



Focused Ultrasound Therapy

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Focused Ultrasound Foundation

Focused Ultrasound Foundation

Unique medical research, education, advocacy organization

- Founded 2006, Charlottesville, Va: Global impact
- Tax exempt non-profit
- Entrepreneurial, high impact, market driven, action and results oriented

Catalyst to accelerate the development and adoption of focused ultrasound

What is Focused Ultrasound?

- Revolutionary, noninvasive, therapeutic technology
- Disruptive alternative/complement to surgery, radiation, drug delivery, immunotherapy
- *Potential* to transform treatment, transform patient lives

Noninvasive therapeutic technology

- Outpatient
- No incisions, less pain: limited/no need for post-procedure pain meds
- Decreased complications: infection, hemorrhage, tissue damage
- Rapid recovery
- Improved outcomes, lower cost

Current use of Focused Ultrasound



565,210

patients have been
treated globally



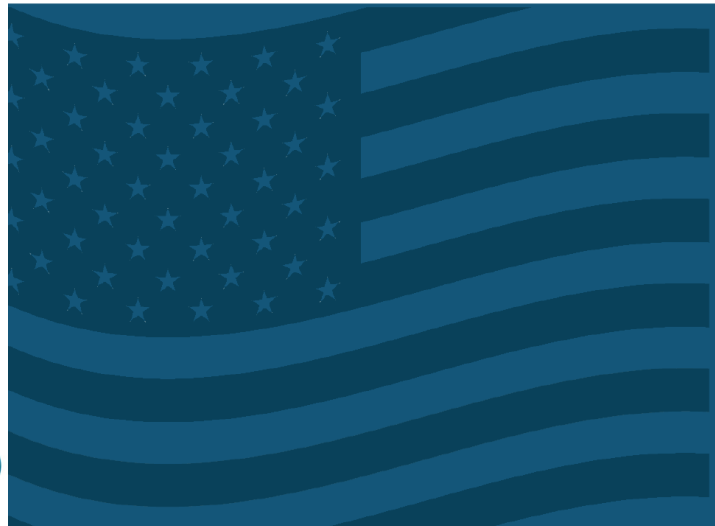
98

indications are in
clinical research



107

indications are in
laboratory research



Nine focused ultrasound applications are **FDA cleared**:

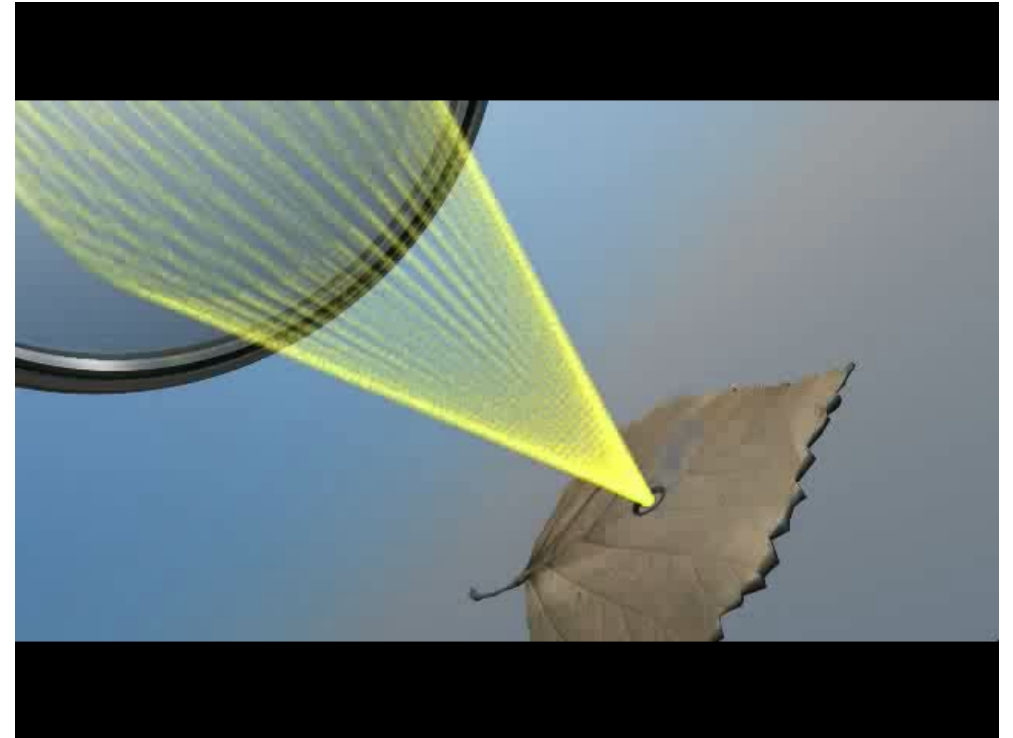
- Benign prostatic hyperplasia
- Bone metastases
- Essential tremor
- Liver tumors
- Osteoid osteoma
- Parkinson's dyskinesia
- Parkinson's tremor
- Prostate cancer
- Uterine fibroids



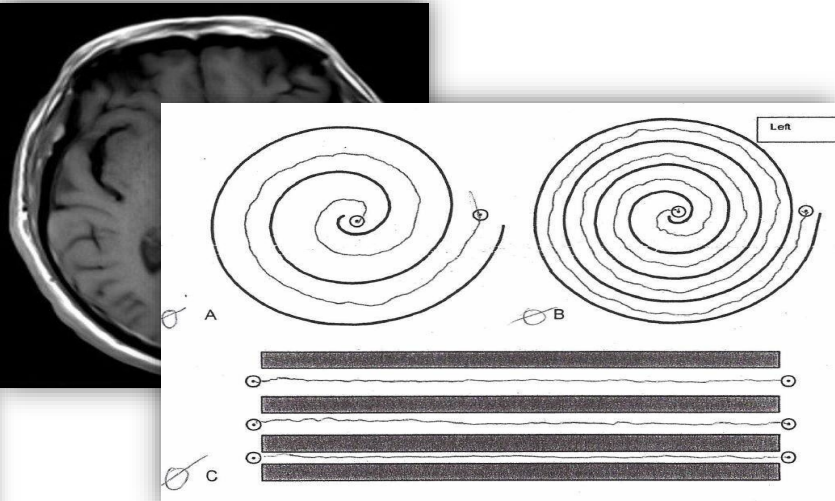
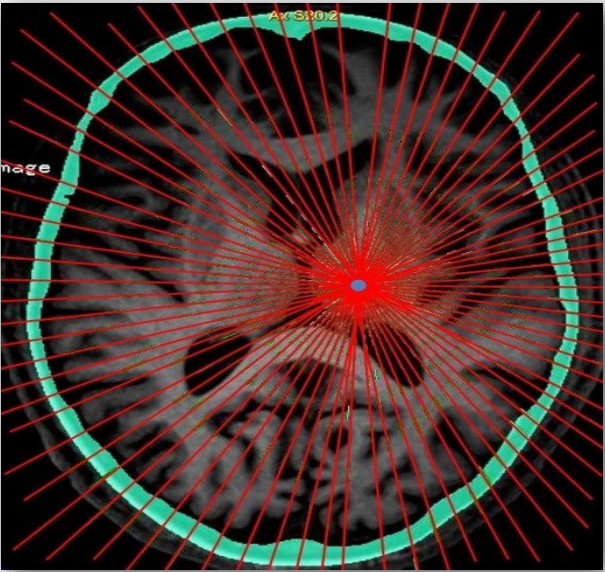
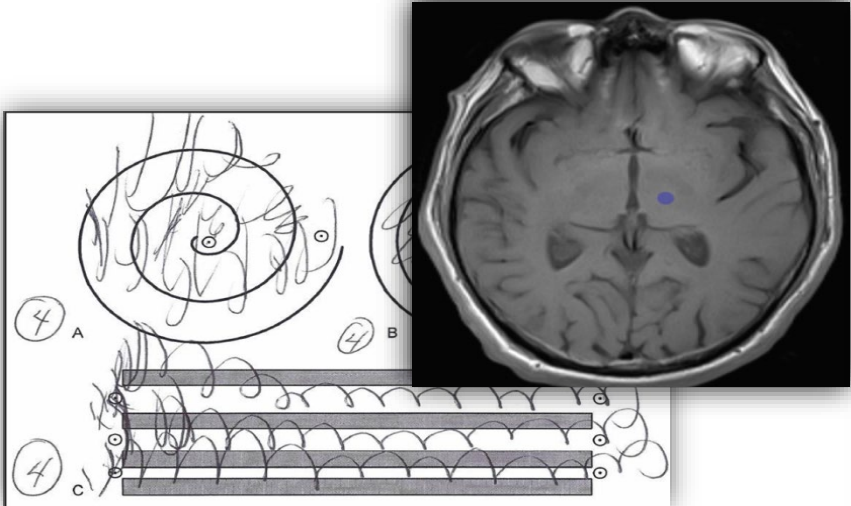
How does it work?

Multiple intersecting beams of ultrasound

- Focused accurately (submillimeter)
- Target in body
- Individual beams pass harmlessly through adjacent tissue
- Profound effect at point of convergence



FUS gives Essential Tremor patients new hope



- Awake, no anesthesia
- No incisions
- No burr holes
- No electrodes
- No infection
- No blood clots
- No brain damage



FUS shows promise for hard-to-treat cancers like Pancreatic Cancer



Baseline

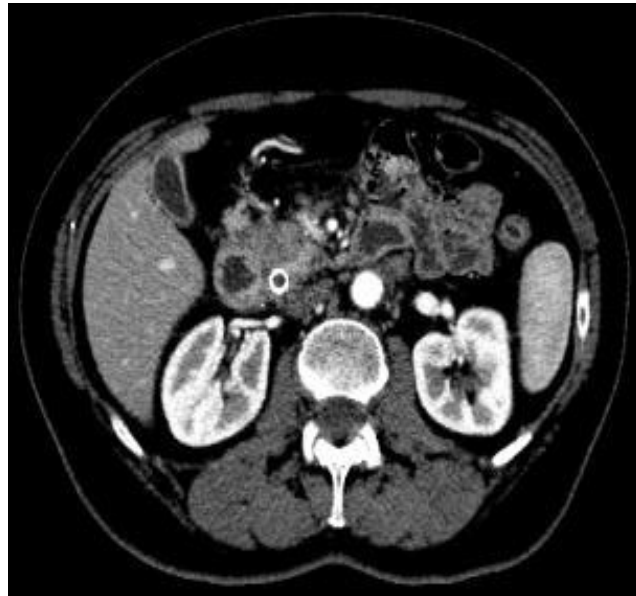


Post treatment



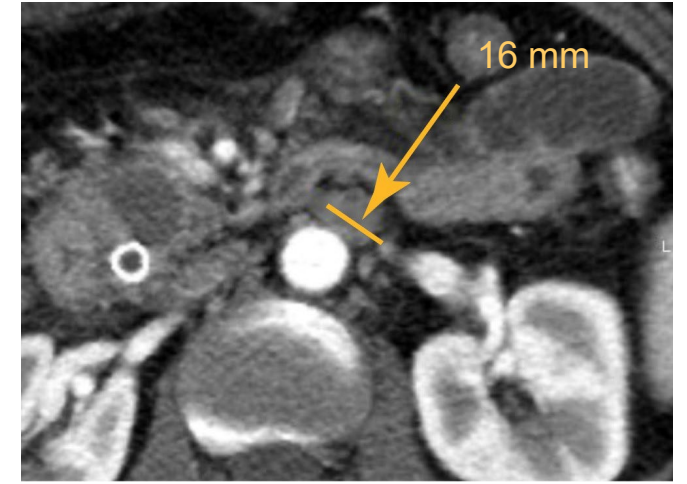
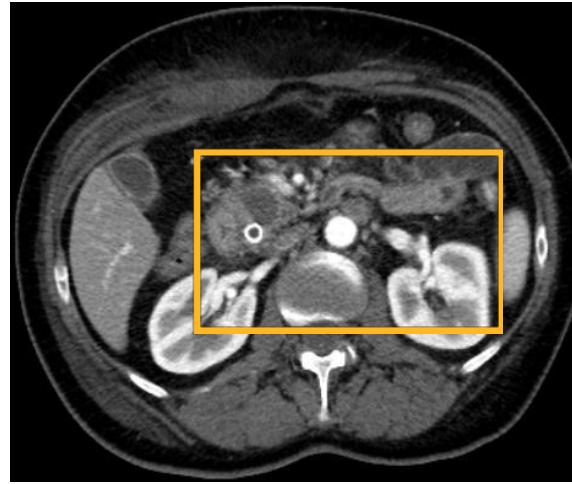
22 Months

Potential for systemic response to FUS cancer treatment

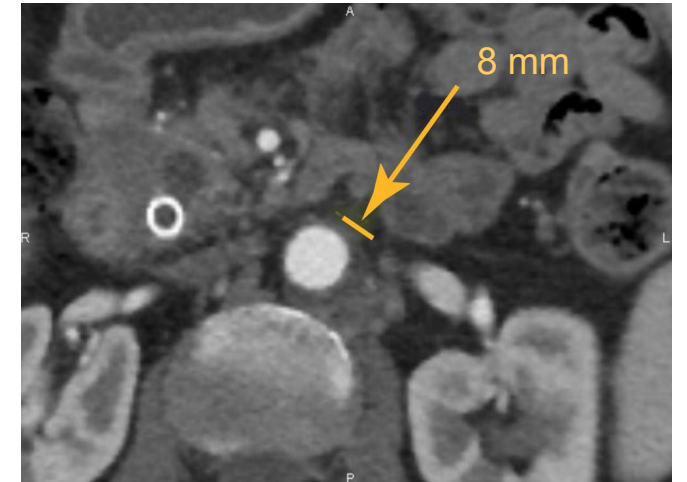
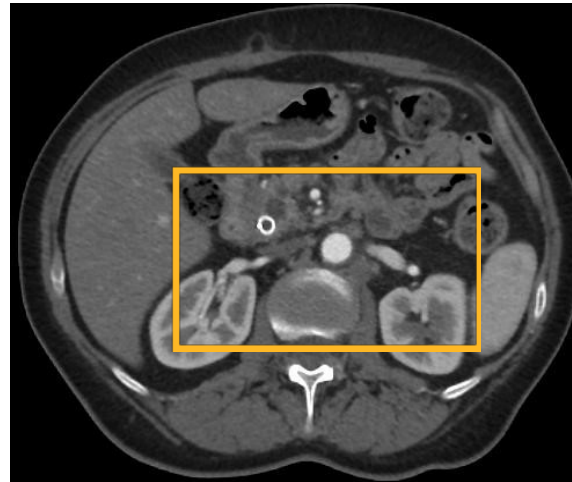


Baseline

2 Days



10 Months



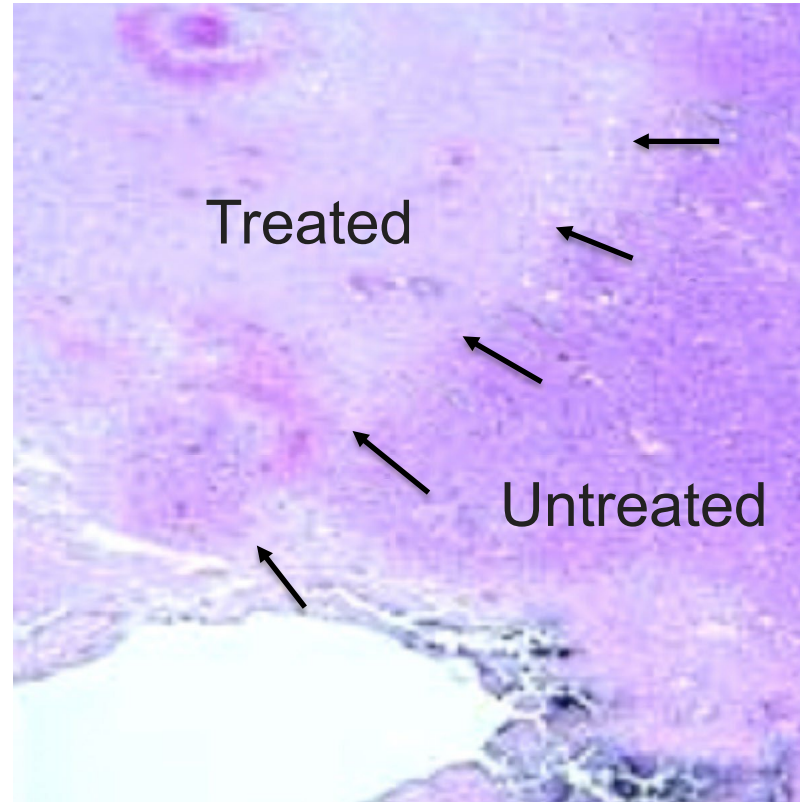
FUS treatment is precise and accurate

Liver



1mm

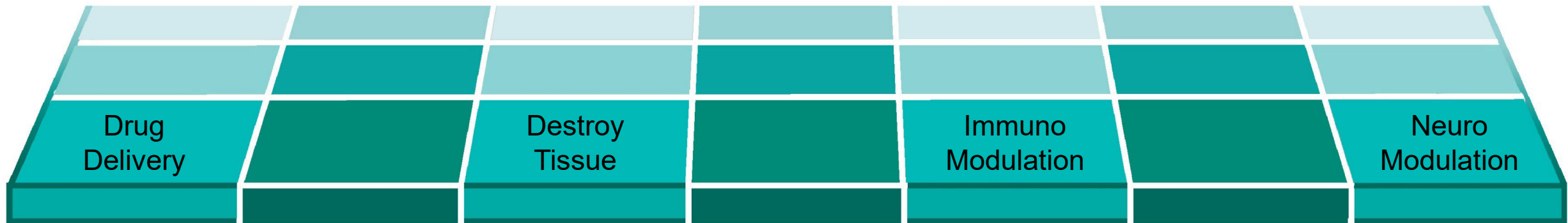
Brain



1mm

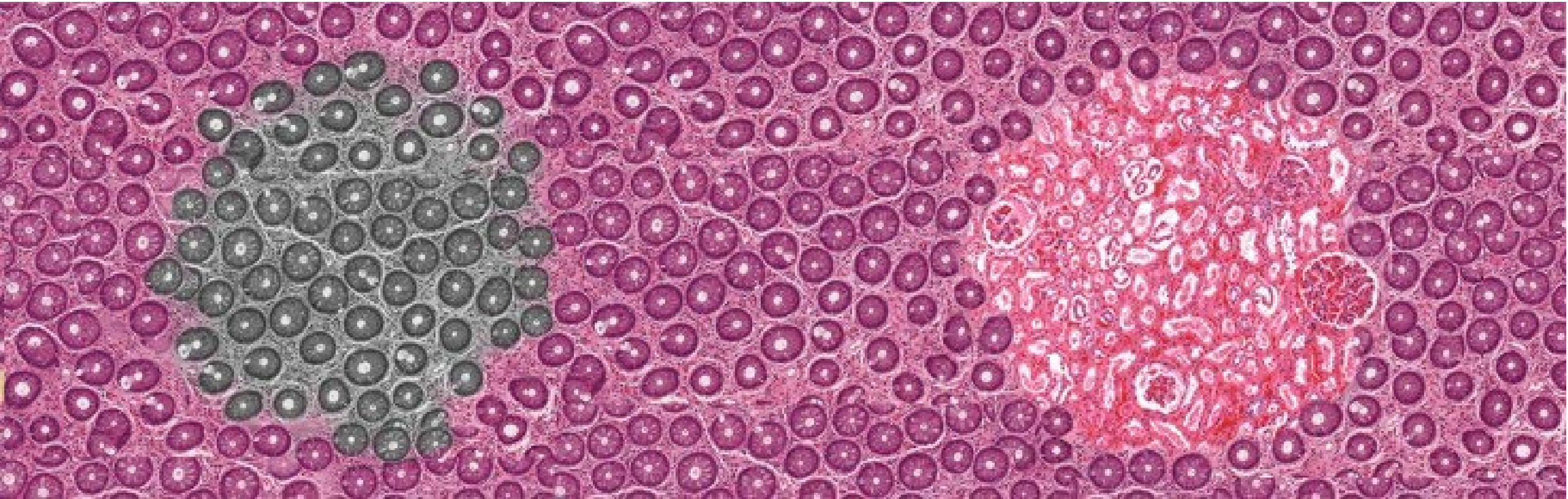
FUS can produce 20+ different biological effects at targets in the body

Platform technology
20+ Biomechanisms



Variety of effects, variety of disorders

FUS can destroy diseased tissue



Thermal Ablation

130°F (56°C) for 1 second = 100% cell death

Histotripsy

Mechanical disruption of cells

FUS can enable localized drug delivery

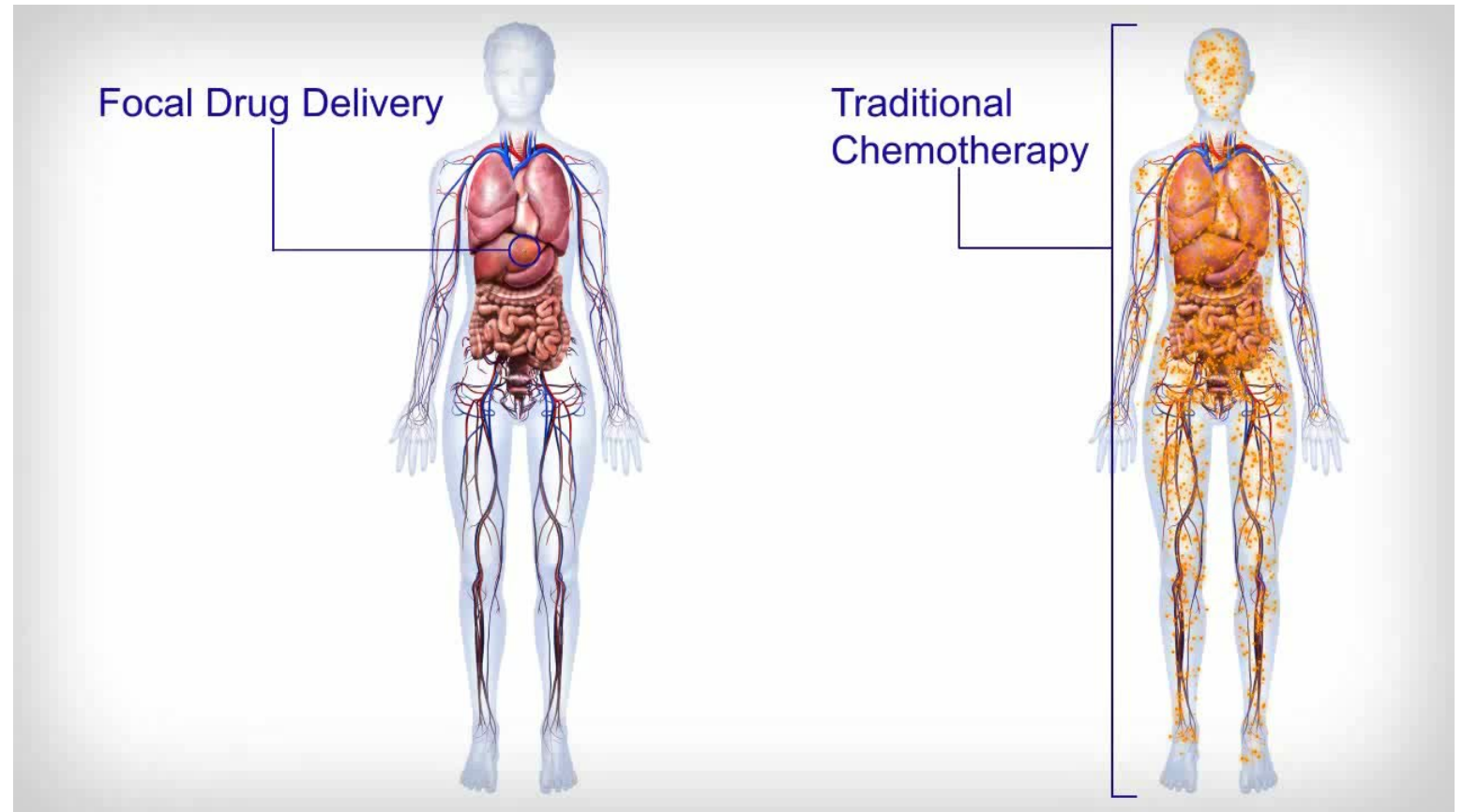
Precisely where needed

Higher concentrations

Lower systemic toxicity

Agents

- Drugs
- Genes
- Growth factors
- Stem cells

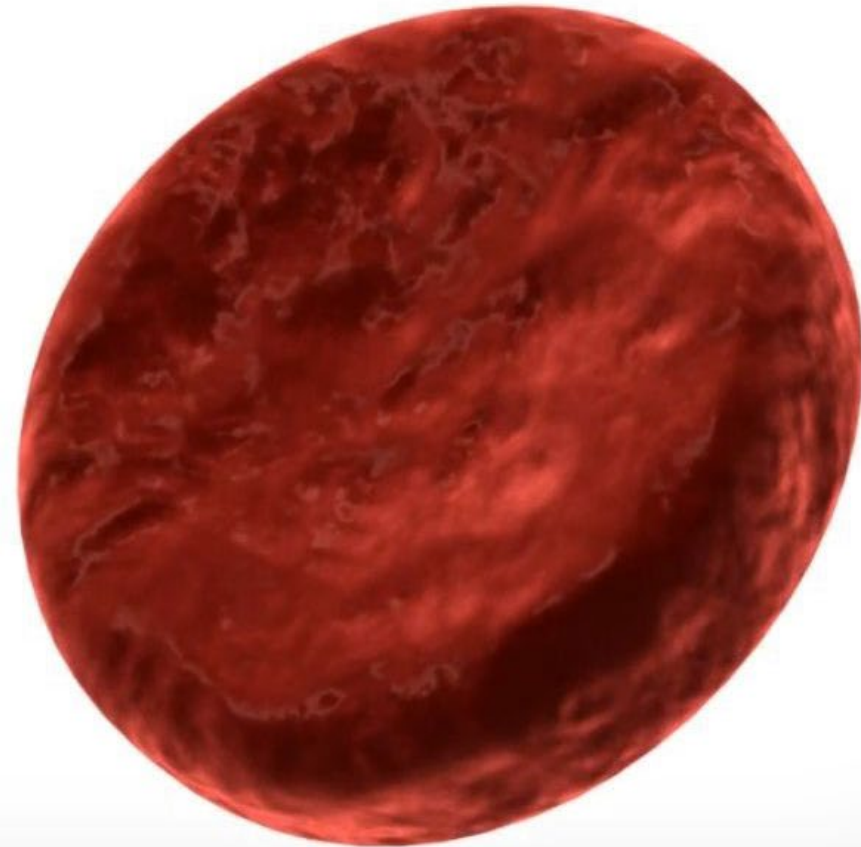


Lipid microbubbles

Microbubble



Red blood cell

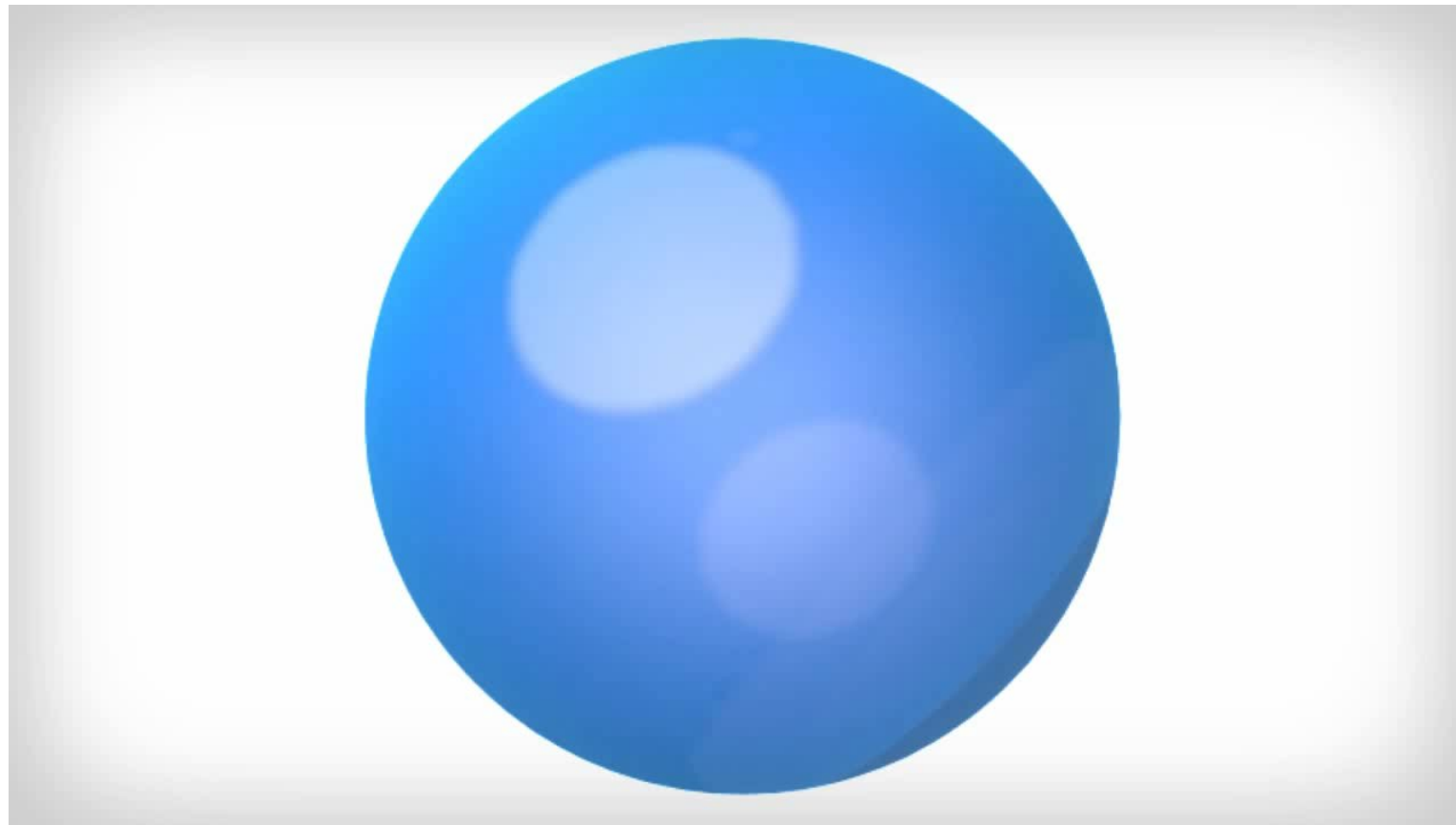


10 microns

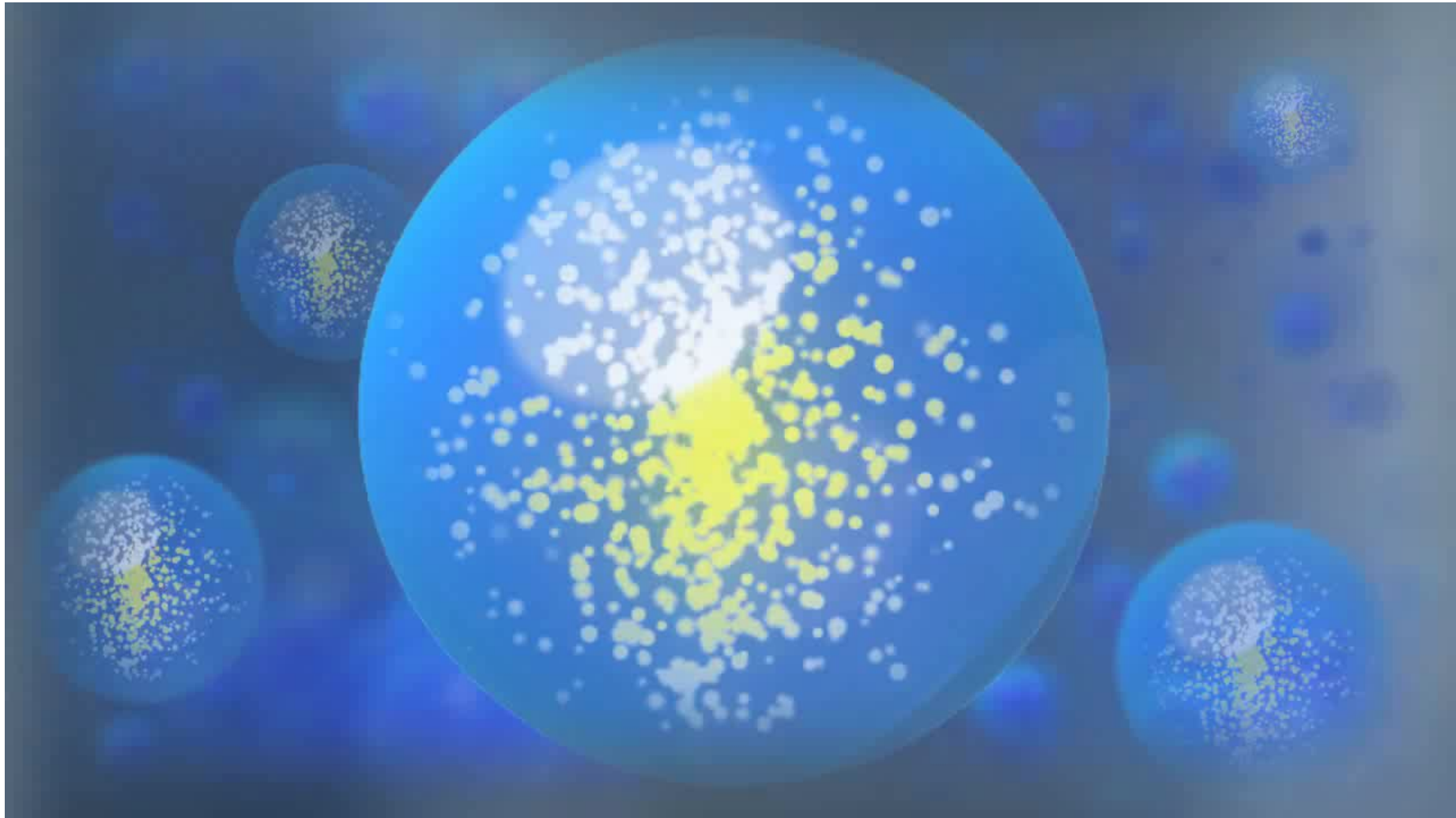


Lipid microbubbles

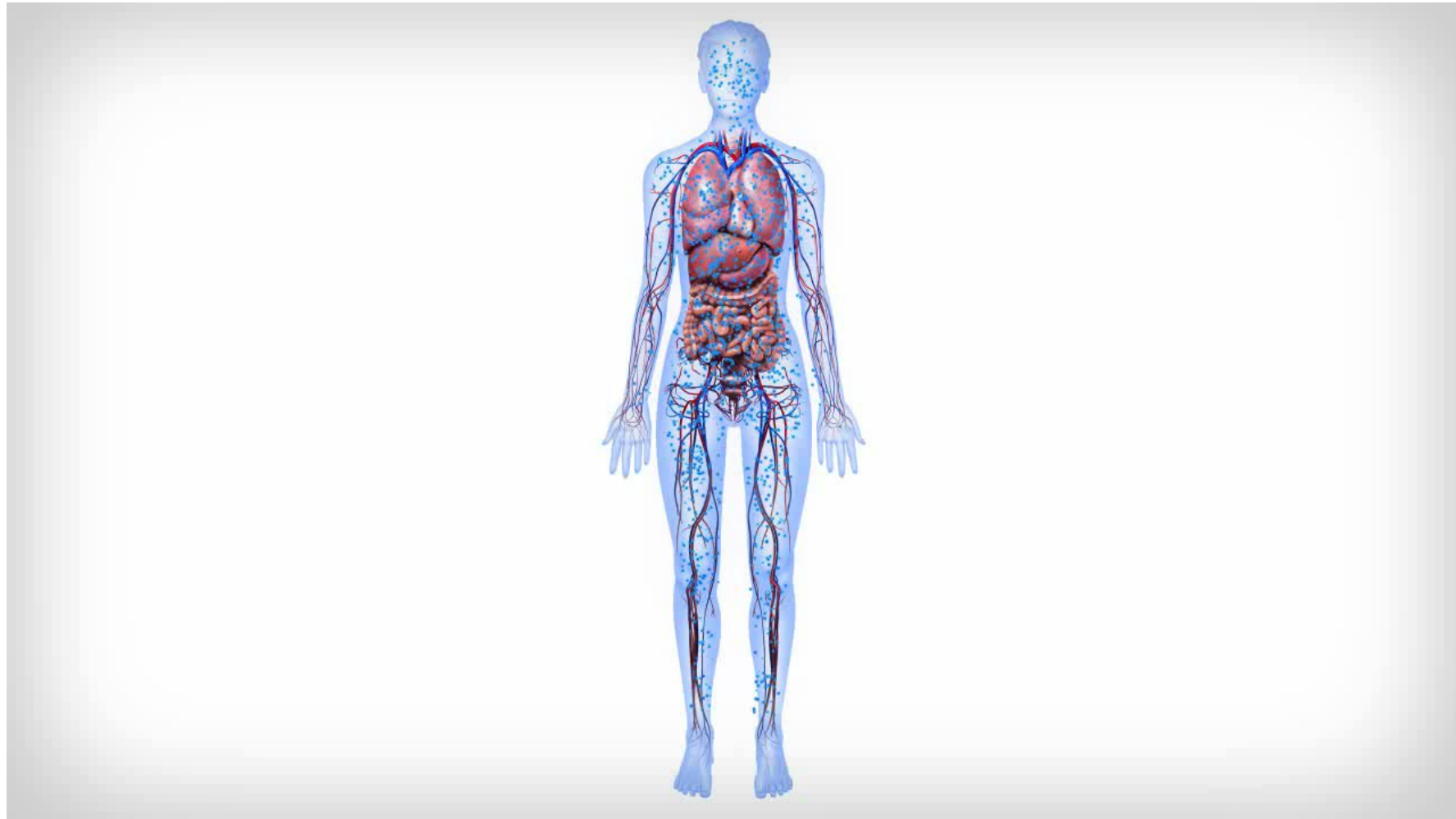
Chemotherapeutic agents, genes, growth factors



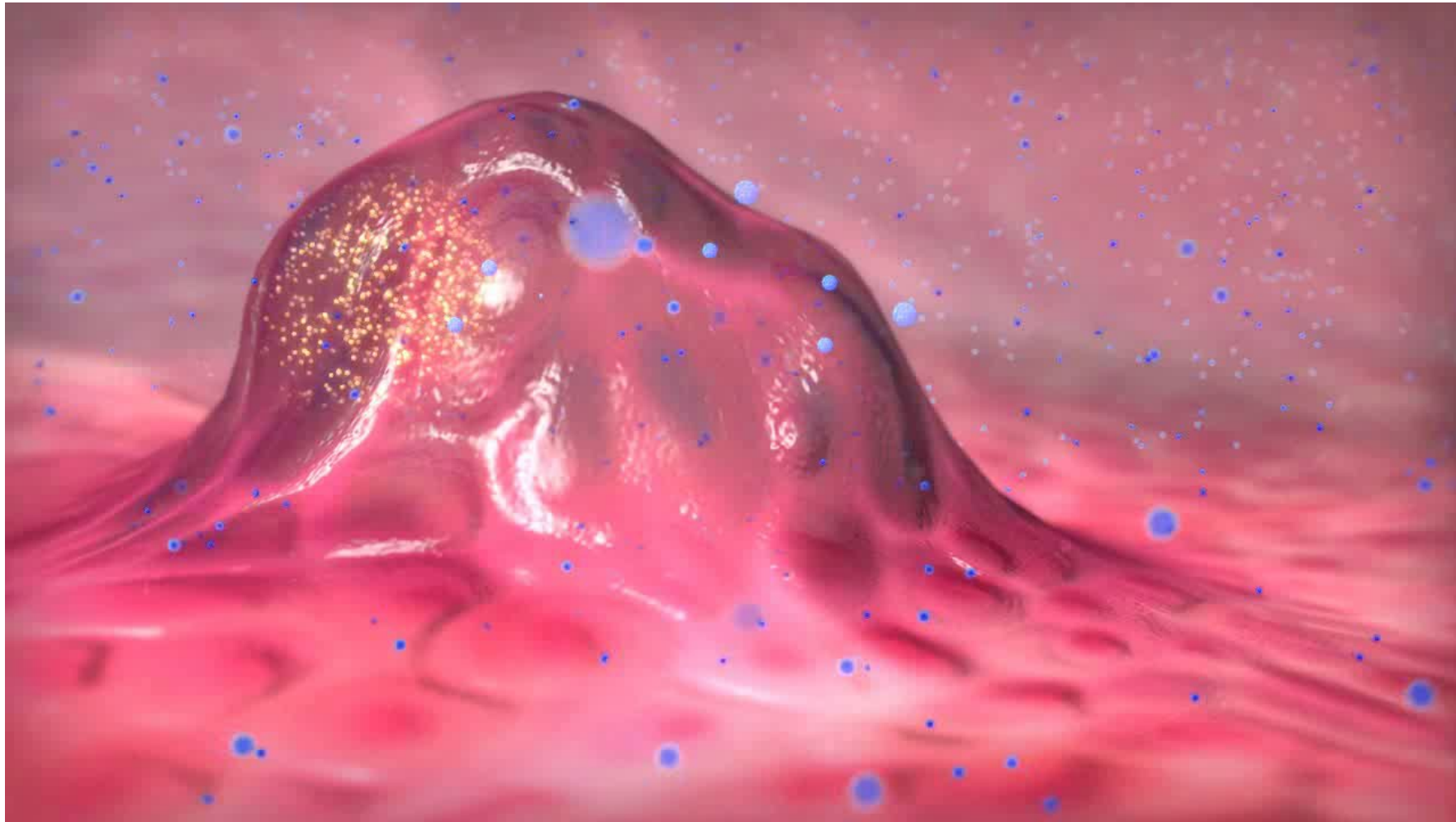
Microbubbles injected



Distribution of microbubbles



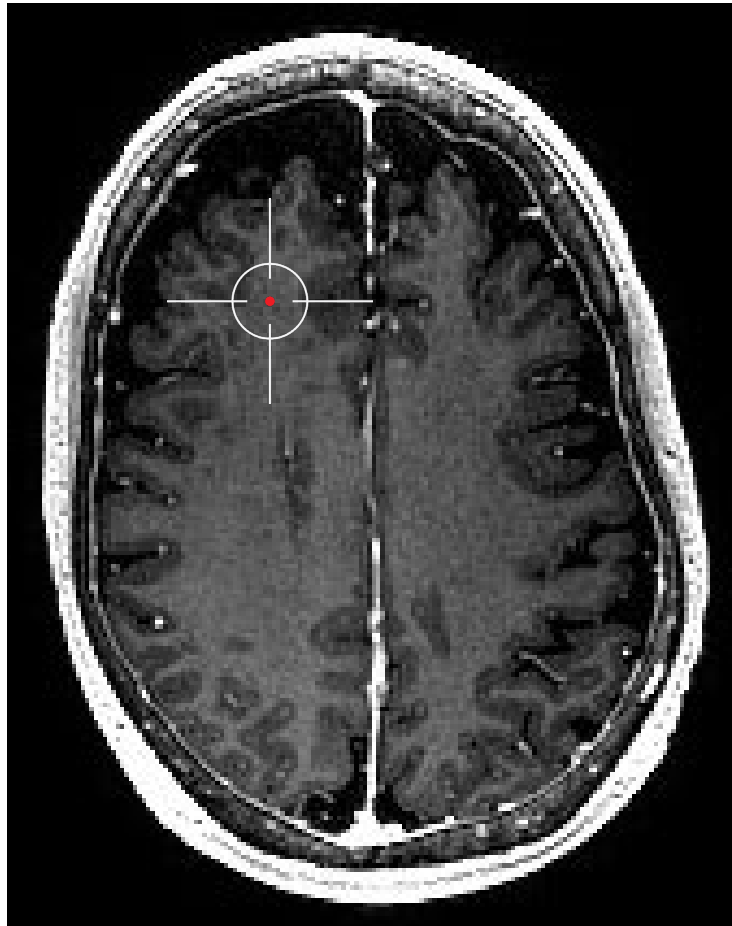
Drugs released at focal point



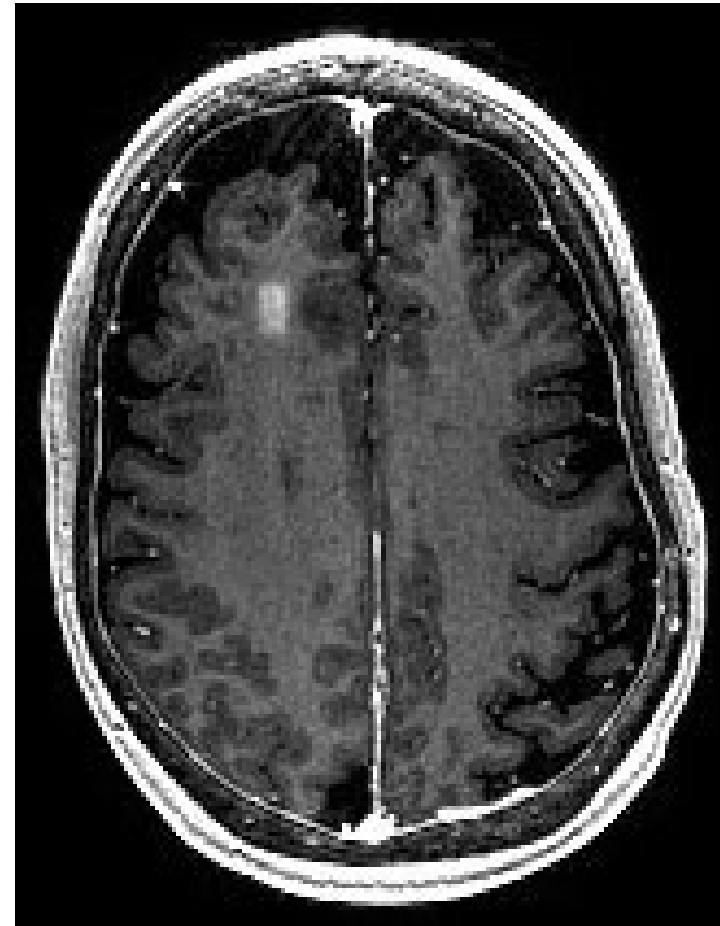
FUS can temporarily open blood-brain barrier



FUS can temporarily open blood-brain barrier



Pre-treatment



Post-treatment

FUS can induce anti-tumor immune response

Tumors are camouflaged from the immune system

FUS destroys camouflage

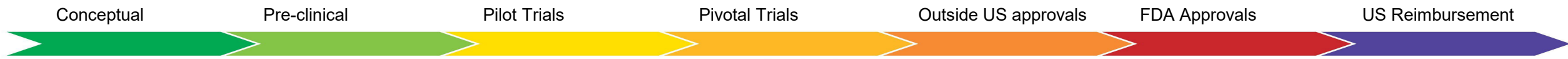
Disrupts tumor cells: exposes antigens, releases proteins

Immune system recognizes and attacks tumors

Enhances effectiveness of immunotherapy drugs



More than 170+ clinical applications in development



Conceptual	Pre-clinical	Pilot Trials	Pivotal Trials	Outside US approvals	FDA Approvals	US Reimbursement
Cardiovascular						
Hypertension	✓	✓	✓	✓	✓	✓
Varicose veins	✓	✓	✓	✓	✓	✓
Atrial fibrillation	✓	✓	✓	✓	✓	✓
Heart valve calcifications	✓	✓	✓	✓	✓	✓
Peripheral artery disease	✓	✓	✓	✓	✓	✓
Arteriovenous malformations	✓	✓	✓	✓	✓	✓
Atherosclerosis	✓	✓	✓	✓	✓	✓
Cardiac hypertrophy	✓	✓	✓	✓	✓	✓
Cardiac pacing	✓	✓	✓	✓	✓	✓
Coarctation of the aorta	✓	✓	✓	✓	✓	✓
Congestive heart failure	✓	✓	✓	✓	✓	✓
Deep vein thrombosis	✓	✓	✓	✓	✓	✓
Fetal heart anomalies	✓	✓	✓	✓	✓	✓
Hematoma	✓	✓	✓	✓	✓	✓
Hemophilia	✓	✓	✓	✓	✓	✓
Hypoplastic left heart syndrome	✓	✓	✓	✓	✓	✓
Mitral regurgitation	✓	✓	✓	✓	✓	✓
Septal perforation	✓	✓	✓	✓	✓	✓
Twin-twin transfusion syndrome	✓	✓	✓	✓	✓	✓
Ventricular tachycardia	✓	✓	✓	✓	✓	✓
Endocrine disorders						
Thyroid nodules	✓	✓	✓	✓	✓	✓
Graves' disease	✓	✓	✓	✓	✓	✓
Hyperparathyroidism	✓	✓	✓	✓	✓	✓
Thyroid cancer	✓	✓	✓	✓	✓	✓
Diabetes	✓	✓	✓	✓	✓	✓
Gastrointestinal						
Liver metastases	✓	✓	✓	✓	✓	✓
Liver tumors	✓	✓	✓	✓	✓	✓
Pancreatic tumors	✓	✓	✓	✓	✓	✓
Biliary tract cancer	✓	✓	✓	✓	✓	✓
Colorectal tumors	✓	✓	✓	✓	✓	✓
Esophageal tumors	✓	✓	✓	✓	✓	✓
Gastric tumors†	✓	✓	✓	✓	✓	✓
Malignant obstructive jaundice	✓	✓	✓	✓	✓	✓
Root canal endodontia	✓	✓	✓	✓	✓	✓
Liver fibrosis	✓	✓	✓	✓	✓	✓
Miscellaneous						
Dercum's disease	✓	✓	✓	✓	✓	✓
Head & neck tumors	✓	✓	✓	✓	✓	✓
Hypersplenism	✓	✓	✓	✓	✓	✓
Lipoma	✓	✓	✓	✓	✓	✓
Melanoma	✓	✓	✓	✓	✓	✓
Multiple tumors ¹	✓	✓	✓	✓	✓	✓
Obesity	✓	✓	✓	✓	✓	✓
Wound healing	✓	✓	✓	✓	✓	✓
Musculoskeletal						
Bone metastases	✓	✓	✓	✓	✓	✓
Osteoid osteoma	✓	✓	✓	✓	✓	✓
Arthritis, facetogenic	✓	✓	✓	✓	✓	✓
Bone cancer	✓	✓	✓	✓	✓	✓
Bone tumors, benign	✓	✓	✓	✓	✓	✓
Epicondylitis	✓	✓	✓	✓	✓	✓
Multiple myeloma ²	✓	✓	✓	✓	✓	✓
Plantar fasciitis	✓	✓	✓	✓	✓	✓
Soft tissue cancer	✓	✓	✓	✓	✓	✓
Soft tissue injury	✓	✓	✓	✓	✓	✓
Soft tissue tumors, benign	✓	✓	✓	✓	✓	✓
Arthritis	✓	✓	✓	✓	✓	✓
Arthritis, ankle	✓	✓	✓	✓	✓	✓
Arthritis, hand	✓	✓	✓	✓	✓	✓
Arthritis, hip	✓	✓	✓	✓	✓	✓
Arthritis, knee	✓	✓	✓	✓	✓	✓
Arthritis, sacroiliac	✓	✓	✓	✓	✓	✓
Desmoid tumors	✓	✓	✓	✓	✓	✓
Disc degeneration	✓	✓	✓	✓	✓	✓
Sacral chordoma	✓	✓	✓	✓	✓	✓
Muscle atrophy	✓	✓	✓	✓	✓	✓
Osteomyelitis	✓	✓	✓	✓	✓	✓
Rotator cuff injury†	✓	✓	✓	✓	✓	✓
Tendon contracture†	✓	✓	✓	✓	✓	✓
Neurological						
Essential tremor	✓	✓	✓	✓	✓	✓
Parkinson's disease, tremor	✓	✓	✓	✓	✓	✓
Depression	✓	✓	✓	✓	✓	✓
Neuropathic pain	✓	✓	✓	✓	✓	✓
Obsessive-compulsive disorder	✓	✓	✓	✓	✓	✓
Parkinson's disease, dyskinesia	✓	✓	✓	✓	✓	✓
Alzheimer's disease	✓	✓	✓	✓	✓	✓
Amyotrophic lateral sclerosis	✓	✓	✓	✓	✓	✓
Astrocytoma	✓	✓	✓	✓	✓	✓
Cancer pain	✓	✓	✓	✓	✓	✓
Dementia	✓	✓	✓	✓	✓	✓
Dystonia	✓	✓	✓	✓	✓	✓
Dystonia, hand ³	✓	✓	✓	✓	✓	✓
Epilepsy	✓	✓	✓	✓	✓	✓
Glioblastoma	✓	✓	✓	✓	✓	✓
Holmes tremor	✓	✓	✓	✓	✓	✓
Huntington's disease	✓	✓	✓	✓	✓	✓
Migraine	✓	✓	✓	✓	✓	✓
Multiple sclerosis	✓	✓	✓	✓	✓	✓
Neuroblastoma	✓	✓	✓	✓	✓	✓
Opioid and other addictions	✓	✓	✓	✓	✓	✓
Painful amputation neuromas	✓	✓	✓	✓	✓	✓
Pontine glioma	✓	✓	✓	✓	✓	✓
Traumatic brain injury	✓	✓	✓	✓	✓	✓
Cavernomas	✓	✓	✓	✓	✓	✓
Hydrocephalus	✓	✓	✓	✓	✓	✓
Neuromyelitis optica†	✓	✓	✓	✓	✓	✓
Parkinson's disease, other ^{4†}	✓	✓	✓	✓	✓	✓
Rett syndrome†	✓	✓	✓	✓	✓	✓
Spinal cord injury	✓	✓	✓	✓	✓	✓
Stroke, intracerebral hemorrhage	✓	✓	✓	✓	✓	✓
Stroke, thromboembolic	✓	✓	✓	✓	✓	✓
Trigeminal neuralgia	✓	✓	✓	✓	✓	✓
Anorexia	✓	✓	✓	✓	✓	✓
Ophthalmological						
Glaucoma	✓	✓	✓	✓	✓	✓
Keratoplasty	✓	✓	✓	✓	✓	✓
Macular degeneration	✓	✓	✓	✓	✓	✓
Pulmonary						
Rhinitis	✓	✓	✓	✓	✓	✓
Lung cancer	✓	✓	✓	✓	✓	✓
Lung metastases	✓	✓	✓	✓	✓	✓
Tuberculosis†	✓	✓	✓	✓	✓	✓
Urological						
Benign prostatic hyperplasia ⁵	✓	✓	✓	✓	✓	✓
Prostate cancer	✓	✓	✓	✓	✓	✓
Kidney tumors	✓	✓	✓	✓	✓	✓
Bladder tumors	✓	✓	✓	✓	✓	✓
Chyluria	✓	✓	✓	✓	✓	✓
Kidney stones	✓	✓	✓	✓	✓	✓
Acute kidney injury	✓	✓	✓	✓	✓	✓
Acute tubular necrosis	✓	✓	✓	✓	✓	✓
Fetal bladder obstruction	✓	✓	✓	✓	✓	✓
Ureterocele	✓	✓	✓	✓	✓	✓
Urinary tract infection †	✓	✓	✓	✓	✓	✓
Vasectomy†	✓	✓	✓	✓	✓	✓
Women's health						
Uterine fibroids	✓	✓	✓	✓	✓	✓
Breast cancer	✓	✓	✓	✓	✓	✓
Breast fibroadenoma	✓	✓	✓	✓	✓	✓
Cervicitis	✓	✓	✓	✓	✓	✓
Uterine adenomyosis	✓	✓	✓	✓	✓	✓
Brain metastases, breast cancer	✓	✓	✓	✓	✓	✓
Cervical tumors	✓	✓	✓	✓	✓	✓
Ectopic pregnancy	✓	✓	✓	✓	✓	✓
Endometrial tumors	✓	✓	✓	✓	✓	✓
Endometriosis	✓	✓	✓	✓	✓	✓
Endometriosis, colorectal	✓	✓	✓	✓	✓	✓
Ovarian tumors	✓	✓	✓	✓	✓	✓
Retained placenta	✓	✓	✓	✓	✓	✓
Vaginal tumors	✓	✓	✓	✓	✓	✓
Vulvar dystrophy	✓	✓	✓	✓	✓	✓
Polycystic ovary syndrome	✓	✓	✓	✓	✓	✓

UVA Focused Ultrasound Center is global leader

- Established in September 2009 – public-private partnership
- Pioneers in FUS research and advancing new patient treatments:
 - First in the world – essential tremor, Parkinson’s tremor, FUS + immunotherapy combination approach (metastatic breast cancer)
 - Cancer (brain, breast, bone, melanoma, pancreas), epilepsy, neuropathic pain, uterine fibroids
- Sustained Commonwealth investment since 2009 has enabled:
 - Hundreds of patients treated
 - Hundreds of jobs created
 - More than \$40 million in additional public/private funding

Foundation and UVA established FUS Cancer Immunotherapy Center in June 2022

Combined investment from UVA, Foundation and Commonwealth of Virginia

- Purchase state-of-the-art focused ultrasound devices
- Hire faculty and staff
- Fund clinical trials and laboratory research studies

Goals

- Optimize the antitumor immunologic effects of focused ultrasound
- Develop new focused ultrasound technologies
- Improve quality of life, longevity, access, and cost of care for patients with a variety of cancers by augmenting the effectiveness of cancer immunotherapy with focused ultrasound

Pioneering new FUS + immunotherapeutic treatments

- Metastatic breast cancer, early-stage breast cancer, glioblastoma, melanoma, pancreatic cancer

Virginia Tech FUS Research Program is growing rapidly

- Multi-disciplinary, large geographic footprint:
 - Fralin Biomedical Research Institute at Virginia Tech Carilion (Roanoke)
 - Carilion Clinic (Roanoke)
 - Biomedical Engineering, Immunology, Veterinary Teaching Hospital (Blacksburg)
 - Virginia-Maryland College of Veterinary Medicine's, Animal Cancer Care and Research Center (Roanoke)
 - Children's National Hospital collaboration (Washington, DC)
- Primary focus areas:
 - Brain - Parkinson's, essential tremor, brain tumors, chronic pain, addiction
 - Pediatric brain tumors
 - Hard to treat cancers – immunotherapy combination approach, comparative oncology
 - Veterinary care
- Recent large gifts from private foundations to support brain and cancer research

2024-2026 Appropriations Request

Advancing focused ultrasound research in Virginia by sustaining the \$4.1 million for UVA in each year of the biennium, and \$1 million per year for Virginia Tech.

The funding supports activities and research at these institutions as designated by the Focused Ultrasound Foundation (FUSF), including coordinated activities between both UVA and Virginia Tech.