2023

Veterinary Medicine

Focused Ultrasound Foundation

Overview

FUS Veterinary Applications

Veterinary medicine offers a unique opportunity to expand research and commercial focused ultrasound applications into a market with reduced regulatory burdens, while also collecting data in naturally occurring disease models to support human clinical trials.

Focused ultrasound's ability to noninvasively treat tissue and enhance the efficacy of some therapies, thus reducing the length of hospital stays and total cost, is a crucial benefit for pet owners who pay out of pocket.

Currently, the most promising focused ultrasound applications in veterinary medicine are in oncology, particularly in indications where surgical approaches may significantly affect quality of life. Veterinary clinical trials have demonstrated that focused ultrasound is easily tolerated and effective in the treatment of soft tissue sarcoma, oral tumors, and osteosarcomas. Ongoing clinical work will investigate focused ultrasound's utility against other aggressive cancers, including bladder cancer, brain cancer, and liver cancer. Excitingly, focused ultrasound is now also in use in emergency veterinary medicine to treat feline uroliths.

XIII. Veterinary Medicine

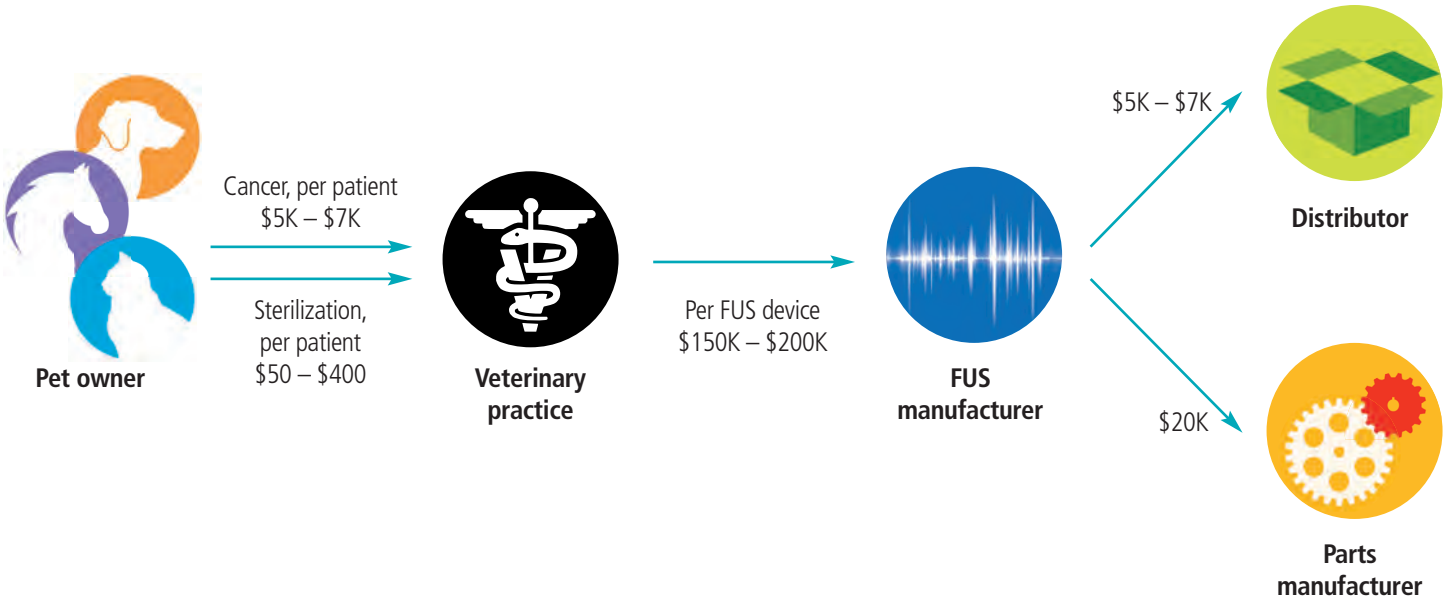
In recent years, the use of focused ultrasound in veterinary medicine has expanded beyond traditional thermally ablative procedures. Histotripsy, sonodynamic therapy, and drug and gene delivery are all currently being explored as alternative treatment approaches. These modalities may offer advantages due to their lower risk of damaging nearby structures such as skin, bone, and nerves. This is especially important in veterinary patients due to their smaller size and the prevalence of lesions on the limbs and body wall.

Focused ultrasound also shows great promise in the management of osteoarthritis, soft tissue injury, and elbow/hip dysplasia. Treatment can enhance blood flow to the damaged tissue, enhancing healing and reducing scar formation. Focused ultrasound can also be used to noninvasively ablate nerve tissue, relieving pain in advanced arthritis.

For more information

www.fusfoundation.org/for-researchers/high-priority-research-areas/veterinary-program.

Value Chain



Potential Market

Focused ultrasound can address many of the common diseases and conditions that affect our pets. For many of these indications, standard of care requires invasive surgery, which often carries significant post-treatment concerns including wound care, infection, pain management, and self-mutilation. The cost for focused ultrasound treatments is heavily dependent on the cost of the equipment. While we are currently projecting that these noninvasive treatments will cost more upfront than surgery, once the added costs and risks of an invasive procedure are accounted for, focused ultrasound may in fact be more cost effective.

This is especially true in oncology cases requiring chemotherapy and/or radiation in addition to surgery, which can add up to an additional $15,000. Factors that can aid in decreasing the cost of focused ultrasound include veterinary-specific device design, rapid large-volume treatment capabilities to decrease total treatment time, and flexible device design that will allow treatment of multiple indications with one unit.

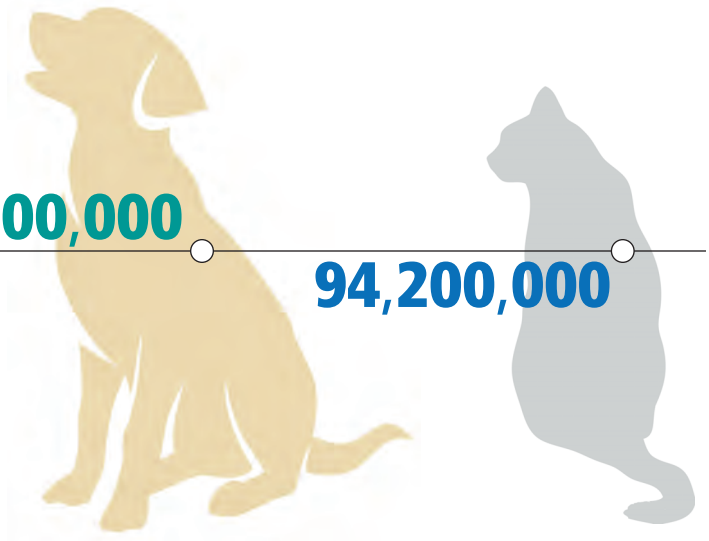
NEW

Potential Market in the US

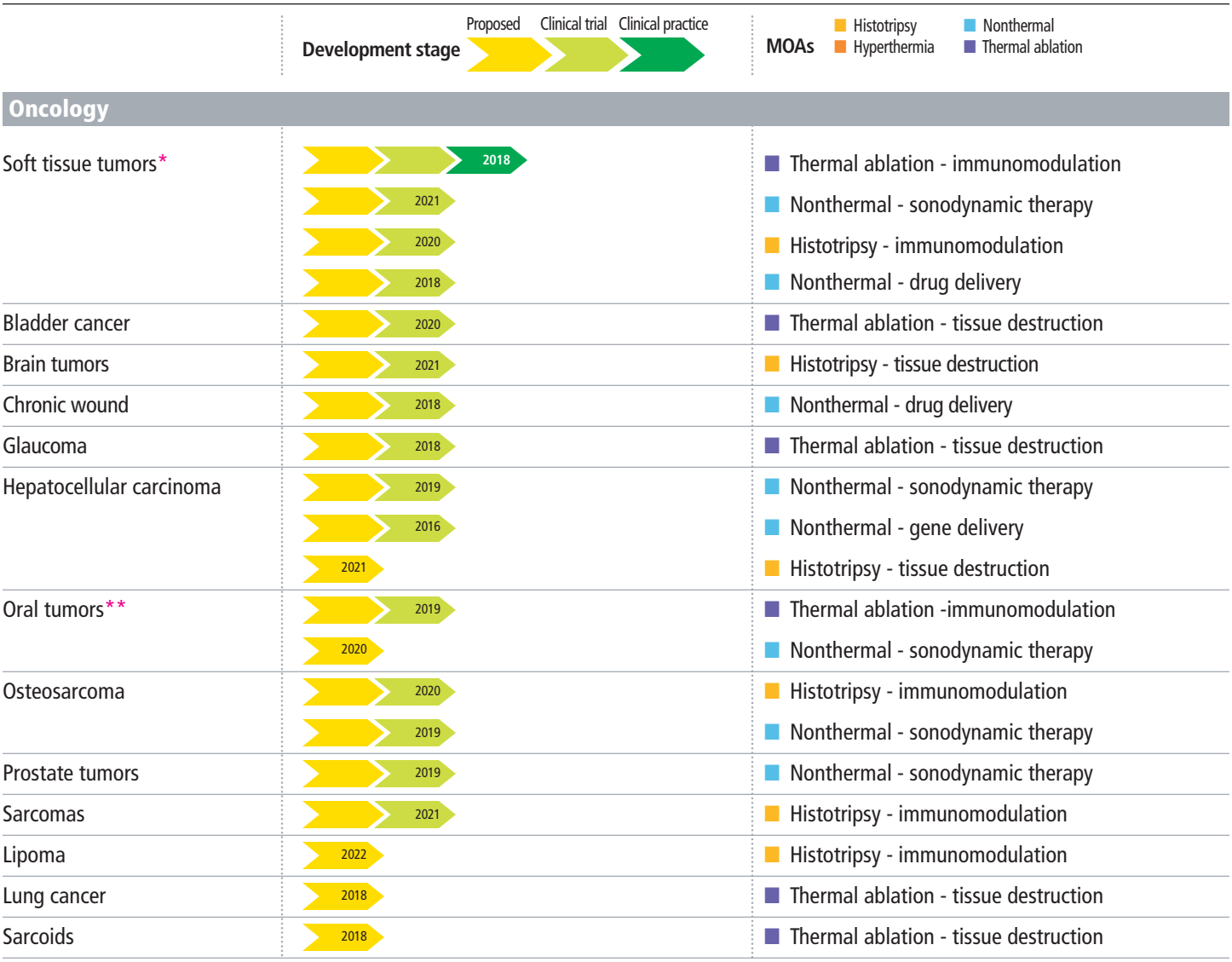
Indication	Incidences per year US	Cost of Surgery	Cost of FUS estimated	Potential market value
Lipoma	269,100	$200 – $500	$1,000	$269,100,000
Urethral obstruction	264,514	$750 – $5,000	$1,000	$264,514,000
Mast cell tumor	112,125	$500 – $1,000	$1,000	$112,125,000
Soft tissue sarcoma	107,640	$500 – $2,000	$1,000	$107,640,000
Osteosarcoma	44,850	$800 – $1,000	$1,000	$ 44,850,000
Brain tumor	13,007	$5,000 – $7,000	$5,000	$ 65,035,000
		Additional costs		
Radiation, any cancer		$4,000 – $10,000		
Chemotherapy, any cancer		$300 – $5,000		

Sources
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3658424/figure/fig1/
https://www.animalsheltering.org/page/pets-by-the-numbers
https://www.embracepetinsurance.com/health/lipoma
https://www.embracepetinsurance.com/health/mast-cell-tumor
https://www.vet.cornell.edu/departments-centers-and-institutes/sprecher-institute-comparative-cancer-research/cancer-care-cuha/cancer-management-frequently-asked-questions
https://www.pawlicy.com/blog/urinary-blockage-in-cats/#cost
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6856054/
https://icatcare.org/advice/feline-lower-urinary-tract-disease-flutd/
https://onlinelibrary.wiley.com/doi/10.1111/jvim.16389
https://www.cbsnews.com/news/the-heartbreak-and-high-costs-of-pet-cancer/

US Canine and Feline Population



State of Research by Indication and MOA

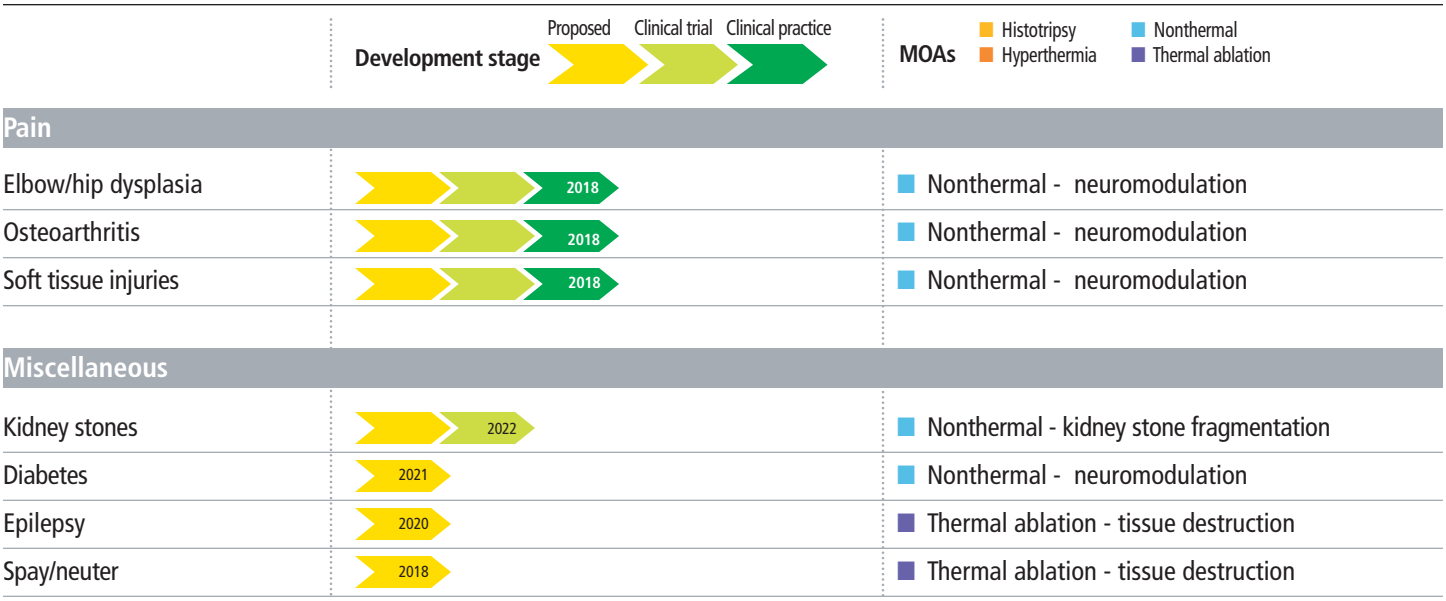


Oncology		
Soft tissue tumors*	2018	Thermal ablation - immunomodulation
	2021	Nonthermal - sonodynamic therapy
	2020	Histotripsy - immunomodulation
	2018	Nonthermal - drug delivery
Bladder cancer	2020	Thermal ablation - tissue destruction
Brain tumors	2021	Histotripsy - tissue destruction
Chronic wound	2018	Nonthermal - drug delivery
Glaucoma	2018	Thermal ablation - tissue destruction
Hepatocellular carcinoma	2019	Nonthermal - sonodynamic therapy
	2016	Nonthermal - gene delivery
	2021	Histotripsy - tissue destruction
Oral tumors**	2019	Thermal ablation -immunomodulation
	2020	Nonthermal - sonodynamic therapy
Osteosarcoma	2020	Histotripsy - immunomodulation
	2019	Nonthermal - sonodynamic therapy
Prostate tumors	2019	Nonthermal - sonodynamic therapy
Sarcomas	2021	Histotripsy - immunomodulation
Lipoma	2022	Histotripsy - immunomodulation
Lung cancer	2018	Thermal ablation - tissue destruction
Sarcoids	2018	Thermal ablation - tissue destruction

*Soft tissue tumors include soft tissue sarcoma and mast cell tumors.

**Oral tumors includes oral melanoma, plasmacytoma (of the gums/lips), ameloblastomas, salivary gland tumors, and squamous cell carcinoma (of the gums/lips).

State of Research by Indication and MOA continued



	Development stage	MOAs
Pain		
Elbow/hip dysplasia	2018	Nonthermal - neuromodulation
Osteoarthritis	2018	Nonthermal - neuromodulation
Soft tissue injuries	2018	Nonthermal - neuromodulation
Miscellaneous		
Kidney stones	2022	Nonthermal - kidney stone fragmentation
Diabetes	2021	Nonthermal - neuromodulation
Epilepsy	2020	Thermal ablation - tissue destruction
Spay/neuter	2018	Thermal ablation - tissue destruction

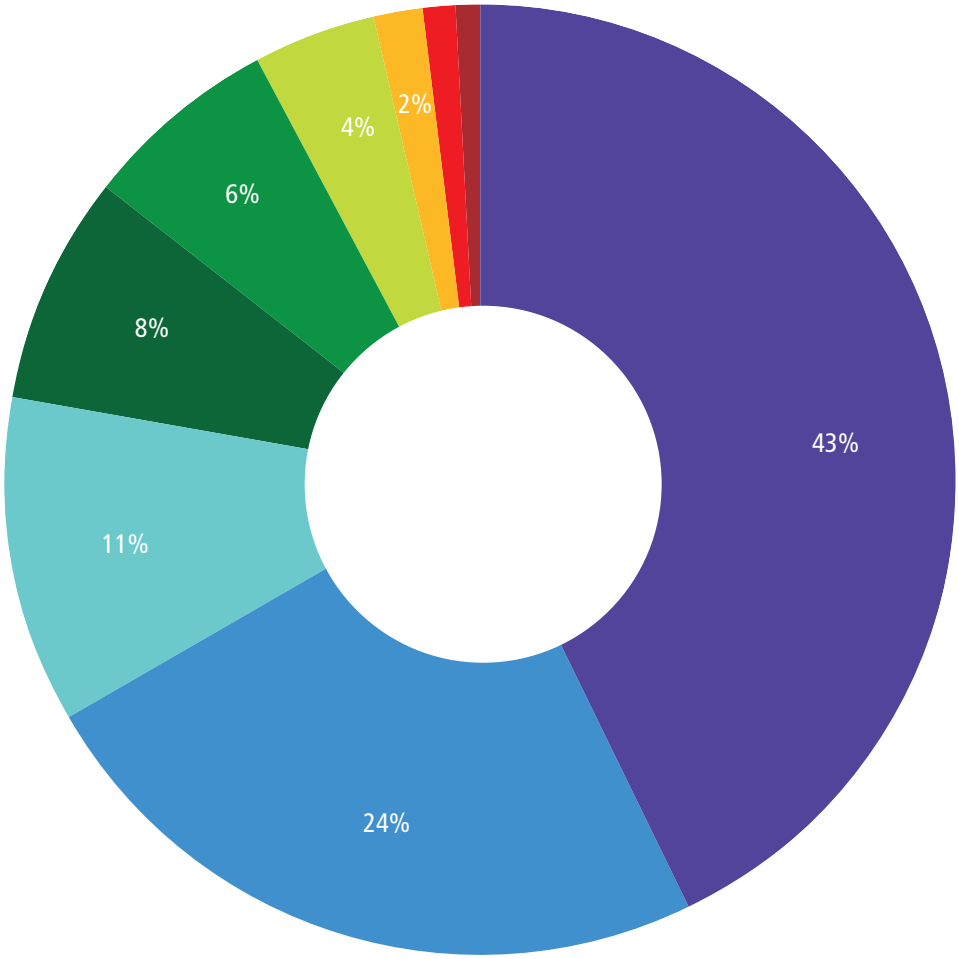
Veterinary advances

As the veterinary focused ultrasound field continues to mature, more technically demanding indications, such as glioblastoma and bladder cancer, are being explored. Focused ultrasound is also now in use for applications in emergency medicine (feline uroliths). Additional modes and bioeffects of focused ultrasound, including histotripsy, sonodynamic therapy, and drug and gene delivery, are now in use in the veterinary space and may offer advantages over more traditional thermally ablative procedures.

Treated Patients by Indication—Cumulative

168 total treatments

- 72 Soft tissue tumors[1]
- 40 Osteoarthritis
- 19 Osteosarcoma[2]
- 13 Hepatocellular carcinoma
- 11 Oral tumors[3]
- 7 Glaucoma
- 3 Chronic wound
- 2 Brain tumor
- 1 Thyroid carcinoma



1 Soft tissue tumors includes soft tissue sarcoma and mast cell tumors.
2 Osteosarcoma includes osteosarcoma and chondrosarcoma.
3 Oral tumors includes oral melanoma, plasmacytoma (of the gums/lips), ameloblastomas, salivary gland tumors, squamous cell carcinoma (of the gums/lips).

Common Cancers in Popular US Dog Breeds

Most popular breeds	Common cancers	Registered dogs per year	Cancer-caused mortality
Labrador Retriever	Lymphoma, Mast cell tumor, Melanoma, Osteosarcoma, Hemangiosarcoma	192,000	31%
German Shepherd	Hemangiosarcoma, Mast cell tumor, Melanoma, Lymphoma	129,000	20%
French Bulldog	Mast cell tumor, Brain tumor, Liver tumor	39, 000	38%
Golden Retriever	Mast cell tumor, Lymphoma, Oral melanoma, Brain tumor, Fibrosarcoma, Histiocytic tumors	93,000	39%
Poodle	Squamous cell carcinoma, Mast cell tumor, Lymphoma	119,000	30%

Mammary and testicular cancer are common in unaltered dogs of all breeds.

Several dog breeds routinely top popularity charts worldwide, notably Labrador and golden retrievers, German shepherd dogs, and poodles. These breeds are genetically predisposed to certain diseases and cancers and can heavily skew the prevalence of these conditions, even if they are rare in other breeds. When assessing clinical unmet needs, it is important to consider the effects of breed popularity and distribution.

NEW

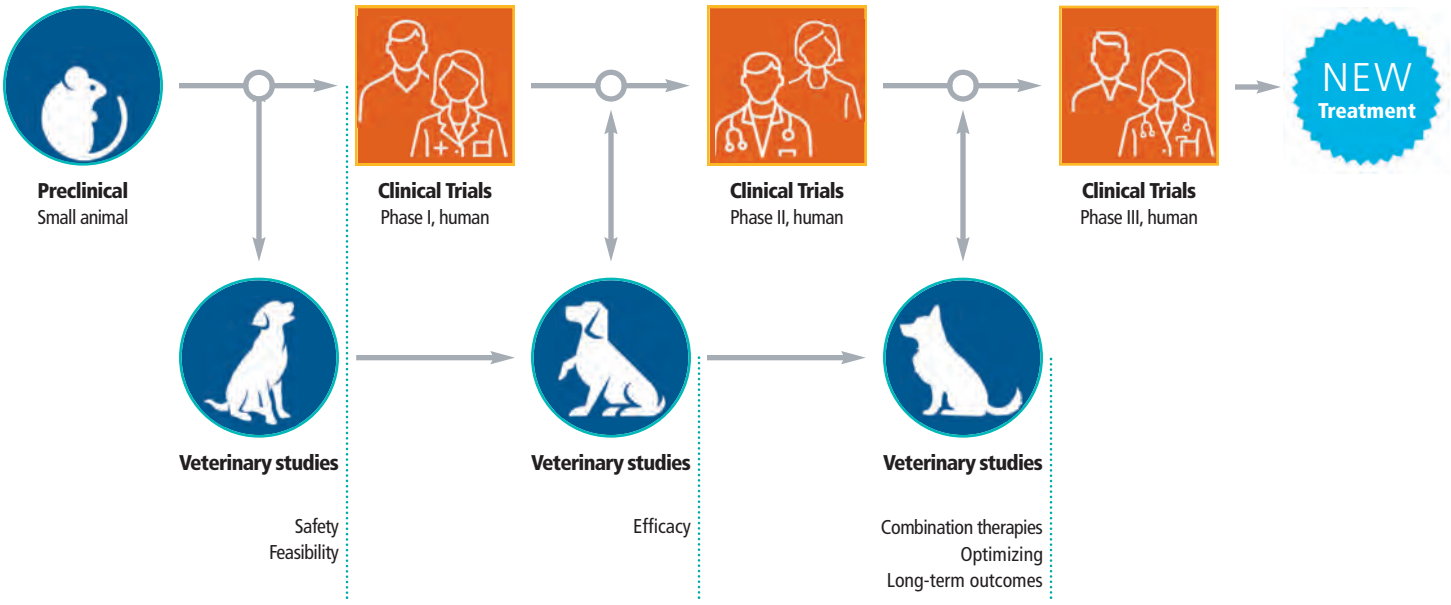
Case Study
Urinary Tract Stones

As with any medical device, regulatory agencies around the world require data from laboratory animal testing before approving focused ultrasound technology for use in humans. However, mouse or rat models often do not accurately represent human disease. Clinical focused ultrasound devices are seldom capable of treating small animals, which further complicates clinical translation. Large animal disease models, while more compatible with clinical focused ultrasound devices, are more expensive and less advanced.

Companion animals can offer the perfect solution to this conundrum. Client-owned animals are exposed to the same environments as their human owners and develop many of the same diseases. Unlike laboratory-induced diseases, these naturally occurring diseases in companion animals are remarkably similar to their human counterparts and respond similarly to therapy. Veterinary trials offer the ability to treat beloved pets while also collecting large-animal data that is more translatable than anything from a laboratory and can dramatically accelerate clinical development.

Bladder stones in pet cats are the only emergency medical condition currently treated using focused ultrasound. Urethral obstruction is one of the most common veterinary emergencies, representing 10% of all emergency cases with an incidence between 1.5 and 9%. Urethral obstruction can be fatal if left untreated, as it causes damage to the kidneys and severe electrolyte imbalances.

Comparative medicine
Integrated and comparative device development plan



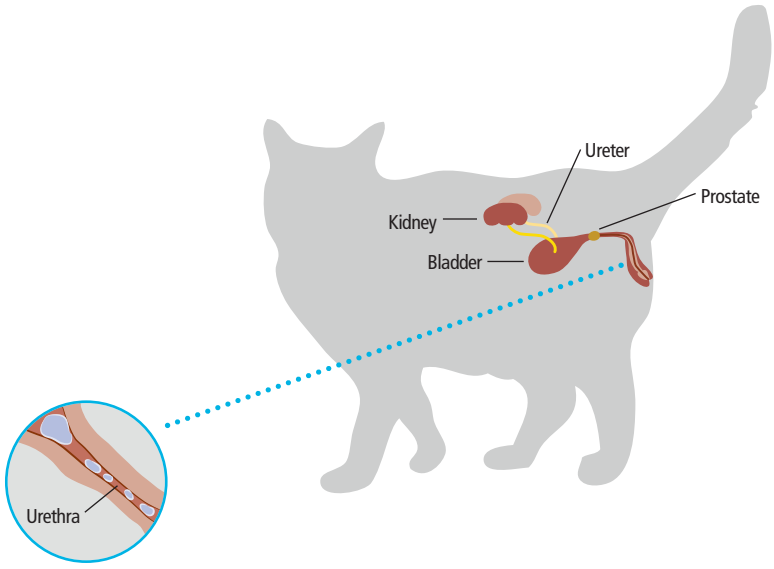
Case Study continued
Urinary Tract Stones

Current standard of care involves placing a catheter and administering supportive care while waiting for the bladder stones to pass. If this is not sufficient, invasive surgery is required to remove stones lodged in the urethra and bladder. Treatment typically requires a multi-day stay in the veterinary hospital and total costs range from $750 for a simple case to well over $5000 in complicated cases. Up to 43% of cats will have a recurrence, adding additional risk and cost.

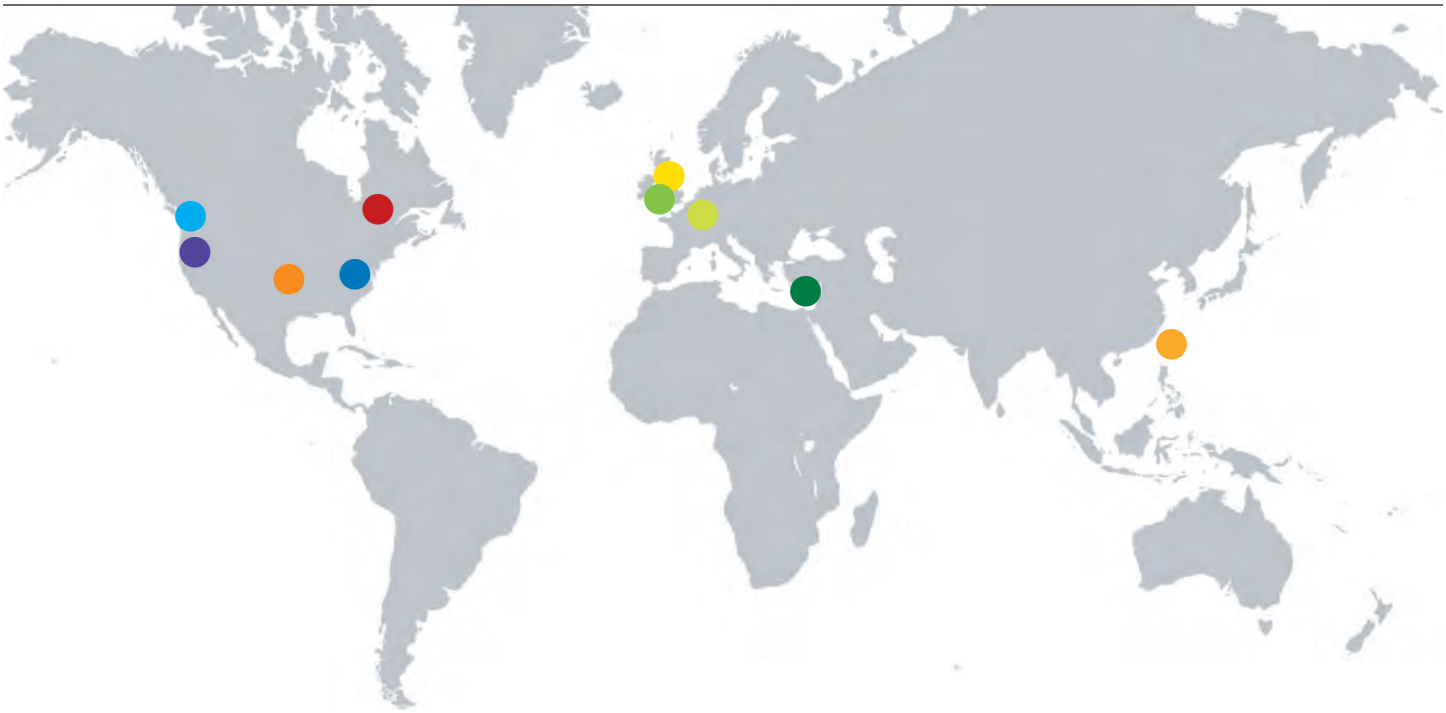
A type of focused ultrasound called lithotripsy may offer a safe, noninvasive, effective method to treat obstructing stones. This form of focused ultrasound produces high pressure mechanical forces that disintegrate bladder stones without the need for surgery. Once the stones have been broken down into smaller pieces, they can be passed to relieve the obstruction.

A veterinary clinical trial, led by Dr. Adam Maxwell of the University of Washington, is using lithotripsy to treat cats with obstructing bladder stones. In addition to developing a new treatment option for pet cats, this trial will provide additional safety and efficacy data for an ongoing human clinical trial testing the same technology. The system used in the human clinical trial was scaled down for veterinary use, and positive results from the veterinary trial will provide excellent supportive data for the use of this smaller device in the pediatric population.

Feline urinary system
Male



Veterinary Program Sites



North America

- Oklahoma State University
- Ontario Veterinary College*
- Stanford University
  In collaboration with University of California, Davis, School of Veterinary Medicine
- Virginia-Maryland College of Veterinary Medicine
- University of Washington*
  In collaboration with University of Minnesota Urolith Center

Europe

- Cyprus University of Technology*
- Institute of Cancer Research
- LabTAU
- Vet LIFU

Asia

- Taipei Animal Hospital*

*Newly identified site in 2022.

Publications

Veterinary publications—Cumulative as of 2022

Antoniou A, Evripidou N, Panayiotou S, Spanoudes K, Damianou C. Treatment of canine and feline sarcoma using MR-guided focused ultrasound system. J Ultrasound. 2022;25(4):895-904. doi:10.1007/s40477-022-00672-5

Arnold L, Hendricks-Wenger A, Coutermarsh-Ott S, et al. Histotripsy Ablation of Bone Tumors: Feasibility Study in Excised Canine Osteosarcoma Tumors. Ultrasound Med Biol. 2021;47(12):3435-3446. doi:10.1016/j.ultrasmedbio.2021.08.004

Carroll J, Coutermarsh-Ott S, Klahn SL, et al. High intensity focused ultrasound for the treatment of solid tumors: a pilot study in canine cancer patients. Int J Hyperthermia. 2022;39(1):855-864. doi:10.1080/02656736.2022.2097323

Foster RS, Bihrle R, Sanghvi N, et al. Production of prostatic lesions in canines using transrectally administered high-intensity focused ultrasound. European urology. 1993;23(2):330-336. http://www.ncbi.nlm.nih.gov/pubmed/7683997

Hendricks-Wenger A, Arnold L, Gannon J, et al. Histotripsy Ablation in Preclinical Animal Models of Cancer and Spontaneous Tumors in Veterinary Patients: A Review. IEEE Trans Ultrason Ferroelectr Freq Control. 2022;69(1):5-26. doi:10.1109/TUFFC.2021.3110083

Horise Y, Maeda M, Konishi Y, et al. Sonodynamic Therapy With Anticancer Micelles and High-Intensity Focused Ultrasound in Treatment of Canine Cancer. Front Pharmacol. 2019;10:545. doi:10.3389/fphar.2019.00545

Isard PF, Mentek M, Clément D, et al. High intensity focused ultrasound cyclocoagulation in dogs with primary glaucoma: a preliminary study. Open Veterinary Journal. 2018;8(3):305. doi:10.4314/ovj.v8i3.9

Kincaide LF, Sanghvi NT, Cummings O, et al. Noninvasive ultrasonic subtotal ablation of the prostate in dogs. American journal of veterinary research. 1996;57(8):1225-1227.

Kumar SU, Telichko AV, Wang H, et al. Acoustically Driven Microbubbles Enable Targeted Delivery of microRNA-Loaded Nanoparticles to Spontaneous Hepatocellular Neoplasia in Canines. Advanced Therapeutics. 2020;3(12):2000120. doi:10.1002/adtp.202000120

Latifi M, Hay A, Carroll J, et al. Focused ultrasound tumour ablation in small animal oncology. Vet Comp Oncol. 2021;19(3):411-419. doi:10.1111/vco.12742

Ranjan A, Kishore D, Ashar H, Neel T, Singh A, More S. Focused ultrasound ablation of a large canine oral tumor achieves efficient tumor remission: a case report. Int J Hyperthermia. 2021;38(1):552-560. doi:10.1080/02656736.2021.1903582

Roberts WW, Teofilovic D, Jahnke RC, Patri J, Risdahl JM, Bertolina JA. Histotripsy of the prostate using a commercial system in a canine model. The Journal of urology. 2014;191(3):860-865. doi:10.1016/j.juro.2013.08.077

Rong S, Woo K, Zhou Q, et al. Septal Ablation Induced by Transthoracic High-Intensity Focused Ultrasound in Canines. Journal of the American Society of Echocardiography. 2013;26(10):1228-1234. doi:10.1016/j.echo.2013.06.020

Ruger L, Yang E, Gannon J, et al. Mechanical High-Intensity Focused Ultrasound (Histotripsy) in Dogs with Spontaneously Occurring Soft Tissue Sarcomas. IEEE Trans Biomed Eng. 2022;PP. doi:10.1109/TBME.2022.3201709

Ruger LN, Hay AN, Gannon JM, et al. Histotripsy Ablation of Spontaneously Occurring Canine Bone Tumors In Vivo. IEEE Trans Biomed Eng. 2022;PP. doi:10.1109/TBME.2022.3191069

Ryu MO, Lee SH, Ahn JO, Song WJ, Li Q, Youn HY. Treatment of solid tumors in dogs using veterinary high-intensity focused ultrasound: A retrospective clinical study. Veterinary journal (London, England : 1997). 2018;234: 126-129. doi:10.1016/j.tvjl.2018.02.019

Seward MC, Daniel GB, Ruth JD, Dervisis N, Partanen A, Yarmolenko PS. Feasibility of targeting canine soft tissue sarcoma with MR-guided high-intensity focused ultrasound. International journal of hyperthermia: the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group. 2019;35(1):205-215. doi:10.1080/02656736.2018.1489072

Spanoudes K, Evripidou N, Giannakou M, Drakos T, Menikou G, Damianou C. A High Intensity Focused Ultrasound System for Veterinary Oncology Applications. J Med Ultrasound. 2021;29(3):195-202. doi:10.4103/JMU.JMU_130_20

Yoo DH, Cho JY, Kwak C, Lee JY, Moon KC, Kim SH. Transabdominal high-intensity focused ultrasound therapy of the prostate and determination of the protective effect of rectal cooling: an experimental study using canine prostates. Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine. 2013;32(8):1419-1425. doi:10.7863/ultra.32.8.1419

Zheng M, Shentu W, Chen D, Sahn DJ, Zhou X. High-Intensity Focused Ultrasound Ablation of Myocardium In Vivo and Instantaneous Biological Response. Echocardiography. 2014;31(9):1146-1153. doi:10.1111/echo.12526