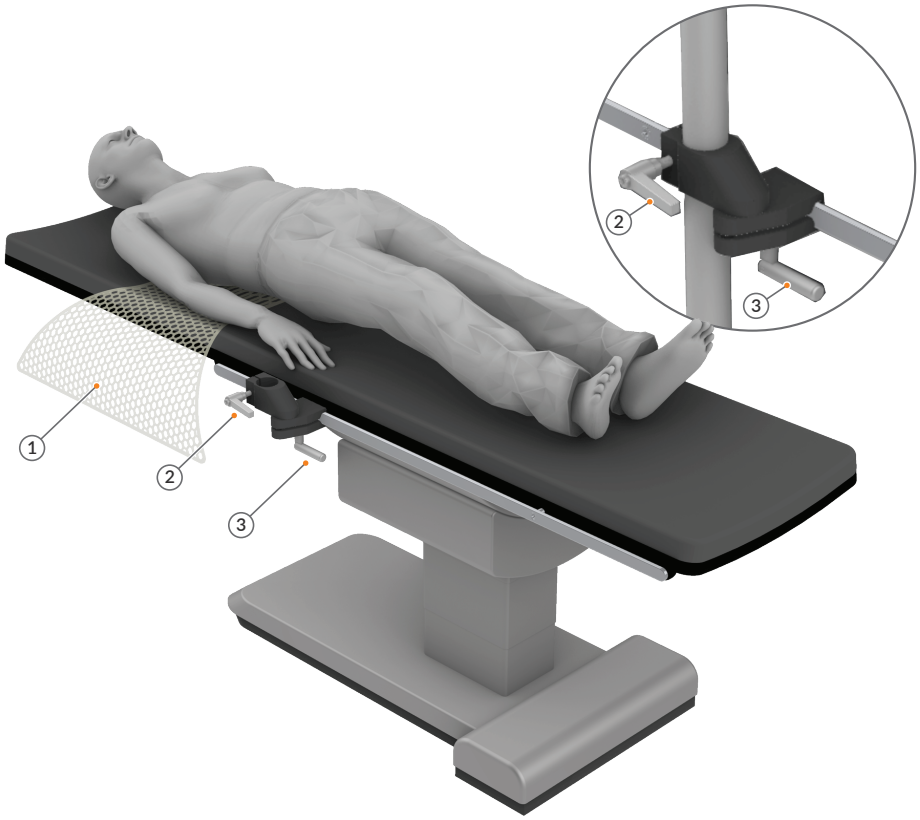
   Important

   Optional: Cover the membrane cradle with an absorbent underpad to prevent the patient from getting temporary red marks on their skin due to lying directly on the membrane cradle.

2. Position the patient on the procedure bed as required for the procedure. The displayed image is only a representative example with the patient in the supine position.
3. Attach the bed rail clamp to a 2.5 cm (1-inch) bed rail on the preferred side of the bed. Rotate the bed rail clamp lever clockwise until the bed rail clamp is secured.

   Typical bed rail clamp placement is:

   - Opposite the treatment cart
   - Between the patient's hip and knee
4. Insert the support arm into the bed rail clamp friction ring. Rotate the friction lever clockwise until the support arm is secured.
5. Select the **Next** button.



① Membrane cradle ② Support arm friction lever ③ Bed rail clamp

Prepare Patient

Caution

Failure to prepare the patient's skin, apply coupling oil, and remove all bubbles and air pockets as instructed will prevent the membrane from acoustically coupling with the patient's skin, preventing visualization in the live ultrasound view.

Be aware that changes to setup can introduce air pockets and bubbles under the membrane or lift it away from the patient's skin.

Do not deliver energy or begin automated treatment if the membrane is not acoustically coupled to the patient's skin, as the following can occur:

- Surface cavitation resulting in patient skin injury
- Incomplete treatment

Coupling oil (castor oil) may cause skin irritation, and patients with an allergy to castor oil may develop hives or rash.

1. Remove body hair from the target area.
2. Configure the ultrasound system to display from the handheld imaging transducer.
3. Enable the **Abdomen** imaging preset on the ultrasound system to improve visualization in the region of interest.
4. Using the handheld imaging transducer, assess the patient's anatomy relative to the planned energy pathway to find the optimal position for the treatment head. Adjust the patient's position as needed.
5. Use a skin marker to mark the target location and other relevant landmarks.



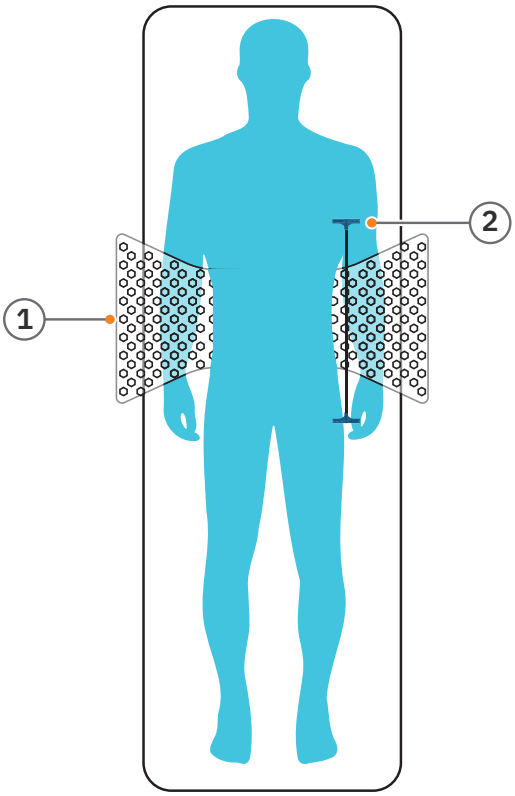


6. Remove the ultrasound gel from the patient's skin.
7. Using a gloved hand, apply coupling oil liberally to the patient's skin and spread it to cover all areas where the membrane will contact the skin.

Important

Coupling oil enables acoustic coupling between the membrane and the patient. Some absorption into the skin is normal, but sufficient oil must remain on the surface to maintain effective coupling.

8. Place the patient's arms under the membrane cradle.
9. Lay the coupling band over the membrane cradle on the preferred side of the patient.
10. Select the **Next** button.



① Membrane cradle is over patient's arms

② Coupling band is placed on membrane cradle

Prepare Patient

Caution

Delivering energy through ultrasound medium that is insufficiently degassed can:

- Prevent the bubble cloud from generating and/or prevent a sustained bubble cloud
- Cause damage to the treatment head

Failure to prepare a sufficient volume of ultrasound medium will delay the procedure.
A histotripsy procedure typically requires 13–15 liters of ultrasound medium.

Do not overfill the reservoir as it adds additional weight on the patient and may cause the ultrasound medium to overflow when the treatment head is introduced.

Leaks from holes in the membrane or from an improper seal between the frame and the membrane may introduce air into the ultrasound medium. If a leak is detected, immediately stop energy delivery and address the leak. Never assemble the frame without the membrane as doing so can damage the frame gasket.

The weight of the ultrasound medium can cause the end of the frame to sag slightly, placing pressure on the patient which could lead to a medical device related pressure injury if the frame rests against the patient for an extended period.

Before transferring ultrasound medium into the reservoir, verify that there is at least 6 cm (2.5 inches) between the frame and the patient to allow for sagging. For patients with compromised skin integrity, consider cushioning or protecting the skin with dressings in high-risk areas.

Allow for slack when attaching the membrane cradle to the frame; do not stretch or pull the membrane cradle taut as it will place unnecessary pressure on the patient's skin which could lead to a medical device related pressure injury if pressed against the patient for an extended period.

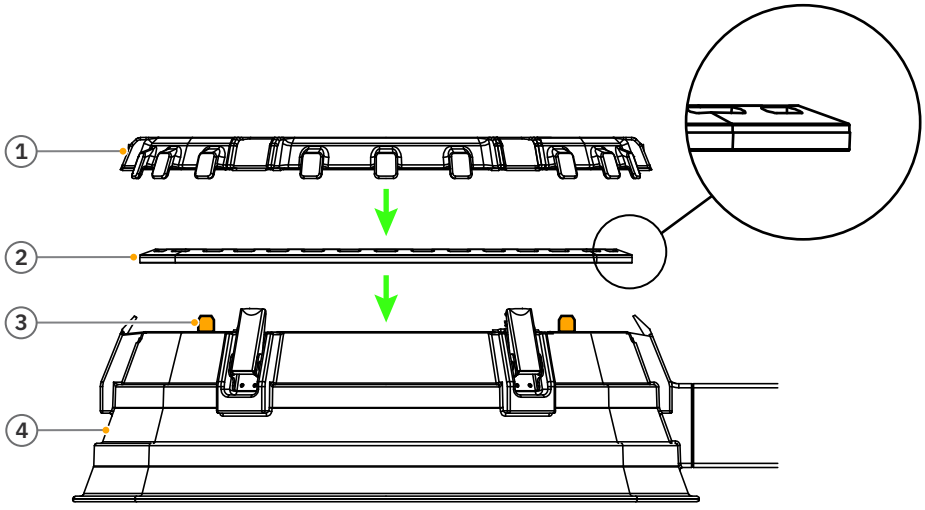
It is normal for the patient to have some temporary red marks on their skin as a result of lying on the membrane cradle during the procedure.

Failure to secure the membrane with the membrane cradle may allow the membrane to bulge or sag, which could:

- Lift the membrane off the patient's skin
- Lower the ultrasound medium level and allow air under the treatment head

Bubbles and air pockets between the membrane and patient's skin can prevent visualization and lead to surface cavitation during energy delivery, resulting in patient injury or incomplete treatment.

1. Attach the membrane to the frame. Using the support arm, rotate the frame so that it is upside down to ease installation.
2. Place the membrane on the upper half of the frame. The membrane has a bowl-like shape that should appear upside down, as shown in the illustration detail bubble. The membrane must be within all four tabs on the upper half of the frame.
3. Place the lower half of the frame over the membrane. If the lower half of the frame does not fit over the membrane, verify the orientation of the membrane.



1. Frame (lower half)
2. Membrane
3. Tab
4. Frame (upper half)

4. Use all eight latches to secure the lower half of the frame to the upper half of the frame.
5. Using the support arm, rotate the frame so that it is right-side-up.

6. Using the support arm, position the frame so that it is over the mark on the patient's skin. The frame should be positioned so that:
   - The treatment head will have the full range of motion necessary for the procedure and will not contact the frame
   - The frame remains approximately 6 cm (2.5 inches) above the patient to prevent frame-to-patient contact and/or excess pressure if it sags from the weight of the ultrasound medium
   - Secure both ends of the membrane cradle to the frame by looping open cells over frame hooks; allow for some slack in the membrane cradle and do not stretch it taut

Important

Before continuing, assess the position of the frame and make necessary adjustments. Try to avoid making changes to the frame position after the reservoir is filled. After the reservoir is filled, the support arm can be used to make small adjustments to the position of the frame. However, the use of an assistant is recommended to help support the frame, keep the frame as level as possible to prevent spillage, and help prevent the membrane from excessive expansion. Keep the membrane cradle attached when making adjustments to help prevent excessive expansion.

7. Using the fluidics system, fill the reservoir until the ultrasound medium is above where the upper half and lower half of the frame meet.

8. Verify there are no leaks between the upper half and lower half of the frame or through the membrane material.

Important

If a leak is observed, check that all latches are engaged.

If the frame latches are equipped with screws, one or more latch screws may need to be tightened to increase latch pressure. To tighten latch screws:

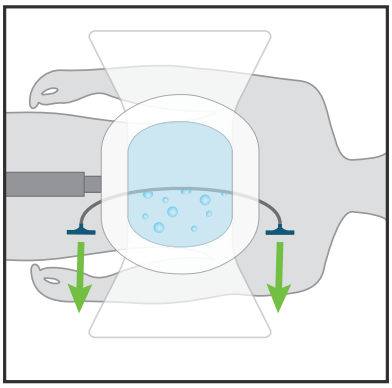
a. Remove all ultrasound medium.

b. Use your hand or a Phillips screwdriver (PH1) to tighten the latch screw nearest to the leak. Do not to overtighten, as excessive pressure may shift the seal and create a leak on the opposite side or make the latch too hard to close without applying excessive force.

c. Refill with ultrasound medium.

d. If the leak persists, tighten the screw further or tighten adjacent latch screws.

9. Holding both coupling band handles, slowly pull the coupling band between the membrane and the patient's skin. As it moves, observe the coupling band through the membrane as it spreads coupling oil and removes bubbles. Repeat this step if any bubbles remain. Ensure the room lighting is sufficient to detect bubbles under or on top of the membrane.



10. Continue filling the reservoir to desired level.

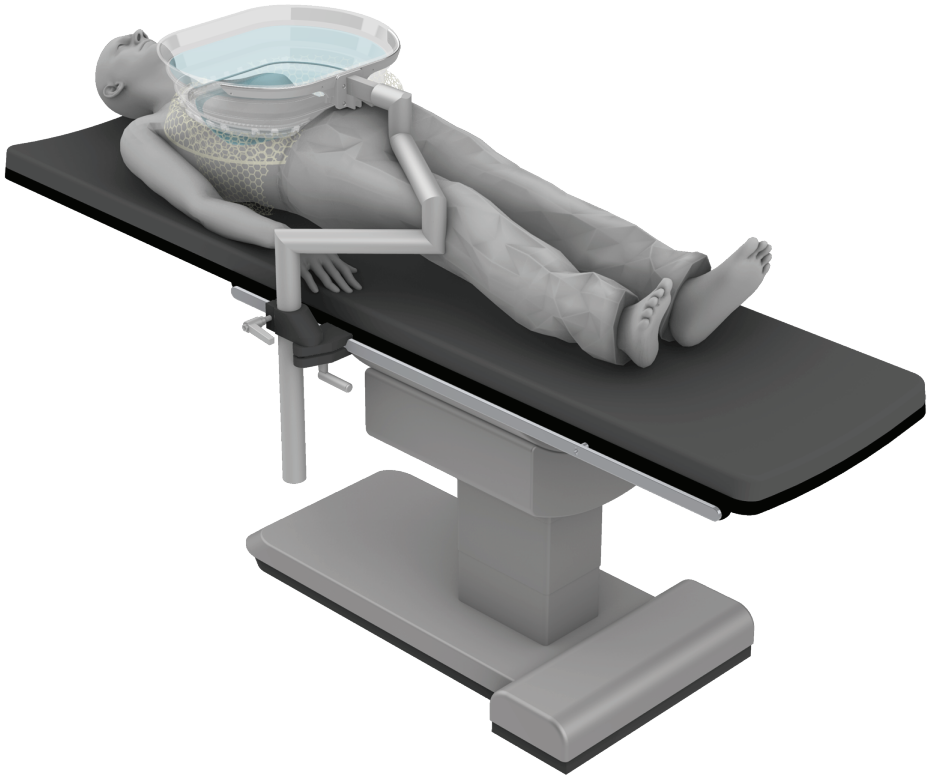
11. Inspect the top of the membrane for bubbles. If present, put on a clean glove, submerge your gloved hand into the ultrasound medium, and gently wipe away the bubbles.

12. Configure the ultrasound system to display from the imaging transducer in the treatment head.

13. Select the **Next** button.

Important

Bubbles or air pockets can form under the membrane if it moves or is adjusted on the patient and/or if the membrane sags after setup. Inspect for air pockets after making any adjustments to the patient or membrane.

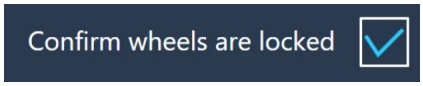


Prepare Patient

Warning

Failure to lock the bed position and lock the treatment cart wheels before energy delivery may result in patient injury.

1. Position the treatment cart for the procedure.
2. Set the bed at the preferred height for the procedure, then lock the bed position.
3. Lock the treatment cart wheels, then select the box to confirm that the wheels are locked.



4. Select the **Next** button.



Calibrate Resistance Detection

Caution

Failure to calibrate resistance detection as instructed may prevent the procedure from proceeding due to resistance limit detection.

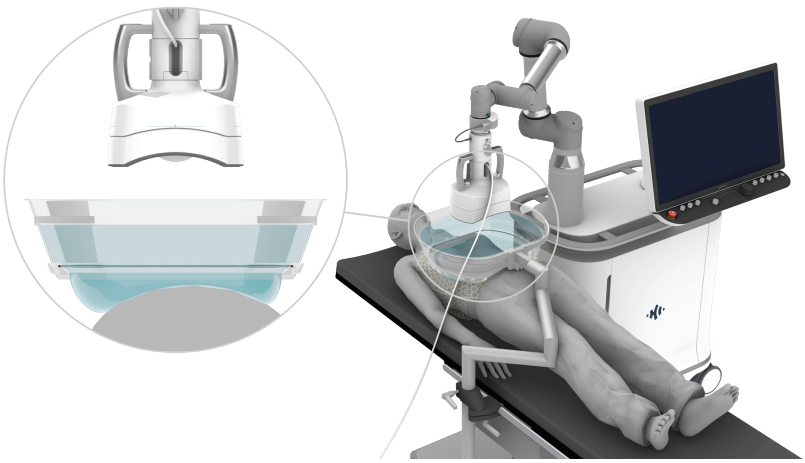
Resistance detection must be recalibrated if changes to the setup are made after calibrating resistance detection. Failing to recalibrate may prolong or prevent the completion of the procedure. Setup changes include:

- Adjusting bed height
- Adding or removing ultrasound medium
- Repositioning the frame

When calibrating resistance detection, verify that nothing is pushing or pulling on the treatment head.

Before moving the treatment arm, verify that the treatment cable and imaging transducer cable are routed and have sufficient slack to allow the full range of motion required for the procedure. A snagged or tightly pulled cable can cause a fault that could delay the procedure.

1. Position the treatment head above the ultrasound medium.
2. Press and hold the **Level Treatment Head** button until movement stops and the Complete message displays.
3. Select the **Next** button.



Calibrate Resistance Detection

Caution

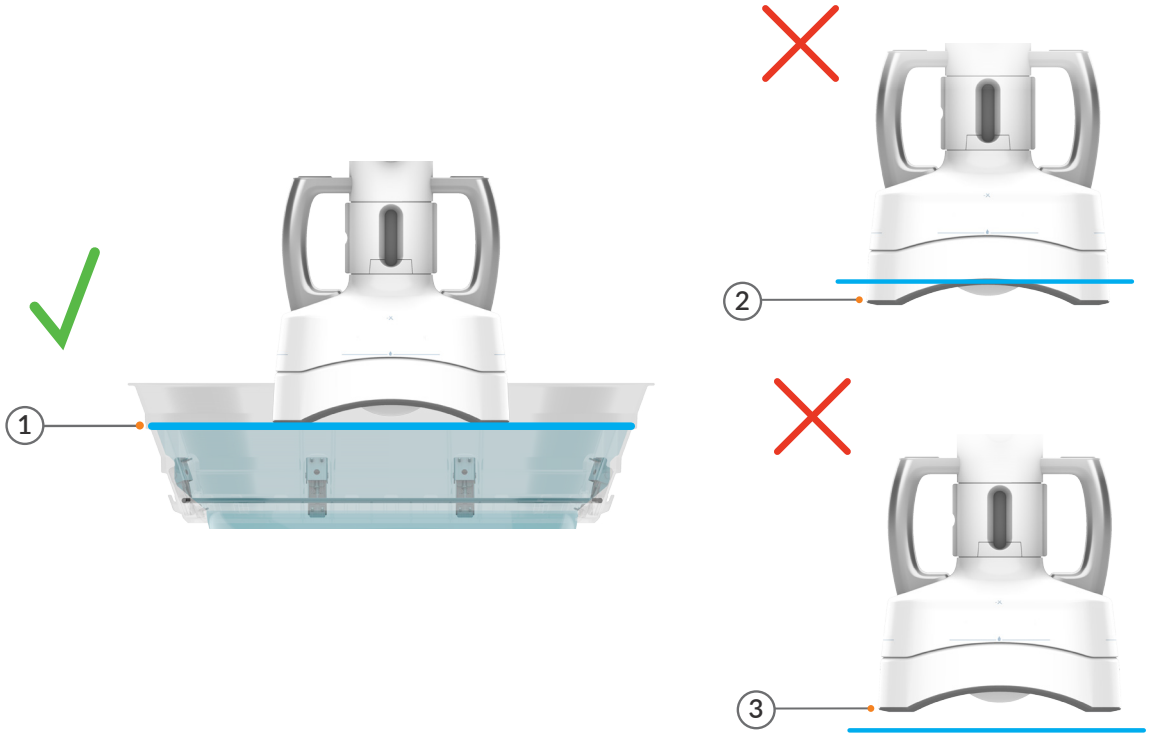
Do not submerge the treatment head when calibrating resistance detection; the treatment head should just touch the surface of the ultrasound medium.

Never submerge the treatment head beyond the bottom of the notch on the imaging transducer rotation lever. Submersion beyond this point could allow ingress that could damage the treatment head.

Important

Even after resistance detection is calibrated, always slow movement whenever the treatment head nears the patient or an object, and monitor resistance detection when moving the treatment head.

1. Use the space mouse to lower the treatment head until its bottom edge just touches the ultrasound medium.
2. Select the **Next** button.



1. Correct: Edge touching ultrasound medium
2. Incorrect: Submerged treatment head
3. Incorrect: Edge not touching surface

Fuse Images

Caution

Take extra precautions when moving the treatment head when its imaging transducer is extended to prevent the imaging transducer from colliding with the frame or patient, as it could cause a fault that could delay the procedure.

During the fuse images task, the sweep (recording) must capture the region of interest. Using a different region to fuse images will result in inaccurate imaging.

Important

If a study was not imported, the fuse images task will not display. If a study was imported, but you do not want to fuse images, select the **Skip Fusion** link to go directly to the Plan phase.

The ultrasound system must be set to the **Abdomen** imaging preset during the Fuse Images task.

Adjust the imaging parameters on the ultrasound system to achieve optimal image quality.

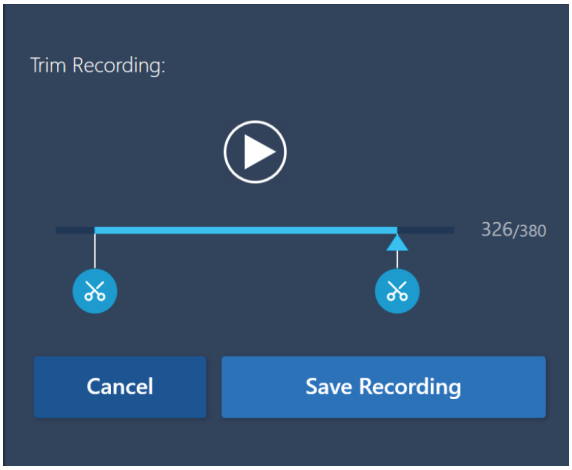
If the patient, bed, or treatment cart moves during the fuse images task (between the sweep and fusion), verify that the images align before proceeding. Movement or shifting may require another fusion.

Air pockets or large bubbles will produce shadows and/or reflection artifacts and will prevent a clear image of the anatomy.

1. Fully extend the imaging transducer, then submerge the treatment head in the ultrasound medium.
2. Lower the treatment head until the imaging transducer provides optimal visualization of the region of interest. Typically, this occurs when the imaging transducer just comes into contact with the membrane, although contact is not strictly necessary.
3. Verify the region of interest is visible in multiple planes.
4. Rotate the imaging transducer to -Y. The imaging transducer must be oriented to -Y to perform the sweep.
5. Start the breath hold, then select the **Breath Held, Start Sweep** button. The automated sweep starts.
6. Release the breath hold when the sweep completes.

Fuse Images

1. Select the play button and review the recording to ensure that the region of interest was captured in the sweep.
2. Trim frames from the recording where the region of interest is obscured. Trim as little as possible. To trim:
   a. Select and drag the trim controls (scissors icons) to the desired frames.
   b. Play the recording to review the results. Adjust the trim if necessary.
   c. Select the **Save Recording** button to apply the trim settings.
3. Select the **Next** button.



Fuse Images

1. Scroll through the ultrasound recording and reference images to locate an easily identifiable landmark in the region of interest (for example, a vessel bifurcation). The landmark must be visible in both the ultrasound recording and the reference images.
2. Activate the **A–Registration Point** button.
3. Using the trackpad, place a registration point on the same landmark:
   - Once in the ultrasound recording
   - Once in a reference image
4. Verify the registration point in both axial and sagittal views.
5. Activate the **B–Registration Point** button, then repeat the scroll, mark, and verify steps to add a second registration point.

Important

Pairs of registration points are identified by the same letter. For example, the letter "A" displays next to the first pair of registration points.

Color indicates the view used to place the registration point.

- Green dot = placed in ultrasound recording
- Red dot = placed in reference image

To correct a registration point location, simply place a new registration point: the previous point is replaced.

The number of registration point pairs to place depends on the degree of alignment between the ultrasound recording and the reference images:

- One pair of registration points (A) is required
- Two pairs of registration points (A and B) are recommended when the ultrasound recording and reference images are approximately aligned
- Three pairs of registration points (A, B, C) is recommended if the ultrasound recording and reference images are substantially misaligned

The **Add Registration Point** button displays after placing pairs A and B. Select it, then repeat the steps in the section to add an additional set of registration points (C).

To delete a registration point (or pair of registration points), select the X on the button.

This icon appears on a registration button after both registration points have been placed. Selecting a button with this icon will set the scroll bars back to the positions they were in when the points were placed.



6. Select the **Fuse** button. The Static Fused Images view displays (static ultrasound image fused with static reference image).

7. Review the fused images and adjust the registration, if necessary.
   - Scroll through the axial and sagittal planes
   - Review alignment throughout the region of interest using identifiable landmarks (for example, a vessel bifurcation) to check alignment
   - If desired, display the registration points (eye icon), then review the distance between a pair of registration points (for example, the distance between red point A and green point A)

8. Select the **Next** button. The Live Fused Images view displays.

Important

The following settings or features are available to perform the review:

- Measuring tool
- Change the blending mode: color or grayscale
- Hide static ultrasound or adjust its opacity (50% is the default opacity)
- Display the registration points (hidden by default)

Select the **Adjust Registration Points** button to modify registration points. Selecting returns you to the beginning of the fuse images task.

The diversion limit is the maximum distance that the image-based algorithm allows registration points to diverge (move away) from each other when fusing images. By default, the diversion limit is set to 10 mm for all pairs of registration points.

The physician can adjust the divergence limit for each pair of registration points. For example, to prioritize registration set A, the physician can set a 2.5 mm divergence limit.

If a diversion limit is changed, the fuse images task must be repeated.

To adjust divergence limits:

a. Select the **Advanced Settings** button.

b. If not already active, select the registration point eye icon to display registration points and the divergence limit controls.

c. Registration point A is selected by default. Select **2.5 mm**, **10 mm**, or **20 mm**.

d. If needed, use the drop-down menu to select other pairs of registration points, then select their divergence limit.

e. Select the **Fuse** button.

Important

The reference image can be manually aligned to the ultrasound image. To manually align:

a. Select the **Advanced Settings** button.

b. Activate the drag  and rotate tools  as needed.

c. Using the trackpad, drag/rotate the reference image so that it aligns to the ultrasound image.

The drop-down menu on the workflow panel facilitates the display of different stages in the fuse images process. Each subsequent stage is built upon the outcome of the preceding one:

Original
No alignment

Landmarks aligned

Aligned with registration points

Landmarks aligned with deformation
Aligned with registration points and by conforming reference images

Automatic registration
Aligned with registration points, by conforming references images, and using an image-based algorithm

If a second fusion is performed, the drop-down menu can be used to select previous results for comparison. All selections are timestamped for identification.

Fuse Images

1. Use the space mouse to move the treatment head and verify that the anatomy is aligned throughout the region of interest.
2. Rotate the imaging transducer and verify that the anatomy is aligned in multiple planes.
3. If fusion results are acceptable, select the **Next** button.

Important

If the fusion results are not acceptable, consider selecting the **Repeat Sweep** button to perform a new sweep.

Warning

After fusing images, always verify that images still align in the Live Fused Images view after making any of these changes:

- Swapping the treatment head
- Adjusting the patient or bed
- Adjusting the treatment cart position
- Adding or removing ultrasound medium

Repeat the fuse images task if images no longer align.

Plan

Position Contours

Warning

Delivering therapeutic ultrasound when anatomical or other obstructions (bone, cartilage, lung, digestive gas, etc.) are along the acoustic pathway can result in thermal injury to non-targeted tissues. Use imaging and the acoustic field indicator overlay to assess and minimize obstruction prior to finalizing the treatment plan.

Anatomical or other obstructions (bone, cartilage, lung, digestive gas, etc.) as well as acoustic aberration along the acoustic pathway can result in mechanical (cavitation) injury to non-targeted tissues.

- Use imaging and the acoustic field indicator overlay to assess and minimize obstructions prior to finalizing the treatment plan
- Monitor the location of the bubble cloud throughout the treatment using real-time ultrasound imaging and suspend therapy if the bubble cloud is not within the PTV

Delivering therapeutic ultrasound when lung tissue is located along the acoustic pathway can result in localized pulmonary tissue edema or hemorrhage. Use imaging and the acoustic field indicator overlay to assess if lung is along the acoustic pathway prior to finalizing the treatment plan. Consider using alternate angles to avoid lung tissue.

Always verify that the PTV encompasses the target tissue (tumor and desired margin) in multiple planes. Misalignment of the PTV can result in unwanted tissue destruction, incomplete treatment, or both.

Respiration may cause the targeted tissue to move relative to the PTV, causing the treatment zone to be larger than the PTV. The system does not account for respiratory motion. Observe the PTV and targeted tissue throughout the respiratory cycle to assess the relative impact of respiratory motion on the treatment plan. Adjust the plan as necessary to ensure safe treatment.

Consider patient-specific risk factors for acute kidney injury (AKI) and/or renal failure based on clinical history and procedural scenarios that may increase stress on kidney function. Factors to consider include, but are not limited to, hydration status, planned treatment volume, number of treatment sessions, use of nephrotoxic agents including NSAIDs, and expected use of imaging contrast agents. The risk of AKI increases as total treatment volume increases. In patients with compromised pre-procedure renal function, AKI may progress to acute renal failure. Renal risk should be evaluated before treatment, and renal function should be monitored for signs of AKI before, during, and after treatment.

Warning

Mechanical injury to critical structures (e.g., vascular structures, liver capsule, bile ducts) may occur when these structures are within the PTV. The likelihood of bleeding and/or mechanical injury may increase with additional and/or subsequent treatments within a treatment session or subsequent sessions. In cases where the tumor violates the liver capsule and/or the liver capsule is compromised from prior intervention or therapy, bleeding events may include intraperitoneal hemorrhage, which can be severe and potentially lead to death.

Caution

Take extra precautions when moving the treatment head when its imaging transducer is extended to prevent the imaging transducer from colliding with the frame or patient, as it could cause a fault that could delay the procedure.

Ensure that the area around the treatment arm is clear before moving the treatment arm. Do not touch the treatment arm when in use. Touching and/or pushing on the treatment arm when it is moving could result in a pinch injury and cause a fault, which could delay the procedure.

1. Align and adjust the PTV:
   a. Using the space mouse, align the target contour to the tumor. When aligning, use imaging and the acoustic field indicator overlay to optimize the acoustic pathway (minimize anatomical or other obstructions) and ensure that there is no excessive blockage.
   b. Activate the **Target Contour** button, then rotate the knobs to set the diameter of the target contour in the three axes (X, Y, Z).
   c. Rotate the imaging transducer to verify that the tumor is within the target contour throughout the respiratory cycle in multiple planes.
   d. The default margin setting is 5 mm; adjust if necessary. To adjust, activate the **Margin Contour** button, then rotate the knob to adjust the setting.
2. Select the **Next** button.

Important

After the next button is selected:

- PTV locks so that it does not move when the treatment head is moved
- Rotational movement of the treatment head (movement around the Rx, Ry, Rz axes) is not available when using the space mouse; the space mouse will only move the treatment head along the X, Y, and Z axes

The system enforces a minimum and maximum PTV:

- Minimum PTV: 15 mm diameter sphere (resulting in a volume of 1.8 cm^3)
- Maximum PTV: 40 mm diameter sphere (resulting in a volume of 33.5 cm^3)

Important

The system enforces that the PTV can be:

- No more than a 2:1 ratio from largest to smallest diameter
- No less than 15 mm in any diameter (X, Y, Z)
- No more than 40 mm in any diameter (X, Y, Z)

The system automatically factors in the margin size (if set). Because the margin contour surrounds the target contour, the margin is accounted for twice in the overall diameter. For example: 20 mm target contour + 5 mm margin + 5 mm margin = 30 mm PTV diameter.

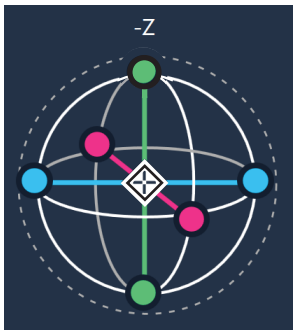
Verify Setup

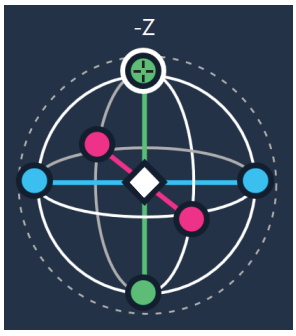
Caution

Failure to perform the survey can lead to excessive force on the patient's abdomen and an aborted procedure if the system detects excessive resistance during treatment.

Take care to prevent the inspection mirror from introducing bubbles or air pockets under the treatment head.

1. Survey the plan to verify that resistance is acceptable. To survey, select a plan point, then press and hold the **Move to Point** button until movement stops and the crosshairs display in the selected plan point.





Important

Surveying the +Z, +X, -X, +Y, -Y plan points verifies that the treatment head will not collide with the frame or apply excessive force on the patient's abdomen during automated treatment.

If changes to setup occur, you must go back and calibrate resistance detection.

Selected plan points are outlined in white. The black crosshairs indicate the current location within the survey.

Important

The following can be adjusted during verify setup:

- Target contour dimensions
- Margin
- Plan location

To adjust PTV alignment, select the **Back** button to go back to the previous screen, then adjust alignment as needed. If any of these adjustments are made, you must resurvey the plan.

2. Survey the superficial plan point (-Z) to verify that the ultrasound medium level is adequate.

   Important

   Recalibrate resistance detection if ultrasound medium is added or removed.

3. Using the inspection mirror, check under the treatment head for air bubbles and air pockets. Take care not to introduce air bubbles with the inspection mirror. If air bubbles or air pockets are present, remove them with the bubble removal tool.

   Important

   Air pockets typically form around the base of the imaging transducer and have a reflective, metallic appearance against the dark background of the transducer face.



4. Select the **Next** button.

Mark Muscle Layer

Warning

Muscle layer depth is one of the measurements used by the software to calculate safe treatment parameters. Failure to correctly mark the muscle layer can result in unintended thermal injury.

Important

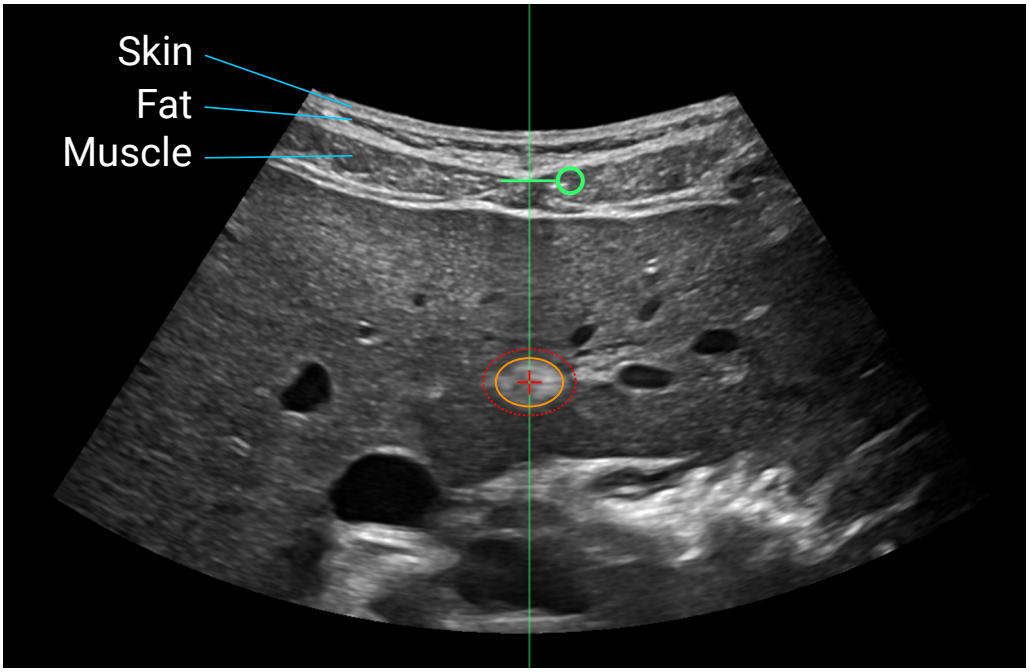
A minimum distance is required between the center of the PTV and the center of the body wall. If the distance is not sufficient, the following message will display:

Treatment is not supported at this depth.

a. Select **OK** to acknowledge the error message and return to the beginning of the Plan phase.

b. End the procedure.

1. Drag the green mark so that it is between the muscle layer and the subcutaneous fat.



2. Verify the location of the mark. If necessary, adjust the location of the mark.
3. Select the **Next** button.

Verify Plan

Warning

Before proceeding to the Treat phase, use live ultrasound to verify that the target contour aligns to the tumor in multiple planes. Do not rely on reference images for location verification, even if they are fused with live ultrasound, as they may not be valid or accurate. Failure to use live ultrasound for verification may lead to unwanted tissue destruction and incomplete or ineffective treatment.

1. While rotating the imaging transducer, verify that the tumor is within the target contour throughout the respiratory cycle.

   Important

   If adjustments to the plan are required, including changing the angle of the treatment head, select the **Adjust Plan** button, then select the **Reset Plan** button to go back to the Position Contours task.

2. Verify the ultrasound medium level is adequate at the superficial plan point (-Z), then evacuate any trapped air from under the treatment head.

   Important

   If you need to add ultrasound medium or adjust the frame, first select the **Adjust Plan** button, then select the **Adjust Setup** button to go back to the Localize phase.

3. After verifying the plan, select the **Next** button.

Treat

Calibrate Crosshairs In Vivo

Warning

When any of the following occur, cumulative thermal exposure will increase, elevating the risk of thermal injury to the skin, body wall, or other tissues:

- User-initiated repetition of tasks where energy is delivered, such as re-performing in vivo calibration or establishing voltage settings for any of the seven plan points
- Prolonged energy delivery when establishing voltage settings
- Exceeding the voltage necessary to sustain the bubble cloud
- Anatomical or other structures (e.g., ribs, lung, bowel) located anywhere within the acoustic pathway—including post-focal—with higher absorption and/or reflection
- Anatomy or obstructions (e.g., bowel gas) within the pre-focal acoustic pathway that require higher voltage settings to sustain the bubble cloud
- Multiple treatments within the same procedure when acoustic pathways may intersect and/or pass through previously treated zones

Note the following system behaviors, which further inform energy delivery considerations related to cumulative thermal exposure:

- The system applies a thermally safe protocol to perform automated treatment but does not account for the energy delivered during treatment planning
- While the mechanism of action is non-thermal, localized temperature rise within the acoustic pathway will occur during energy delivery/deposition—particularly in transition zones such as the skin, body wall, or in tissues that absorb/obstruct ultrasound energy, such as bone
- The system enforces a 30-second timeout when establishing a voltage setting but does not limit cumulative energy delivery

While some repetition or extended energy delivery may be required to verify a sustained bubble cloud, procedural goals should be met using the minimum voltage and duration necessary, while limiting or preventing unnecessary repetition. When clinically appropriate, users may consider pausing between energy delivery tasks to allow tissue cooling before proceeding.

Do not make any setup changes during the Treat phase. Repositioning the treatment cart, bed, or patient will cause misalignment between the PTV and the targeted tissue. Delivering therapeutic ultrasound when the PTV is misaligned with targeted tissue will result in unwanted tissue destruction or incomplete treatment.

Failure to calibrate the crosshairs in vivo as instructed can result in injury to the patient or incomplete treatment.

Warning

The imaging transducer must be aligned to -Y and in the home position (fully retracted) when calibrating crosshairs. Calibrating crosshairs when the imaging transducer is not oriented to -Y or is not in the home position can result in injury to the patient or incomplete treatment.

The bubble cloud must be visible in the live ultrasound to calibrate the crosshairs in vivo.

Caution

Do not deliver energy when air pockets or bubbles are trapped under the treatment head, as system damage can occur. Submerge the treatment head and remove all air pockets and bubbles as instructed in this user guide.

Be aware that changes to setup can introduce air pockets and bubbles under the treatment head. For example:

- Ultrasound medium level lowers (inadequate submersion)
- Treatment head is raised too high (inadequate submersion)
- Additional ultrasound medium is poured into the reservoir too quickly or too close to the treatment head

Failure to prepare the patient's skin, apply coupling oil, and remove all bubbles and air pockets as instructed will prevent the membrane from acoustically coupling with the patient's skin, preventing visualization in the live ultrasound view.

Be aware that changes to setup can introduce air pockets and bubbles under the membrane or lift it away from the patient's skin.

Do not deliver energy or begin automated treatment if the membrane is not acoustically coupled to the patient's skin, as the following can occur:

- Surface cavitation resulting in patient skin injury
- Incomplete treatment

Important

Before calibration and before a bubble cloud is generated, the application displays the crosshairs where it estimates the bubble cloud center will be. The physician calibrates the crosshairs so that they are precisely in the center of the bubble cloud.

When generating the bubble cloud for in vivo calibration, it is possible for the bubble cloud location to be misaligned with the crosshairs such that the bubble cloud is partially or entirely outside of the PTV. The risk is higher with a smaller PTV, or when acoustic aberration and/or anatomical obstruction exists in the acoustic pathway. However, once in vivo crosshair calibration is successfully completed, the likelihood of a bubble cloud generating outside of the PTV is low.

Important

Visualizing bubble cloud alignment with the crosshairs confirms that histotripsy treatment is occurring in the planned location. Various factors can obscure or prevent visualization of a sustained bubble cloud, including ultrasound artifacts, ultrasound system settings, attenuation, aberration, and acoustic blockage (bone, gas, and cartilage). For troubleshooting information, refer to *Visualizing a Bubble Cloud on page 7-3*.

The voltage required to sustain a bubble cloud will vary based upon the acoustic path, tissue properties and depth.

After selecting the **Enable Voltage Knob** toggle, you have 30 seconds to press the voltage knob. If the time lapses, select the button again.

1. Enable the **Histotripsy** imaging preset on the ultrasound system to improve visualization of the bubble cloud.

   Important

   Failure to use the **Histotripsy** imaging preset will prevent optimal visualization of the bubble cloud, which is required to perform calibration.

2. Verify that the imaging transducer is oriented to -Y and is in the home position (fully retracted).
3. Select the **Enable Voltage Knob** toggle.
4. Press the voltage knob to activate it. By default, the voltage is set to 0%.
5. Rotate the voltage knob to increase voltage until you can visualize a sustained bubble cloud.
6. Use the trackpad to mark the center of the bubble cloud.
7. Press the voltage knob to deactivate it and stop energy delivery.

8. The results display.

Offset	Y ± mm Z ± mm	Distance that the crosshairs moved to align to the mark. If the Z-axis offset is ± 5 mm or greater, a message displays to consider verifying setup.
Offset Limit	Within range	Indicates the offset is within the acceptable range for calibration.
	Out-of-range	Out of range means that the distance is too great to allow calibration. This may indicate the presence of anatomical obstructions and/or acoustic aberrations in the acoustic pathway. It could also indicate an issue with the setup or equipment.

9. Select the **Accept** button.

Important

When the **Accept** button is selected, the crosshairs are calibrated and the treatment arm will move the treatment head so that crosshairs are at the center of the PTV.

Z-axis offset was +5 mm or greater: Perform a new survey to verify that the ultrasound medium level is adequate when the treatment head is at the superficial plan point (-Z) as the treatment head was significantly raised for calibration.

Z-axis offset was -5 mm or greater: Perform a new survey to verify resistance is acceptable at the deepest plan point (+Z) as the treatment head was significantly lowered for calibration.

Calibrate Crosshairs In Vivo

Warning

Muscle layer depth is one of the measurements used by the software to calculate safe treatment parameters. Failure to correctly mark the muscle layer can result in unintended thermal injury.

Important

In vivo crosshair calibration may adjust the location of the muscle layer mark.

1. Verify that the green mark is located between the muscle layer and the subcutaneous fat. If necessary, adjust the location of the mark.
2. Select the **Next** button.

Establish Voltage Settings

Warning

Exceeding the voltage necessary to sustain a bubble cloud in any of the seven plan points and/or failing to calibrate crosshairs that are misaligned with the bubble cloud may result in thermal or cavitational injury to non-targeted tissue.

When establishing a voltage setting, always try to minimize energy duration as prolonged energy delivery can result in patient thermal injury.

Do not continue establishing voltage settings if the crosshairs are significantly misaligned with the bubble cloud as it may indicate:

- In vivo calibration was not performed correctly
- Setup issue (for example, the presence of an air pocket)
- System malfunction

When establishing voltage settings, immediately stop energy delivery if the patient, bed, or treatment cart move. Movement can cause the PTV to become misaligned with the targeted tissue resulting in unwanted tissue destruction.

Important

Acoustic cavitation (bubble cloud formation) is only created when there is sufficient negative pressure to exceed the cavitation threshold, making it a threshold phenomenon. Therefore, when establishing voltage settings, use the minimum voltage required to generate a sustained bubble cloud. There is no benefit to increase the voltage beyond the threshold voltage (the voltage required to generate a sustained bubble cloud).

Raising the voltage beyond the threshold voltage can:

- Cause cavitation outside of the PTV
- Cause the system to prolong the procedure time to maintain a thermally safe protocol
- Create an unsafe treatment plan, which will prevent you from proceeding

The voltage required to sustain a bubble cloud throughout respiration will vary based upon the acoustic path, tissue properties and depth.

Cavitation produces a high-pitched audible signal. As the voltage setting is increased from 0%, cavitation is typically heard before a bubble cloud is established. Once the bubble cloud initiates and is sustained, the sound is consistent and robust and can be slightly louder with a subtle rise in pitch. Audible confirmation of this change is covered with demonstrations during required system training. Detecting this audible change reliably often requires a trained ear and familiarity with the expected sound pattern.

The change in sound associated with bubble cloud formation may be difficult to detect under certain conditions:

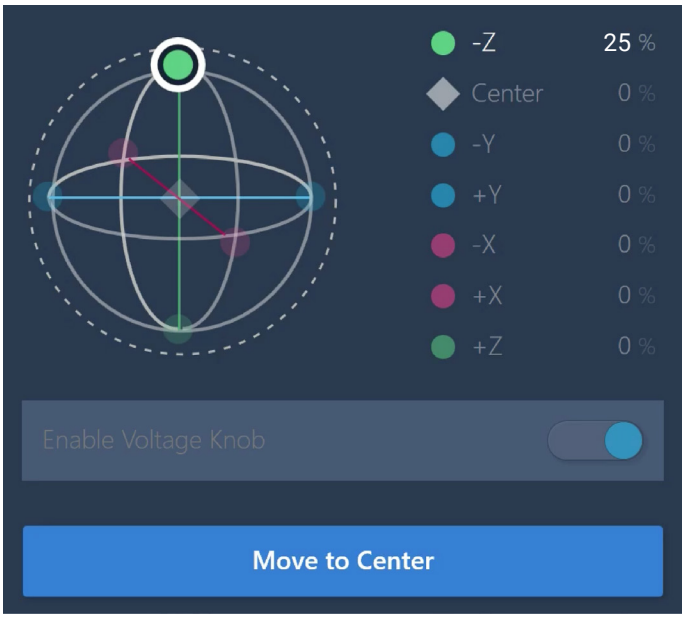
- Users with high-frequency hearing loss
- Transducer hum may mask the change
- Rooms with louder ambient noise or competing equipment sounds
- Certain tumor locations or deeper targets with increased soft tissue between the skin and focal zone

Do not rely on sound alone to verify that the bubble cloud is sustained unless familiar with the expected audio profile—visualization remains the primary method for confirmation.

Keep the imaging transducer in its home position (fully retracted) before and during energy delivery to prevent a system error.

1. Select the **Enable Voltage Knob** toggle.
2. Press the voltage knob to activate it. By default, the voltage is set to 0%.
3. Rotate the voltage knob to increase voltage until you can visualize and/or hear that the bubble cloud is sustained throughout respiration.
4. If the bubble cloud is visible, verify that it is in the expected location and that the crosshairs align with the bubble cloud. Do not continue if the crosshairs are significantly misaligned.

5. Press the voltage knob to stop energy delivery. The established voltage setting (e.g., 25%) displays next to the plan point.
6. Select the **Move to...** button. The treatment head will automatically move to the next plan point. Repeat the steps in this section until the voltage is set for all seven plan points.



7. Select the **Accept** button.

Automated Treatment

1. Review the automated treatment plan details.



2. If the plan is acceptable, select the **Next** button.

Important

If the plan is not acceptable, either go back and adjust the plan or end the procedure.

Automated Treatment

Warning

During automated treatment, carefully monitor the patient and the system. Failure to monitor automated treatment can result in unwanted tissue destruction and incomplete treatment. Immediately suspend therapy if the:

- Bubble cloud is not confined within the PTV
- Patient, bed, or treatment cart move

Movement can cause the PTV to become misaligned with the targeted tissue. Do not resume treatment after movement. Evaluate to confirm there are no complications, then begin a new treatment session, if desired.

Delivering energy without consistent bubble cloud visualization increases the risk that a bubble cloud to crosshair misalignment may occur undetected, resulting in cavitational injury to non-targeted tissue. However, once in vivo crosshair calibration is successfully performed, the potential of a bubble cloud being significantly misaligned with the crosshairs is low.

Caution

During automated treatment, observe the treatment head's submersion in the ultrasound medium. If the ultrasound medium level falls below the point it was at when setup was verified, immediately stop energy delivery. Delivering energy when the treatment head is not adequately submerged can result in system damage and incomplete treatment.

Resistance detection must be recalibrated if changes to the setup are made after calibrating resistance detection. Failing to recalibrate may prolong or prevent the completion of the procedure. Setup changes include:

- Adjusting bed height
- Adding or removing ultrasound medium
- Repositioning the frame

During automated treatment, do not apply excessive force on the treatment head when using the imaging transducer rotation lever or imaging transducer translation dial. Applying force on the treatment head can cause a fault that can abort automated treatment and require a repeat of the workflow.

Ensure that the area around the treatment arm is clear before moving the treatment arm. Do not touch the treatment arm when in use. Touching and/or pushing on the treatment arm when it is moving could result in a pinch injury and cause a fault, which could delay the procedure.

Caution

Failure to prepare the patient's skin, apply coupling oil, and remove all bubbles and air pockets as instructed will prevent the membrane from acoustically coupling with the patient's skin, preventing visualization in the live ultrasound view.

Be aware that changes to setup can introduce air pockets and bubbles under the membrane or lift it away from the patient's skin.

Do not deliver energy or begin automated treatment if the membrane is not acoustically coupled to the patient's skin, as the following can occur:

- Surface cavitation resulting in patient skin injury
- Incomplete treatment

Important

Energy delivery can be stopped at any point by pressing the voltage knob.

The space mouse is disabled while automated treatment is in progress.

Visualizing bubble cloud alignment with the crosshairs confirms that histotripsy treatment is occurring in the planned location. Various factors can obscure or prevent visualization of a sustained bubble cloud, including ultrasound artifacts, ultrasound system settings, attenuation, aberration, and acoustic blockage (bone, gas, and cartilage). For troubleshooting information, refer to *Visualizing a Bubble Cloud on page 7-3*.

The bubble cloud must be sustained during treatment for the procedure to be effective. For troubleshooting information, refer to *Sustaining a Bubble Cloud on page 7-2*.

If the bubble cloud is not sustained, consider increasing the average voltage. The average voltage setting adjusts the voltage values for all points in the plan. If the average voltage is increased, the remaining treatment time may also increase to maintain thermal safety.

To increase average voltage:

a. Enable voltage adjustment (switch toggle to on the position).
b. Use the voltage knob or buttons to increase average voltage until the bubble cloud is sustained.

Keep the imaging transducer in its home position (fully retracted) before and during energy delivery to prevent a system error.

1. Select the **Enable Voltage Knob** toggle.
2. Press the voltage knob to start automated treatment. The remaining treatment time displays.
3. During automated treatment, continually monitor patient motion to ensure that the PTV aligns to the target tissue and that treatment is safe and medically appropriate. Rotate the imaging transducer to view the treatment zone in multiple planes.

Important
If the bubble cloud is not sustained, you can increase the average voltage. To increase average voltage, toggle **Enable Voltage Adjustment** on, then rotate the voltage knob to increase the average voltage.
After automated treatment, energy delivery automatically stops, and the workflow advances to the Review Treatment task.



Review Treatment

1. Press the voltage knob to toggle it back to its default (deactivated) state for the next treatment session.
2. Use live ultrasound to review the treatment zone.
3. Optional: Use the pane capture tool to save an image of the treatment zone, then compare it against an image taken before treatment.
4. Move the treatment head up and out of the ultrasound medium. Allow the treatment head to drain into the reservoir, then move the treatment head away from the patient.
5. Fully retract the imaging transducer if it was extended to perform the review.
6. Unlock the treatment cart wheels and move the treatment cart away from the patient.
7. Enter comments in the Treatment Session text field, if desired.
8. Select the **End Treatment Session** button. The Treatment Session window displays.

Options after Treatment

The following options are available from the Treatment Session window:

- Export the treatment report
- Add a new treatment session (select the **Add Session** button to continue)
- Select **Exit** from the main menu to continue to the System Exit task

After Treatment

1. Position the fluidics cart near the bed.
2. Using the fluidics system, remove as much ultrasound medium from the reservoir as possible.
3. Move the fluidics cart away from the bed.
4. Using a towel or a sponge, remove the remaining ultrasound medium.
5. Unhook the membrane cradle from the frame hooks.
6. Place the patient's arms over the membrane cradle to allow patient transfer from the bed.
7. Pivot the support arm away from the patient.

Important

If you need to move the treatment cart or the ultrasound system to access the patient, you can do so now. However, movement will be limited due to cable connections. When moving the systems away from the bed, take care not to put strain on the cables.

8. Remove the coupling oil from the patient's skin.
9. Using the support arm, turn the frame upside down. Release all latches, then remove the lower half of the frame.
10. Remove the membrane.
11. Remove the support arm from the bed rail clamp.
12. Remove the bed rail clamp from the bed.
13. Put the bed rail clamp friction ring around the support arm before storage.

System Exit

Remove Treatment Head

Caution

Do not drop or roughly handle the treatment head as it may damage the therapy transducer or imaging transducer components. Take care when handling the treatment head, especially during setup and transport. Before removing or attaching the treatment head, ensure the imaging transducer is in the home position (fully retracted) to protect it against physical damage. Keep the imaging transducer in the home position during storage.

Important

To prevent accidental damage, it is recommended to clean the treatment head while it is still attached to the treatment arm and in the ready position.

If you do not want to remove the treatment head, select **Skip Remove Treatment Head** and continue to *Prepare for Shutdown on page 6-69*.

1. Select **Exit** from the main menu.
2. Select Press and hold the **Ready Position** button until the treatment arm stops and the **Ready Position** status displays.
3. Verify that the imaging transducer is in the home position (fully retracted).
4. Optional: Use the handheld imaging transducer to evaluate the treatment zone. Enable the **Abdomen** imaging preset for optimal visualization.
5. Disconnect the treatment head imaging transducer from the ultrasound system.
6. Disconnect the treatment head I/O cable from the treatment arm. To disconnect, pull back the outer sleeve of the connector, and then gently pull the connector out from the receptacle.
7. Remove the splash guard and EMI shield.
8. Unlock the treatment cable connector, then remove the treatment cable from the treatment cart.
9. Reattach the splash guard.
10. While holding the treatment head, press the lock release mechanism to detach the treatment head from the treatment arm.
11. Verify that the treatment head and EMI shield are clean and dry, then store them in the treatment head storage case. Refer to *Transport and Storage on page 6-71*.
12. Select the **Next** button.

Prepare for Shutdown

Caution

Do not turn off the main power switch or unplug the treatment cart until the sequenced shutdown has completed.

Important

For Samsung R20 Ultrasound System safety and use information (including cleaning), refer to the manufacturer's instructions for use.

1. Press and hold the **Storage Position** button until the treatment arm stops and the **Storage Position** status displays.
2. Select the **Shutdown** button. The treatment cart performs a sequenced shutdown.
3. If the treatment cart will stay plugged in to the power outlet, it is recommended to keep the main power switch in the "on" position, enabling the UPS to charge its battery when needed.

   Important

   If you need to unplug the treatment cart from the power outlet, first allow completion of the sequenced shutdown (wait for fan noise to stop), then switch the main power to the "off" position.

4. If disconnecting the treatment cart power cord, store it in the treatment cart cable storage keeper.
5. Shut down the ultrasound system.
6. Disconnect the ultrasound system power cord from the outlet.
7. Disconnect the Ethernet cable that establishes the connection between the systems, and store it on the ultrasound system.
8. If connected, disconnect the LAN Ethernet cable from the treatment cart and store as needed.

Discard

Discard the ultrasound medium and all single-use accessories according to hospital or clinical protocol. This includes the:

- Membrane
- Membrane cradle
- Coupling band
- Coupling oil
- Inspection mirror
- Bubble removal tool

Transport and Storage

Follow the guidelines below for transport and storage information.

Caution

When transporting the treatment cart, use care and move slowly to avoid damage. The treatment cart wheels are designed for smooth surfaces; rough surfaces can damage the wheels. Because the treatment cart is heavy, it is recommended that two people transport it over inclines to prevent injury or damage.

Only use the handrail to move the treatment cart. Do not attempt to move the treatment cart using any other component, such as the treatment arm or monitor.

To prevent damage during transportation, ensure that the:

- Treatment head is removed and stored in the provided case
- Treatment arm is in the storage position
- Monitor arm secures the monitor within the treatment cart handrail

1. Ensure that the treatment head imaging transducer is fully retracted before storage.
2. Store the treatment head and EMI shield in the treatment head storage case.
3. Store the lower half of the frame with the upper half, but do not latch them together, as this can damage the frame gasket when the membrane is not in place.
4. Store the support arm in its storage case.
5. Store the handheld imaging transducer on the ultrasound system.
6. Put the treatment cart wheels in drive mode.
7. Transport the system to a proper storage location.

   Important

   Avoid storing the treatment cart, treatment heads, and coupling kits in areas with extreme temperatures or direct sunlight.

8. Transport the ultrasound system to a proper storage location.

   Important

   Refer to the Samsung R20 Ultrasound System User Manual for handling and transport information.

7 Troubleshooting

When an error displays, the application provides the necessary steps on how to resolve it. This chapter provides information on how to:

- Sustain and visualize a bubble cloud.
- How to perform a hard shutdown.

Sustaining a Bubble Cloud

Warning

Delivering therapeutic ultrasound when anatomical or other obstructions (bone, cartilage, lung, digestive gas, etc.) are along the acoustic pathway can result in thermal injury to non-targeted tissues. Use imaging and the acoustic field indicator overlay to assess and minimize obstruction prior to finalizing the treatment plan.

Important

Some tumor locations will not be treatable due to excessive anatomical obstruction and/or acoustic aberration.

If the bubble cloud is not sustained throughout respiration after the troubleshooting steps have been exhausted, it is unlikely that the system will be able to deliver the desired effect for this particular patient.

If the bubble cloud is not sustained, consider the following:

- Treatment not currently active
- Ultrasound medium level might be too low, allowing air under the treatment head
- Bubbles may have formed under the membrane or under the treatment head
- Bubble cloud encountered a fibrous tissue structure
- Excessive anatomical obstructions in the acoustic pathway
  - Use imaging and the acoustic field indicator overlay to assess and minimize anatomical obstructions
  - Consider manipulating patient anatomy to improve the acoustic pathway to the target tissue
- Voltage too low
  - Increase average voltage until the bubble cloud is sustained

Important

To adjust the average voltage setting during automated treatment, toggle the Enable Voltage setting, then rotate the voltage knob or use the voltage buttons.

If the average voltage is increased, the treatment time may increase to maintain thermal safety.

Visualizing a Bubble Cloud

Warning

Delivering energy without consistent bubble cloud visualization increases the risk that a bubble cloud to crosshair misalignment may occur undetected, resulting in cavitational injury to non-targeted tissue. However, once in vivo crosshair calibration is successfully performed, the potential of a bubble cloud being significantly misaligned with the crosshairs is low.

Various factors can obscure or prevent visualization of a sustained bubble cloud, including ultrasound artifacts, ultrasound system settings, attenuation, aberration, and excessive anatomical obstruction.

If you can hear a sustained bubble cloud but cannot visualize it in the Live Ultrasound or Live Fused Images view, consider performing one or more of these troubleshooting steps to improve visualization:

- Rotate the imaging transducer
- Adjust the B-mode ultrasound image settings:
  - Gain and/or TGC
  - Dynamic range
  - Center frequency
- Adjust the angle of the treatment head. An alternate treatment head angle may reduce ultrasound artifacts. Use imaging and the acoustic field indicator overlay to assess and minimize anatomical obstructions.

Important

Repeat all tasks in the Plan phase if any adjustments are made to the position or angle of the treatment head.

Hard Shutdown

Caution

Do not turn off the main power switch or unplug the treatment cart until the sequenced shutdown has completed.

If the treatment cart does not respond to the normal shutdown procedure, perform a hard shutdown. To perform a hard shutdown, press and hold the power button for several seconds.

8 Cleaning

How to safely clean the system.

Cleaning Safety

Observe the following precautions when cleaning the system.

Warning

When cleaning, do not apply liquids directly onto the control panel or let them seep inside the treatment cart. Ingress liquid can result in electric shock or risk of fire.

Caution

The use of cleaning agents or use of cleaning products other than those specified may damage equipment and void the warranty.

Do not use chemicals (cleaning agents) to clean the touchscreen, as they may cause damage.

To clean the touchscreen, use a soft, non-abrasive cloth with a small amount of water. Do not use paper towels as they may cause light scratches.

Do not drop or roughly handle the treatment head as it may damage the therapy transducer or imaging transducer components. Take care when handling the treatment head, especially during setup and transport. Before removing or attaching the treatment head, ensure the imaging transducer is in the home position (fully retracted) to protect it against physical damage. Keep the imaging transducer in the home position during storage.

Use a soft cloth to clean the treatment head. Do not use a brush.

Do not attempt to remove or disassemble treatment head components.

Do not allow connectors or electrical contacts to come into contact with cleaning solutions.

Do not apply, spray, or spill liquids on the control panel or treatment cable connection points.

Never use sterilization methods (autoclave, ultraviolet, gamma radiation, gas, steam, or heat sterilization) on the treatment head. Sterilization methods may severely damage treatment head components.

Important

Repeated cleaning has minimal effect on the therapy transducer and imaging transducer in the treatment head. End of life is typically determined by wear and damage from use.

Cleaning Protocol

Reusable Equipment

- Treatment cart
- Treatment heads and EMI shields
- Support arm (includes frame and bed rail clamp)

Frequency

- Before use: Clean all reusable equipment
- After use: Inspect all reusable equipment and clean if any visual contamination is present

Approved Cleaning Products

- CaviWipes™ germicidal wipe or equivalent

Cleaning Action

- Use a gentle wiping action
- Use a scrubbing action only when required to remove stubborn soil

Cleaning Instructions

Important

Clean the treatment head with the imaging transducer fully extended. Allow the imaging transducer to air dry or dry it with a non-abrasive cloth before retracting it for storage.

It is recommended to clean the treatment head while it is attached to the treatment arm to prevent accidental damage.

With the exception of the touchscreen, follow these steps to clean system equipment.

1. Wipe surfaces clean with a fresh germicidal wipe. Use additional wipes as needed.
2. After surfaces appear clean, wipe once more with a fresh germicidal wipe.
3. Soak a soft, non-abrasive cloth with water, then wipe surfaces to remove residual cleaning agents.

Cleaning the Touchscreen

1. Moisten a soft, non-abrasive cloth with water.
2. Gently wipe the screen.

Samsung R20 Ultrasound System

Clean the Samsung R20 Ultrasound System, including the handheld imaging transducer, according to the manufacturer's instructions for use.

9 Service

Service Schedule

Warning

Unauthorized modification of the system is strictly prohibited due to the presence of internal components such as lead-acid battery and high-voltage electronics, and may lead to severe adverse consequences including, but not limited to:

- Electric shock
- Fire or explosion
- Chemical burns
- Incomplete or ineffective treatment
- Thermal or cavitation injury

Failure to comply may result in serious harm to the user or patient, as well as damage to the device.

Caution

Preventive maintenance and system service can be performed only by HistoSonics service or an authorized service provider.

The ultrasound system provided with the system has been configured for use with the treatment cart. Do not service or reconfigure the ultrasound system settings. If service is needed, contact HistoSonics or an authorized service provider.

Reconfiguring does not include making adjustments to optimize visualization. For example, adjusting gain, depth, width, etc.

With the exception of temporarily removing the splash guard to allow attaching/detaching the treatment cable, do not remove panels or covers from the treatment cart.

Inspection, functional checks, cleaning, and maintenance must be performed according to the following schedule:

Task	Frequency	By	Reference
Visual inspection and system check	Daily, prior to every use	User	*Inspect Before Use on page 6-2*
Cleaning	Follow cleaning protocol	User	*Cleaning Protocol on page 8-3*
Preventive maintenance	Annually	HistoSonics	

Preventive Maintenance

The system is not designed with any user-serviceable components.

Caution

Preventive maintenance and system service can be performed only by HistoSonics service or an authorized service provider.

Replacement Components

Important

Ethernet cables can be sourced and replaced by the user. Use a CAT5e Ethernet cable or faster. The system verifies that Ethernet port speeds are sufficient during startup.

The following may be obtained from HistoSonics and replaced by the user:

Description	Catalog/Part Number
Support Arm (includes Frame and Bed Rail Clamp)	EDNSA1001
Handheld Imaging Transducer	CA1-7S
Treatment Cart Power Cord – US 120 V - 15' (4.6 m)	XCA30840
Treatment Cart Power Cord – EU 240 V - 20' (6.1 m)	XCA30138
Treatment Cart Power Cord – UK 240 V - 20' (6.1 m)	XCA30363
CAT6 Ethernet Cable – 14' (4.3 m)	XCA30598
User Guide	Call for current version

Expected Service Life

The expected service life of the system is two years and includes the following equipment.

Treatment cart	EDNTC1001
Treatment head, 12 cm	EDNTH12
Treatment head, 14 cm	EDNTH14
Support arm (includes frame and bed rail clamp)	EDNSA1001

Warranty

Please refer to your purchase or use contract for warranty information. Contact HistoSonics for more information about warranties.

Disposal

Caution

Follow local governing ordinances and recycling plans regarding disposal or recycling of device components.

Contact HistoSonics for disposal information when the system reaches the end of its service life and must be removed from service.

10 Specifications

System specifications, testing and performance.

Description of Essential Performance

The system is designed to reduce the likelihood of the following events as far as possible while maintaining the intended benefits to the patient:

- Production of unwanted or excessive ultrasound output
- Unwanted targeting of tissue regions away from the intended target region
- Production of unwanted thermal or mechanical tissue damage outside of the PTV
- Production of excessive reflection of ultrasonic power at the transducer-patient interface

Automated Treatment Duration

To ensure a thermally safe protocol, the system determines the required treatment time based on the PTV size, target depth, plan point voltage settings, and treatment head model.

PTV Diameters (X,Y,Z)	Total Volume	Approximate Treatment Time (Minutes)
15 mm	1.8 cm^3	2–5
20 mm	4.2 cm^3	4–10
25 mm	8.2 cm^3	7–18
30 mm	14.1 cm^3	12–31
35 mm	22.5 cm^3	18–45
40 mm	33.5 cm^3	26–63

Ultrasound Medium Specifications

Caution

Delivering energy through ultrasound medium that is insufficiently degassed can:

- Prevent the bubble cloud from generating and/or prevent a sustained bubble cloud
- Cause damage to the treatment head

When preparing ultrasound medium, the water must be degassed to have less than a 50% dissolved oxygen level and have a temperature between 15°C and 25°C.

HistoSonics manufactures a fluidics system that degases water within the required specifications, as well as measures the water temperature. Use of HistoSonics' fluidics system is not required if there is a clinical water source that meets these specifications. Refer to *Substituting Fluidics Equipment on page 6-6*.

Procedure Bed Requirements

The procedure bed must have a 2.5 cm (1-inch) bed rail to attach the bed rail clamp.

Treatment Cart Specifications

Physical Characteristics	
Footprint	100 cm x 64.6 cm (39 inches x 25 inches)
Weight	268 kg (590 lb)
Height (measured from top of LCD display to floor)	164 cm (64.5 inches)
Height (transport/storage mode)	166 cm (65.5 inches)

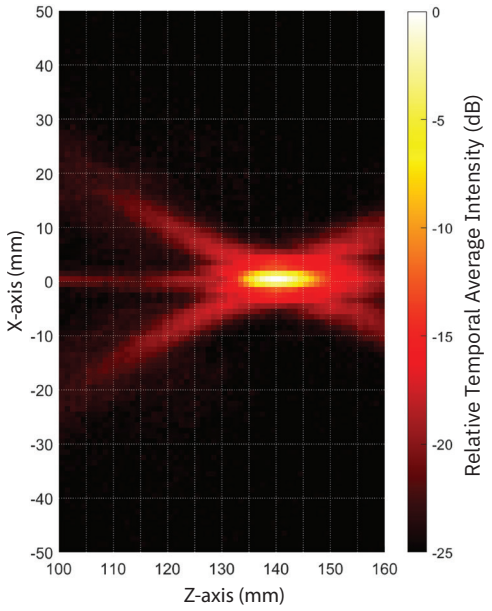
Targeting Accuracy

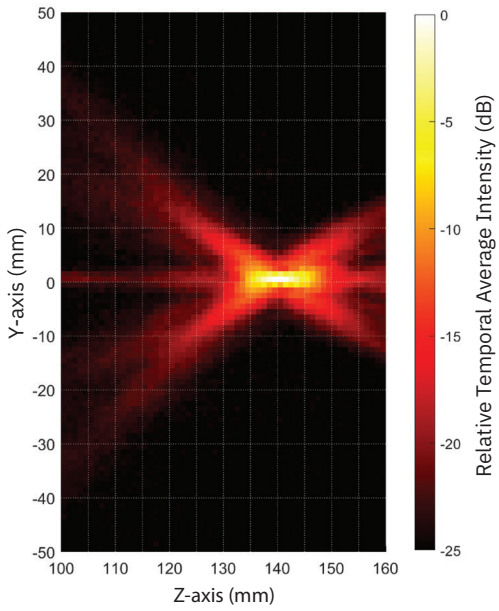
Acoustic characterization performed per IEC 60601-2-62 determined that the system targeting accuracy is less than 2.5 mm. Targeting accuracy was determined by measuring the distance between the therapy transducer focal point and the software crosshairs when aligned to the center of the bubble cloud.

The procedural workflow requires the user to perform in vivo crosshair calibration, which centers the crosshairs over the bubble cloud to correct for acoustic aberration, refraction, and blockage due to bone, cartilage, or gas which can affect the alignment of the bubble cloud with respect to the crosshairs.

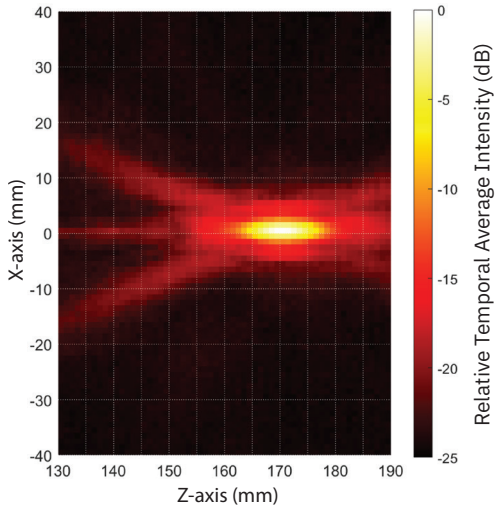
Ultrasound Field Distribution

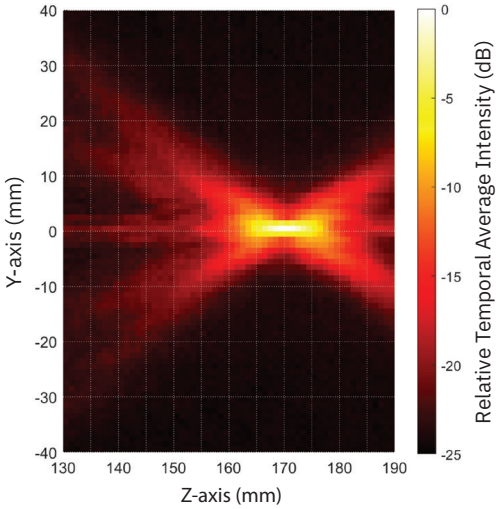
12 cm Treatment Head REF EDNTH12	
Beam width at focus	2.49 mm
Orthogonal beam width at focus	1.97 mm
Focal volume	24.5 mm^3





14 cm Treatment Head REF EDNTH14	
Beam width at focus	2.64 mm
Orthogonal beam width at focus	1.88 mm
Focal volume	26.4 mm^3





Environmental Conditions

Caution

HistoSonics cannot guarantee the performance of the system if stored or used outside of the specified environmental conditions.

Avoid exposing the system to flammable liquids or gases, corrosive substances, strong electrical or magnetic fields, and equipment that emits high-frequency waves.

Treatment Cart and Treatment Heads	Temperature Limit	Humidity Limit
Operation	15°C to 30°C (59°F to 86°F)	30% to 75% RH (non-condensing)
Shipping/Storage	-15°C to 50°C (5°F to 122°F)	10% to 75% RH (non-condensing)

Coupling Kit and Support Arm	Temperature Limit	Humidity Limit
Operation	10°C to 40°C (50°F to 104°F)	30% to 75% RH (non-condensing)
Shipping/Storage	-15°C to 50°C (5°F to 122°F)	10% to 75% RH (non-condensing)

Electrical Requirements

Treatment Cart REF EDNTC1001	
Line voltage (must be held within +/- 10% of specified line voltage)	120 V ~ | 240 V ~
Line frequency	50—60 Hz
Power consumption	1350 VA

Electromagnetic Compatibility (EMC) Requirements

Warning

The system is not compatible with an MRI environment.

Do not use the system outside of the EMC specifications provided in this user guide.

To meet electromagnetic compatibility requirements (EMC), avoid using the treatment cart adjacent to other equipment. Do not place other equipment on top of the treatment cart.

Use of components such as treatment heads, imaging transducers, and cables other than those specified by HistoSonics may result in increased emissions or decreased system immunity.

Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the treatment cart. Otherwise, the degradation of system performance could result.

Caution

Avoid exposing the system to flammable liquids or gases, corrosive substances, strong electrical or magnetic fields, and equipment that emits high-frequency waves.

The emissions characteristics of this equipment make it suitable for use in industrial areas and hospitals (CISPR 11 Class A). If it is used in a residential ENVIRONMENT (for which CISPR 11 class B is normally required) this equipment might not offer adequate protection to radio-frequency communication services. The user might need to take mitigation measures, such as relocating or re-orienting the equipment.

The system has special precautions regarding electromagnetic compatibility. Contact HistoSonics if additional information or assistance is required relative to the following requirements:

- Always use the system according to the EMC information provided in this user guide.
- Portable and mobile RF communications equipment can affect the system.
- The imaging transducer cable must be raised above the ground during scanning.
- The system has been tested and found to comply with the limits for Class A equipment, pursuant to IEC 60601-1-2 for emissions and immunity for non-life-supporting equipment. These limits are designed to provide reasonable protection against harmful interference in a commercial environment. The system generates, uses, and can radiate electromagnetic energy. If the system is not operated in accordance with these instructions, it may cause harmful interference to surrounding equipment.
- The system is intended for use in an electromagnetic environment specified in this section. The user of the system should ensure that it is used in such an environment.

- If the system is suspected of causing harmful interference for other surrounding equipment, try to correct the interference by one or more of the following methods:
  - Shut down the system, check for equipment interference, then turn the system back on to verify that the interference is coming from the system.
  - Move the other equipment farther away from the treatment cart.
  - Connect the other equipment to an outlet on a circuit different from that to which the system is connected.

<table>
<tr><th>Immunity/Test</th><th colspan="3">Electrostatic Environment Requirements</th></tr>
<tr><td>Electrostatic discharge</td><td colspan="3" rowspan="4">Compliant to +15 kV. Floors should be wood, concrete, or ceramic tile. If floors are synthetic, the relative humidity should be at least 30%.
Electrical power quality should be that of a typical commercial or hospital environment. See Electrical Power Requirements.
Mains power quality should be that of a typical commercial or hospital environment. If the user requires continued operation during power mains interruptions, it is recommended that the equipment be powered from an external uninterruptible power supply.
Portable and mobile communication equipment should be separated from the treatment cart by no less than 19 feet (6 meters).
The treatment cart is intended for use in an electromagnetic environment in which radiated disturbances are controlled. The user can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment and the treatment cart as recommended below, according to the maximum output power of the communications equipment.</td></tr>
<tr><td>EFT and surge</td></tr>
<tr><td>Voltage dips/ dropout</td></tr>
<tr><td>Conducted radio-frequency (RF)</td></tr>
<tr><td rowspan="5">Radiated RF</td><td>Maximum Output Power (watts)</td><td>Separation (150 kHz–800 MHz)</td><td>Separation (800 MHz–5 GHz)</td></tr>
<tr><td>0.01</td><td>15 inches (38 cm)</td><td>30 inches (76 cm)</td></tr>
<tr><td>0.1</td><td>15 inches (38 cm)</td><td>30 inches (76 cm)</td></tr>
<tr><td>1</td><td>46 inches (117 cm)</td><td>8 feet (2.4 m)</td></tr>
<tr><td>10</td><td>12 feet (3.7 m)</td><td>24 feet (7.3 m)</td></tr>
<tr><td>Proximity fields from RF wireless communications equipment</td><td colspan="3">Compliant to 28 V/m per IEC 60601-1-2. Maintain separation between RF sources (e.g. mobile phones, WiFi routers, Bluetooth devices) and all accessible surfaces of the treatment cart. Recommended minimum separation is 12 inches (30 cm), or greater depending on RF source output.</td></tr>
<tr><td>Proximity magnetic fields (9 kHz—13.56 MHz)</td><td colspan="3">Compliant with IEC 60601-1-2 proximity magnetic field testing. Avoid placing RFID readers, NFC-enabled smartphones, or inductive chargers within 6 inches (15 cm) of the treatment cart or connected accessories during use.</td></tr>
</table>

EMC Compliance Summary

The system was evaluated for electromagnetic compatibility in accordance with IEC 60601-1-2:2020. The following emissions and immunity tests were performed to confirm that electromagnetic disturbances do not affect the system's essential performance or basic safety.

Essential performance was monitored throughout testing and includes the following functions:

- Continuous live ultrasound imaging
- PTV overlays (e.g., contours) displayed on live ultrasound within tolerance
- Correct and consistent output effect (bubble cloud) across the PTV within tolerance
- Accurate motion of the treatment arm
- Therapy status is indicated and remains under user control at all times
- Safe operation of the system with no interruption or degradation during test conditions

Test	Standard	Test Level
Conducted emissions	CISPR 11	Class A, Group 1
Radiated emissions	CISPR 11	Class A, Group 1
Electrostatic discharge (ESD)	IEC 61000-4-2	±8 kV contact, ±2/4/8/15 kV air
Radiated RF immunity	IEC 61000-4-3	3 V/m, 80–2700 MHz, 80% AM
Proximity RF fields	IEC 60601-1-2 §8.10	As defined in the standard
Electrical fast transients (EFT)	IEC 61000-4-4	±2 kV (AC), ±1 kV (I/O), 100 kHz
Surge immunity	IEC 61000-4-5	±0.5/1 kV L–L, ±0.5/1/2 kV L–G
Conducted RF immunity	IEC 61000-4-6	3 V, 0.15–80 MHz; 6 V (ISM/Amateur bands)
Power frequency magnetic field	IEC 61000-4-8	30 A/m, 50/60 Hz
Voltage interruptions	IEC 61000-4-11	100% reduction for 5 seconds
Proximity magnetic field immunity	IEC 60601-1-2 §8.11	As defined in the standard

Samsung R20 Ultrasound System

The Samsung R20 Ultrasound System that is distributed by HistoSonics has been configured to be compatible for use with the system. The handheld imaging transducer (CA1-7S) which is also distributed by HistoSonics has been tested to confirm compatibility with the system.

A Appendix

Clinical Submission Report Summary

Two prospective, multi-center, single-arm trials were conducted (one in the US, one in Western Europe) to assess the safety and efficacy of histotripsy for the destruction of primary or metastatic tumors located in the liver.

Key inclusion/exclusion criteria are presented below. For a complete list of inclusion/exclusion criteria, visit:

clinicaltrials.gov/study/NCT04572633
clinicaltrials.gov/study/NCT04573881

Key Inclusion Criteria	Key Exclusion Criteria
Subject is diagnosed with hepatocellular carcinoma (HCC) or liver metastases (mets) from other primary cancers.	Subject is eligible for surgical resection.
The tumor(s) selected for histotripsy treatment must be ≤3 cm in longest diameter.	The Planned Treatment Volume intended to cover the targeted tumor includes or encompasses any portion of the main portal vein, common hepatic duct, common bile duct, gallbladder or stomach/ bowel.
Subject has not responded to and/or has relapsed and/or is intolerant of other available therapies including locoregional therapies, chemotherapy, immunotherapy and targeted therapies.	Subject has a planned cancer treatment (e.g. resection, chemotherapy, etc.) after the planned index-procedure date and prior to completion of the 30-day follow-up visit.

As the trials were developed with an identical study design using the same device, the data from all 47 subjects enrolled were pooled for analysis. The pooled data contains 23 subjects treated in the US and 24 subjects treated in Europe. Data from the first 44/47 subjects enrolled were analyzed for primary effectiveness and primary safety. Co-primary endpoints of primary effectiveness and primary safety were defined with a pre-specified performance goal to indicate success. Results for both endpoints needed to be positive for the trial to be considered a success.

The primary effectiveness endpoint was technical success, defined as the treatment volume/ treatment dimensions being greater than or equal to the targeted tumor with complete tumor coverage as assessed by a Core Laboratory ≤36 hours post-index procedure, with a performance goal of 70%. The first 40 consecutive subjects with sufficient imaging data to assess primary effectiveness included treatment of 44 total tumors. The >70% performance goal for the primary efficacy endpoint was met with 42/44 (95.5% [95% CI 83.72 – 100%]) of the lesions having achieved technical success within 36 hours of the procedure.

The primary safety endpoint of the clinical studies was defined as index-procedure related major complications of Common Terminology Criteria for Adverse Events (CTCAE) Grade 3 or higher toxicities as adjudicated by a Clinical Events Committee (CEC) with a performance goal of 25%. All 44 subjects enrolled were included in the analysis of the primary safety endpoint. The <25% performance goal for the primary safety endpoint was met with a reported procedure-related major complication rate (CTCAE ≥3) of 3/44 (6.8% [95% CI 2.35 – 18.23%]) within 30 days post-procedure. The safety conclusion is further supported by the secondary safety analysis which provides evidence that all adverse events reported within 30 days of the procedure are consistent with the established risk-analysis of the System.

Index-procedure related Adverse Events CTCAE Grade 3 or higher occurring in the population included pleuritic pain (1 patient, 2%), sepsis (1 patient, 2%), and hepatic failure (1 patient, 2%), all of which are well documented risks of focal liver treatments in subjects with liver tumors and are not unique to histotripsy. The most common Adverse Device Effects (ADE) include procedural pain (24.0%), abdominal pain (22.0%), and pyrexia (12.0%). All reported ADEs are consistent with the known risks of the investigational device and were included in the risk analysis.

Demographic Information

Demographics and other baseline characteristics presented in this section reflect subjects evaluated for primary effectiveness and primary safety (N=44).

As shown in **Table 1**, the mean age was 63.9 ± 12.32 years. Fifty percent (50%) of the total population was female, including 38.1% (8/21) US subjects and 60.9% (14/23) EU/UK subjects. Most subjects enrolled in the US and EU/UK were white (95.2% and 95.7%, respectively). The one (1) subject with a race reported as "other" self-identified as Arabic. Most subjects were Child-Pugh Class A (84.1%). HCC diagnosis was most common in the US (52.4%) and diagnosis of liver metastases was most common in the EU/UK (69.6%).

Table 1: Subject Demographics and Baseline Characteristics

Category	Sub-category	Statistics	Total
Enrolled Subjects			44
Age (Years)		Non-missing (N)	44
		Mean (SD)	63.9 (12.32)
		Median	65.0
		Min, Max	36, 89
		Missing (N)	0
Sex	Male	n (%)	22 (50.0)
	Female	n (%)	22 (50.0)
	Missing	n (%)	0
Ethnicity	Hispanic/Latino	n (%)	5 (11.4)
	Not Hispanic/ Latino	n (%)	39 (88.6)
	Missing	n (%)	0
Race	Black or African American	n (%)	1 (2.3)
	White	n (%)	42 (95.5)
	Other	n (%)	1 (2.3)
	Missing	n (%)	0

Category	Sub-category	Statistics	Total
Body Mass Index (BMI) (kg/m²)	<18.5	n (%)	4 (9.1)
	18.5 to <25	n (%)	13 (29.5)
	25.0 to <30	n (%)	17 (38.6)
	≥30.0	n (%)	9 (20.5)
	Missing	n (%)	1 (2.3)
Time since liver tumor diagnosis (days)		Non-missing (N)	43
		Mean (SD)	411.4 (492.38)
		Median	245.0
		Min, Max	15, 2776
		Missing (N)	1
Type of tumor	Hepatocellular Carcinoma	n (%)	18 (40.9)
	Liver metastasis	n (%)	26 (59.1)
	Missing	n (%)	0
Renal function (eGFR, mL/min/1.73m²)	<15.0	n (%)	0
	15.0 to <30	n (%)	0
	30.0 to <60	n (%)	5 (11.4)
	60.0 to <90	n (%)	15 (34.1)
	≥90.0	n (%)	24 (54.5)
	Missing	n (%)	0
ECOG Performance Status	0	n (%)	28 (63.6)
	1	n (%)	14 (31.8)
	2	n (%)	2 (4.5)
	3	n (%)	0
	4	n (%)	0
	Missing	n (%)	0
Child-Pugh Class	A	n (%)	37 (84.1)
	B	n (%)	6 (13.6)
	C	n (%)	0
	Missing	n (%)	1 (2.3)

Tumor Type Information

The baseline tumor information for the subjects with HCC is presented in **Table 2**. Of the eighteen (18) subjects with HCC, two (2) had metastatic disease (i.e., stage IV) at the time of diagnosis. Most of the subjects diagnosed with HCC had ≤5 liver tumors (94.4%). Prior treatments/therapies for subjects diagnosed with HCC included surgery (22.2%), liver ablation (22.2%), intra-arterial treatment (50.0%), and chemotherapy (16.7%). The lack of chemotherapy and higher reported rates of local regional therapy is typical of HCC and expected[1].

Table 2: Baseline Hepatocellular Carcinoma (HCC) Tumor Information

Category	Sub-category	Total, n (%)
Subjects with HCC		18
Disease stage at diagnosis	I	7 (38.9)
	II	8 (44.4)
	IIIA	0
	IIIB	1 (5.6)
	IIIC	0
	IVA	1 (5.6)
	IVB	1 (5.6)
	Missing	0
Number of liver tumors	1 - 5	17 (94.4)
	6 - 10	0
	11 - 15	1 (5.6)
	16 - 20	0
	>20	0
	Missing	0
Prior surgery	Yes	4 (22.2)
	No	14 (77.8)
	Missing	0
Prior liver ablation	Yes	4 (22.2)
	No	14 (77.8)
	Missing	0
Prior intra-arterial treatment	Yes	9 (50.0)
	No	9 (50.0)
	Missing	0
Prior chemotherapy	Yes	3 (16.7)
	No	15 (83.3)
	Missing	0

The baseline tumor information for metastatic non-HCC subjects (N=26) is presented in **Table 3**. While all subjects with liver metastases have stage IV cancer, only 61.5% (N=16) had stage IV disease at the time of primary tumor diagnosis. The primary tumor location was colon or rectum in 38.5% of subjects with liver metastases. Five subjects had pancreatic metastases (19.2%) and four (15.4%) were breast. The seven (7) primary tumor locations classified as "other" were brain (N=1), liver neuroendocrine tumor (N=1), ovary (N=1), uveal melanoma (N=2), bronchial carcinoma (N=1), and large cell neuroendocrine lung (N=1).

Among subjects with liver metastases, 30.8% had ≥6 liver tumors and therefore represented non-oligometastatic progression. Prior treatments/therapies for liver metastases included ablation (15.4%), resection (7.7%), and intra-arterial treatment (11.5%). Twelve subjects (46.2%) had chemotherapy/targeted therapy for metastatic disease. In addition to these prior treatments/therapies, one (1) subject had neoadjuvant radiotherapy and two (2) subjects had adjuvant chemotherapy for metastatic disease. The presence of multiple prior therapies is consistent with the inclusion/exclusion criteria of the study which required subjects to have failed or been intolerant to other available therapies prior to eligibility for the trial.

Table 3: Baseline Metastasis Tumor Information

Category	Sub-category	Total, n (%)
Subjects with liver metastases		26
Primary tumor, disease stage at initial diagnosis	I	1 (3.8)
	II	2 (7.7)
	IIIA	2 (7.7)
	IIIB	2 (7.7)
	IIIC	0
	IVA	11 (42.3)
	IVB	5 (19.2)
	Missing	3 (11.5)
Primary tumor, location	Colon: right	4 (15.4)
	Colon: left	1 (3.8)
	Rectum	5 (19.2)
	Breast	4 (15.4)
	Pancreas	5 (19.2)
	Other	7 (26.9)
	Missing	0
Primary tumor, prior surgery	Yes	16 (61.5)
	No	10 (38.5)
	Missing	0

Category	Sub-category	Total, n (%)
Prior intra-arterial treatment for primary tumor	Yes	0
	No	26 (100)
	Missing	0
Received neoadjuvant/ adjuvant therapy for primary tumor (i.e., chemotherapy, targeted therapy, radiotherapy)	Yes	20 (76.9)
	No	6 (23.1)
	Missing	0
Metastatic location	Liver-only metastases	13 (50.0)
	Extra-hepatic disease	13 (50.0)
	Missing	0
Number of liver tumors	1 - 5	17 (65.4)
	6 - 10	3 (11.5)
	11 - 15	0
	16 - 20	1 (3.8)
	>20	4 (15.4)
	Missing	1 (3.8)
Prior liver metastases ablation	Yes	4 (15.4)
	No	22 (84.6)
	Missing	0
Prior liver metastases resection	Yes	2 (7.7)
	No	24 (92.3)
	Missing	0
Received neoadjuvant/adjuvant therapy for metastatic disease (i.e., chemotherapy, targeted therapy, radiotherapy)	Yes	3 (11.5)
	No	23 (88.5)
	Missing	0
Prior intra-arterial treatment for metastatic tumor	Yes	3 (11.5)
	No	23 (88.5)
	Missing	0
Received chemotherapy/targeted therapy for metastatic disease	Yes	12 (46.2)
	No	14 (53.8)
	Missing	0
Number of lines of chemotherapy/targeted therapy	1	6 (23.1)
	2	4 (15.4)
	≥3	2 (7.7)
	Did not receive therapy/missing	14 (53.8)

Primary Efficacy Endpoint

There were forty-four (44) lesions treated in the forty (40) FAS subjects. Technical success occurred in 42/44 of the lesions treated. The observed rate of technical success was 95.5% (42/44) with a two-sided 95% confidence interval of 83.72% - 100% by bootstrap re-sampling (**Table 4**). The lower bound of 83.72% was greater than the pre-defined performance goal of 70% indicating the null hypothesis was rejected and the technical success goal was met successfully.

Table 4: Primary Efficacy Endpoint: Technical Success

Region	n/N	% [95% CI]*
Overall Technical Success	42/44	95.5% (83.72% - 100%)
US Subjects	21/23	91.3% (70.00% - 100%)
EU/UK Subjects	21/21	100% (100% - 100%)

*Estimated by bootstrap sampling with replacement method to account for potential within-subject lesion correlations. Subject is the bootstrap sampling unit, 1,000,000 iterations for bootstrap resampling were performed, and the bootstrap method was the bias-corrected and accelerated (BCA) method[2].

Primary Safety Endpoint

All the enrolled cohort (N=44) subjects were included in the analysis. Index-procedure related major complications (CTCAE grade 3 or higher) occurred in 3/44 of the subjects enrolled. The observed rate of the primary safety endpoint was 6.8% with a two-sided 95% confidence interval of 2.35% – 18.23% (**Table 5**). The upper bound of 18.23% was less than the pre-defined performance goal of 25% indicating the null hypothesis was rejected and the primary safety goal was met successfully.

Table 5: Primary Safety Endpoint: Index-Procedure Related Major Complications

Region	n/N	% [95% CI][3]
Overall Primary Safety Rate	3/44	6.8% (2.35% - 18.23%)
US Subjects	0/21	0% (0% - 15.46%)
EU/UK Subjects	3/23	13.0% (4.54% - 32.13%)

Adverse Device Effects (ADEs) are reported on all 47 subjects enrolled in **Table 6**. Events classified by the CEC as causal relationship, probably related, possibly related, or missing a response to relationship to the device were classified as device-related. Since the study is ongoing, the reporting of events after the first 6 months is limited and may include site-reported seriousness and device relatedness not yet CEC adjudicated. Of the two-hundred-and-twelve (212) reported AEs, fifty (50) or 23.6% were classified as device-related. The most commonly reported ADEs (those with an incidence rate >5%) include procedural pain (24.0%), abdominal pain (22.0%), and pyrexia (12.0%). All reported ADEs are consistent with the known risks of the investigational device and were included in the risk analysis.

Table 6: Adverse Device Effects (ADE)

System Organ Class	Preferred Term	Total Subjects (N=47) n (%)	Total Events (N=50) n (%)
Gastrointestinal disorders		13 (27.7)	14 (28.0)
	Abdominal pain	11 (23.4)	11 (22.0)
	Abdominal distension	1 (2.1)	1 (2.0)
	Abdominal pain upper	1 (2.1)	1 (2.0)
	Vomiting	1 (2.1)	1 (2.0)
Injury, poisoning and procedural complications		14 (29.8)	15 (30.0)
	Procedural pain	12 (25.5)	12 (24.0)
	Post procedural discomfort	1 (2.1)	1 (2.0)
	Post procedural oedema	1 (2.1)	1 (2.0)
	Postoperative thrombosis	1 (2.1)	1 (2.0)
General disorders and administration site complications		8 (17.0)	9 (18.0)
	Pyrexia	6 (12.8)	6 (12.0)
	Chest pain	1 (2.1)	1 (2.0)
	Fatigue	1 (2.1)	1 (2.0)
	Pain	1 (2.1)	1 (2.0)

System Organ Class	Preferred Term	Total Subjects (N=47) n (%)	Total Events (N=50) n (%)
Hepatobiliary disorders		6 (12.8)	6 (12.0)
	Hepatic hypoperfusion	2 (4.3)	2 (4.0)
	Biloma	1 (2.1)	1 (2.0)
	Hepatic failure	1 (2.1)	1 (2.0)
	Hepatic lesion	1 (2.1)	1 (2.0)
	Portal vein thrombosis	1 (2.1)	1 (2.0)
Infections and infestations		1 (2.1)	1 (2.0)
	Sepsis	1 (2.1)	1 (2.0)
Investigations		1 (2.1)	1 (2.0)
	Gamma-glutamyltransferase increased	1 (2.1)	1 (2.0)
Musculoskeletal and connective tissue disorders		1 (2.1)	1 (2.0)
	Musculoskeletal chest pain	1 (2.1)	1 (2.0)
Psychiatric disorders		1 (2.1)	1 (2.0)
	Apathy	1 (2.1)	1 (2.0)
Respiratory, thoracic and mediastinal disorders		1 (2.1)	1 (2.0)
	Pleuritic pain	1 (2.1)	1 (2.0)
Skin and subcutaneous tissue disorders		1 (2.1)	1 (2.0)
	Rash	1 (2.1)	1 (2.0)
Total		34 (72.3)	50 (100)

Serious Adverse Device Effects (SADEs) are reported on all 47 subjects enrolled in **Table 7**. Events classified by the CEC as causal relationship, probably related, possibly related, or missing a response to relationship to the device were classified as device-related. Of the reported fifty (50) ADEs, six (6) (12.0%) were classified as SADEs with 12.8% of the trial population experiencing an SADE. Since the study is ongoing, the reporting of events after the first 6 months is limited and may include site-reported seriousness and device relatedness not yet CEC adjudicated. There was no predominant SADE reported and all were consistent with the known risks of the investigational device and were included in the risk analysis.

Table 7: Serious Adverse Device Effects (SADE)

System Organ Class	Preferred Term	Total Subjects (N=47) n (%)	Total Events (N=6) n (%)
Hepatobiliary disorders		2 (4.3)	2 (33.3)
	Hepatic failure	1 (2.1)	1 (16.7)
	Portal vein thrombosis	1 (2.1)	1 (16.7)
Infections and infestations		1 (2.1)	1 (16.7)
	Sepsis	1 (2.1)	1 (16.7)
Injury, poisoning and procedural complications		2 (4.3)	2 (33.3)
	Postoperative thrombosis	1 (2.1)	1 (16.7)
	Procedural pain	1 (2.1)	1 (16.7)
Respiratory, thoracic and mediastinal disorders		1 (2.1)	1 (16.7)
	Pleuritic pain	1 (2.1)	1 (16.7)
Total		6 (12.8)	6 (100)

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HISTOSONICS™

HistoSonics, Inc.
16305 36th Avenue North, Suite 300
Plymouth, MN 55446
USA

EU REP Obelis S.A.
Boulevard Général Wahis, 53
1030 Brussels
BELGIUM

CE 2797

histosonics.com • 612-351-0361 • info@histosonics.com

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