



Histotripsy of Liver

MEET EDISON™

**A NEW THERAPEUTIC PLATFORM FOR TREATING TUMORS
using the novel science of histotripsy**

• HISTOTRIPSY DEVELOPMENT AND CLINICAL DATA

- 20 years of research on the science of histotripsy generating over 100 peer reviewed articles, and on-going
- HistoSonics, Inc. was founded in 2009 to advance the development of image-guided histotripsy
- THERESA Study completed in 2020 demonstrated acute safety and efficacy in patients suffering from advanced stage liver tumors
- Currently 2 active clinical trials ongoing, one in US and similar study in Europe, evaluating broader safety and efficacy in both primary and secondary liver tumors
- Category III CPT code awarded for histotripsy of liver malignancy, July 2021,



- **HISTOTRIPSY PLATFORM**

Non-invasive, non-ionizing and non-thermal beam therapy to destroy liver tumors

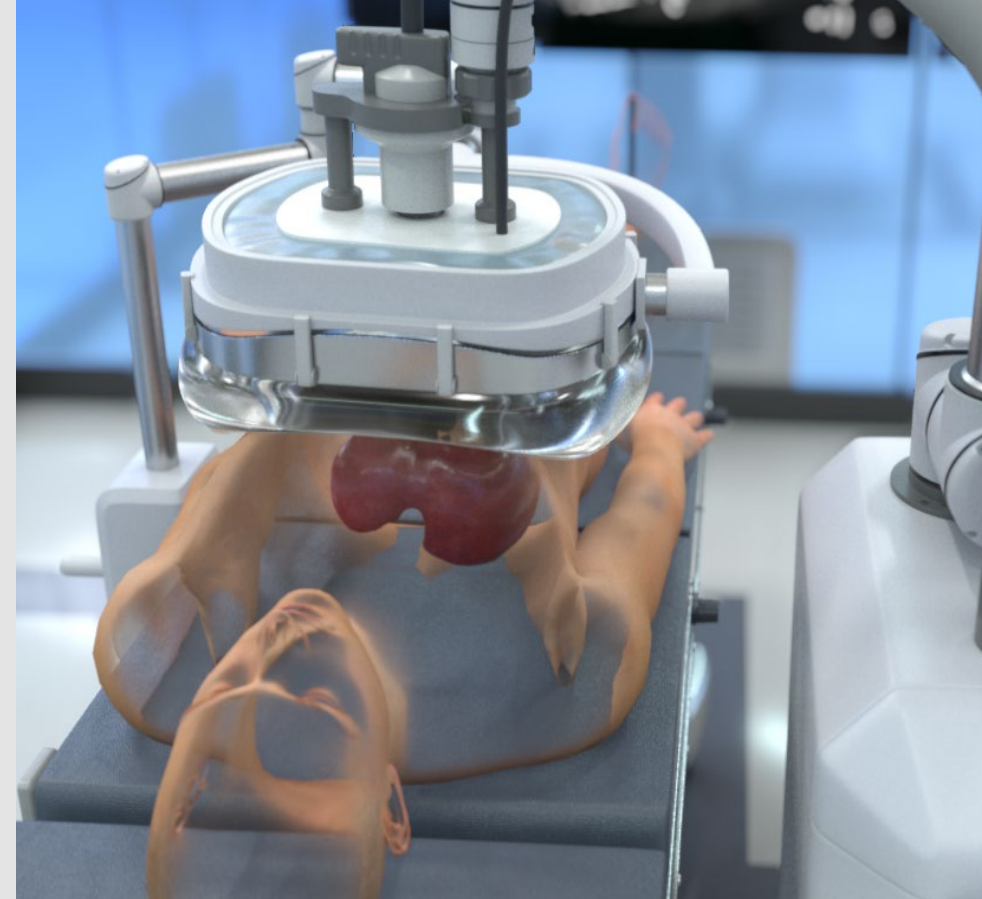


Platform supports use and availability in multiple hospital settings to improve patient access to external beam therapy

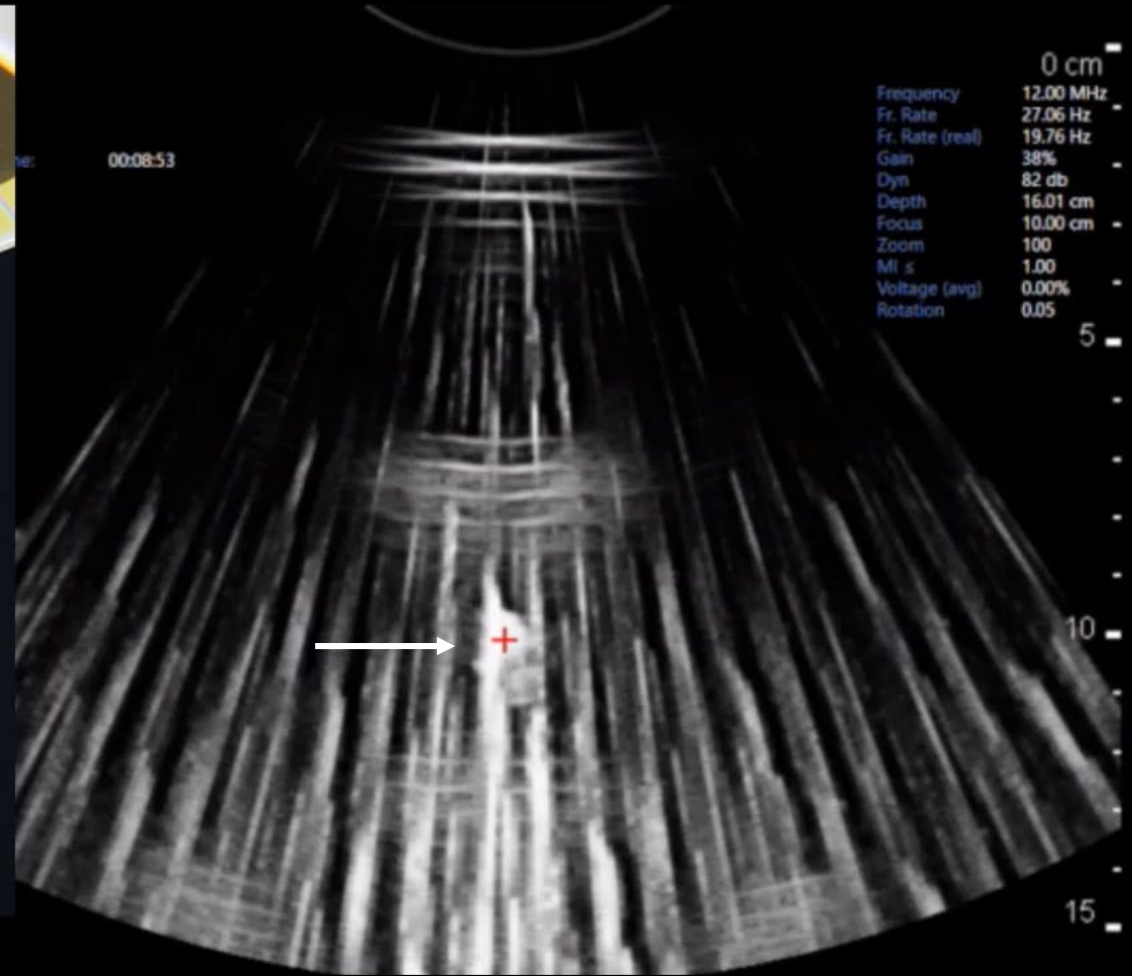
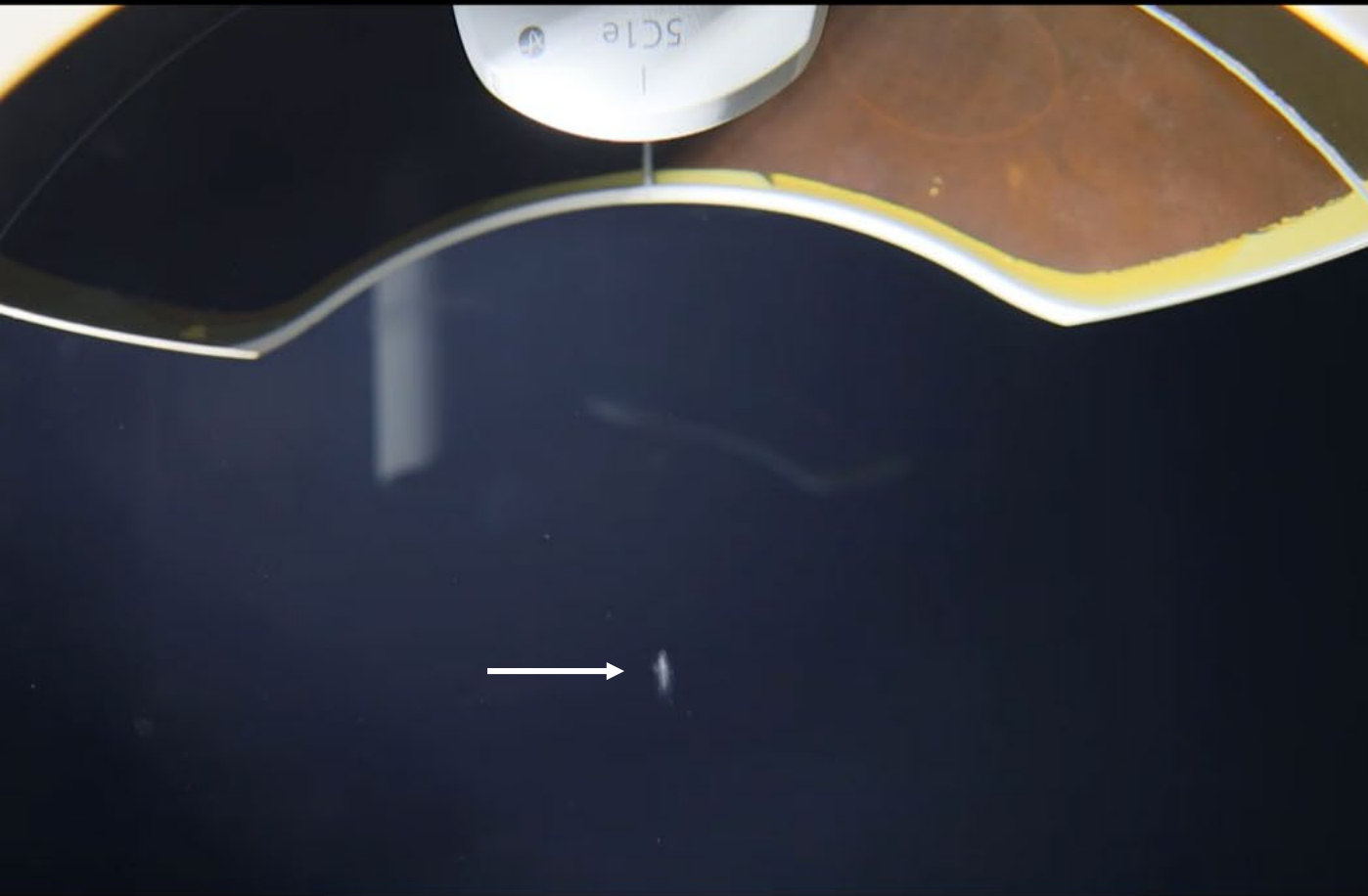
• HISTOTRIPSY: AN ENTIRELY NEW PLATFORM FOR TREATING TUMORS

DELIVERING PRECISE GUIDED PERSONALIZED THERAPY

- Completely **non-invasive, non-thermal** precise guided **beam therapy**
- **Destroys and liquifies** tissues at a **sub-cellular level**, with tissue selectivity
- **Rapid resorption/healing** of treatment site
- Conformal treatment under **complete real time visualized physician control**
- Ability to calculate tumor specific energy dose
- **Safe through and around** critical structures **without damage to vital, healthy tissue**
- Patients report minimal to **no pain** at any time from procedure or device



Histotripsy is the process whereby focused beam of sonic energy creates a “bubble-cloud” that mechanically destroys diseased, targeted tissue at a sub-cellular level



HISTOTRIPSY TREATMENT OR “BUBBLE CLOUD” DESTROYS TAREGETED TUMORS BUT DOES NOT DAMAGE INTEREVENING TISSUES

• HISTOTRIPSY TREATMENT OBSERVED IN REAL TIME

Histotripsy mechanism
observable in real time
during treatment



Histotripsy treated
tissue effect in real
time



- **High-amplitude, short-pulsing** (microsecond) sonic **energy** is directed at the targeted tissue
- **Pressure** created by this focused energy **creates a “bubble cloud” and sub-cellular mechanical destruction** of targeted tissue
- **No heat or radiation into patient** eliminating thermal or radiation induced side effects
- Intra-tumoral energy deliver calculations optimize cellular destruction and preserve critical structuresCan be delivered **through and around critical structures**



Untreated

Treated

Cell cut in half

Precision delivery

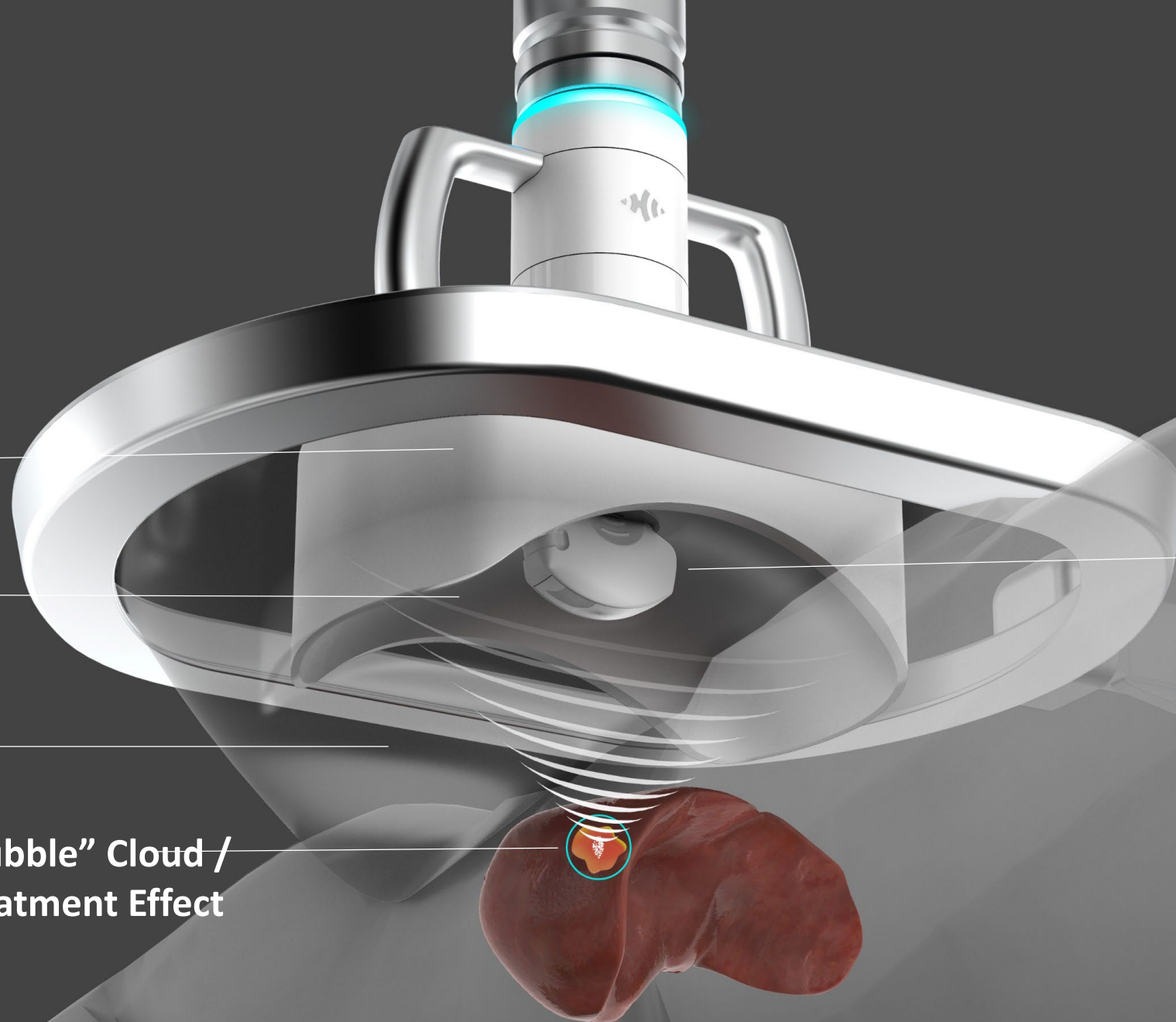
Treatment Head

**Histotripsy
Therapy Transducer**

**Proprietary Coupling
Device**

**Therapy “Bubble” Cloud /
Focused Treatment Effect**

**Imaging Probe/
Real-time
Visualization**



• HISTOTRIPSY PROCEDURES: EXTERNAL BEAM PLANNING AND TREATMENT

Target tumors with personalized therapy for each tumor



Simulation of beam paths performed to optimize therapy deliver time and identify organs of interest.

Physicians contour and plan treatments according to the shape and size of each target.

Inside the targeted tissue, energy is dosed to at least 7 points inside the tumor to inform the treating physicians of the energy required to create a bubble cloud and cellular destruction, delivering a personalized treatment for each target.

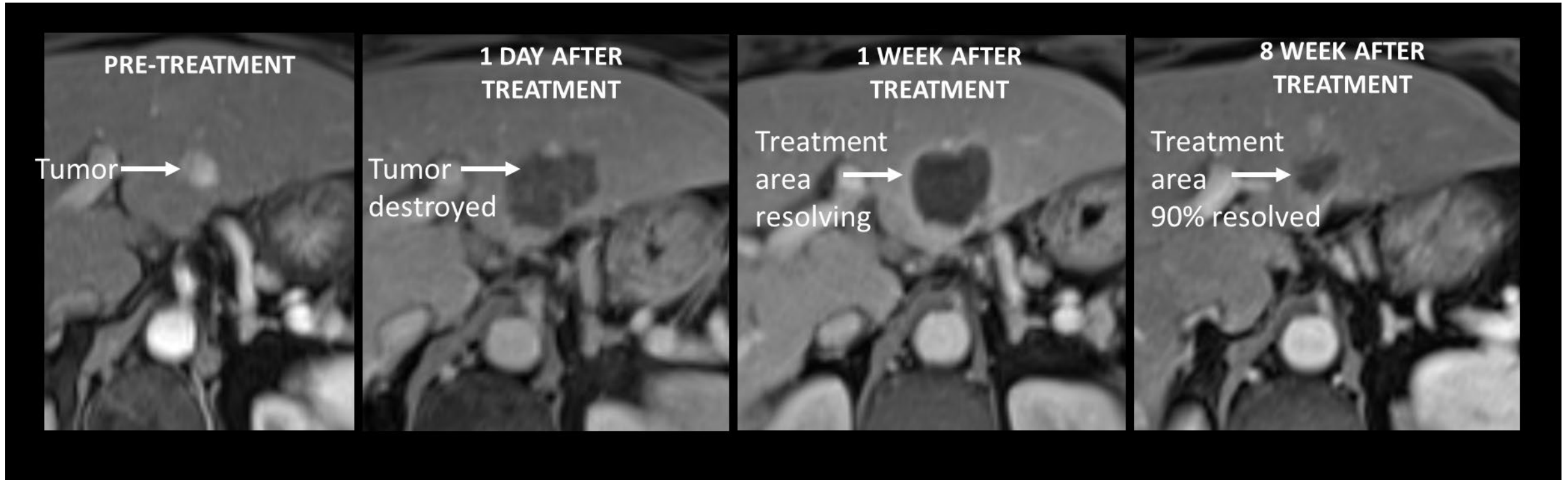
Treatment is initiated and controlled by the physician who monitors in real-time while the system automatically moves the bubble cloud through the treatment plan.

• THERESA LIVER STUDY: OVERVIEW OF 8 PATIENTS

- **All 8 patients had multi-focal liver malignancy:** colorectal mets (N=5), breast met (N=1), hepatocellular carcinoma (HCC) (N=1), cholangiocarcinoma (N=1)
- **11 total treatments:** 1 treatment (N=6), 2 treatments (N=1), 3 treatments (N=1)
- **Primary endpoint met in all cases,** defined as acute technical success and creation of a treatment zone per the pre-planned volume, as assessed by MRI 1-day post-procedure
- Procedures were performed general anesthesia in operating room setting
- **All procedures well tolerated with no patient discomfort or pain at any time points,** including all follow-up visits
 - Patient with 3 treatments had fever for 2 days and then resolved, consistent with other modalities
- **No collateral damage** to intervening/overlying tissue and critical structures preserved
- **Although not the aim, 2 of 8 patients** appeared to have **biological response** based on biomarkers and non-targeted tumor response
- **Significant involution/healing of treatment site in all patients:** >70% volume reduction at 2 months

- **EVOLUTION OF TREATMENT OVER 2 MONTHS**

Patients treated in Theresa Study demonstrated rapid involution of treatment sites



HISTOTRIPSY THERAPY

Non-invasive

Hypofractionated delivery

Effective at sub-cellular levels

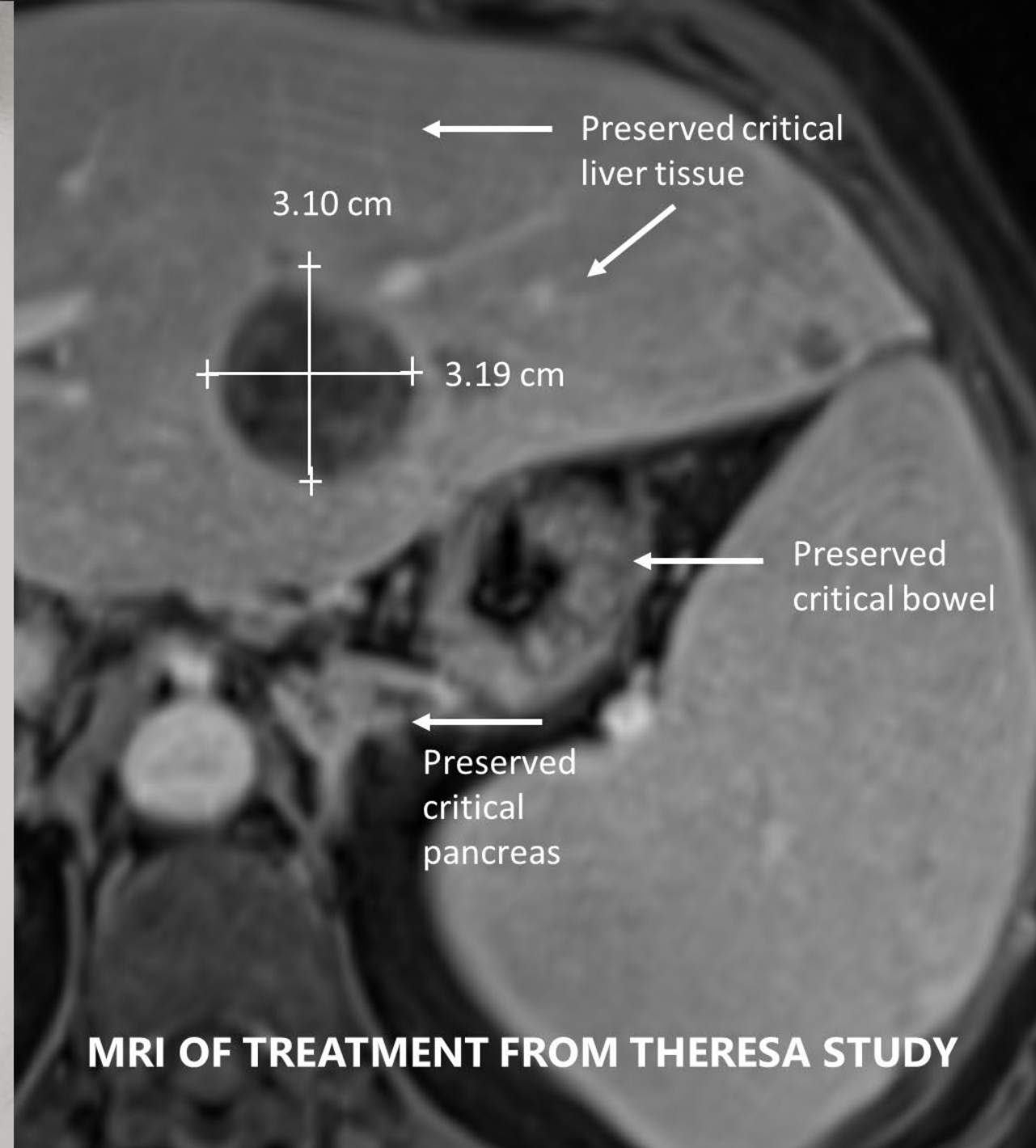
Critical structure and intervening tissue sparing

Delivered with precision and control

Rapid involution and healing of the treatment site

Minimal to no pain

Quick recovery



THANK YOU