

Focused Ultrasound *for Pancreatic Cancer*

Overview

Focused ultrasound is an early stage, noninvasive therapeutic technology with the potential to improve the quality of life and decrease the cost of care for patients with pancreatic cancer. This novel technology precisely focuses beams of ultrasound energy on targets deep in the body without damaging surrounding normal tissue. Where the beams converge, the ultrasound can produce a variety of therapeutic effects enabling the patient to be treated without incisions or radiation. These effects can work alone or in combination with other treatments to help these patients.

Benefits

Current treatment options for pancreatic cancer include combinations of surgery, radiation, chemotherapy, embolization or other ablative methods, yet these are not effective for most patients. Focused ultrasound can be used alone and in combination with other therapies to treat pancreatic cancer by reducing tumor size and spread and even “debulk” the tumor prior to surgical resection. Focused ultrasound can also decrease the pain often associated with pancreatic cancer by decreasing tumor size and ablating the sensory nerves surrounding the tumor.

Advantages

- **Noninvasive – no incisions, rapid recovery and no risk of infection or bleeding**
- **Image guided – precise targeting leads to minimal damage to surrounding normal tissue**
- **No ionizing radiation – can be safely repeated if necessary**

State of the Field

Focused ultrasound treatment for pancreatic cancer has regulatory approval in Europe, Korea, Russia and China. Multiple published studies have reported significant reduction in tumor size and pain. In order to further improve treatment outcomes, the Foundation is establishing the Pancreatic Cancer International Registry (ARRAY), which will capture treatment details from leading sites that can be used to optimize patient selection and treatment parameters.

Due to new evidence supporting the potential impact of focused ultrasound on the immune system, the Foundation recently held a workshop that included experts in oncology, immunology, surgery and focused ultrasound that agreed on a road map to advance the field. A new clinical research project will study patients with late stage pancreatic cancer receiving FUS and chemotherapy versus chemotherapy alone. Additional preclinical and clinical projects will study the ability of focused ultrasound to enhance targeted drug delivery to the tumor and evaluate if even only partial focused ultrasound ablation following immune agonist administration can produce a reliable abscopal (i.e. disappearing metastases) effect.

For more information visit www.fusfoundation.org/diseases-and-conditions/gastrointestinal/pancreatic-cancer

Focused Ultrasound for Pancreatic Cancer

Mechanisms of Action

Focused ultrasound delivers a variety of effects on tissue and the following mechanisms are currently in use or under investigation for the treatment of pancreatic cancer.

TISSUE DESTRUCTION

- **Thermal ablation:** coagulative cell death
- **Histotripsy:** mechanical cell disruption

THERAPEUTIC AGENT DELIVERY

- **Carrier mediated vehicle:** activate encapsulated therapies
- **Stromal disruption:** disturb the tumor microenvironment to permit drug infiltration

IMMUNOMODULATION

- **Tumor cell disruption:** exposure of tumor antigens improves the anti-tumor immune response
- **Immune cell trafficking:** enhanced delivery of immune cells to the target site

RADIATION SENSITIZATION

- **Hyperthermic preconditioning:** increased blood flow enhances efficacy of primary treatment

Research Project Inventory

Preclinical Laboratory Studies

- *Focused Ultrasound Driven Drug Release From Theranostic Nanoparticles For The treatment Of Pancreatic Cancer (S White, Froedtert & the Medical College of Wisconsin)
- *Focused ultrasound immunomodulation for pancreatic cancer (F Padilla, University of Virginia Health System)
- *Image-Guided Drug Delivery to Tumors using Ultrasound-Activated Perfluorocarbon Nanoemulsions as Drug Carriers (N Rapoport, University of Utah)
- *MR-guided HIFU enhanced targeted drug delivery for treatment of pancreas cancer: a pre-clinical study (JH Hwang, University of Washington)
- *Defining Basic Properties of Physical Immunotherapy using HIFU and Immune Checkpoint Inhibition (G Haar, Institute of Cancer Research)
- *Development of Novel Porcine Models of Orthotopic Pancreatic Cancer for FUS and Histotripsy Tumor Ablation Applications" (Irving Coy Allen, Ph.D. at Virginia Polytechnic Institute and State University)
- Contrast-enhanced ultrasound evaluation of pancreatic cancer xenografts in nude mice after irradiation with sub-threshold focused ultrasound for tumor ablation (LX Jiang, Shanghai Institute of Ultrasound in Medicine)
- Cavitation-induced release of liposomal chemotherapy in orthotopic murine pancreatic cancer models: A feasibility study (F Prat, Inserm)
- High-intensity focused ultrasound enhances the effect of bufalin by inducing apoptosis in pancreatic cancer cells (Z Meng, Shanghai Medical College)
- In vivo study of enhanced chemotherapy combined with ultrasound image-guided focused ultrasound (USgFUS) treatment for pancreatic cancer in a xenograft mouse model (JY Lee, Seoul National University Hospital)

* The Focused Ultrasound Foundation is fully or partially funding these projects

Focused Ultrasound *for Pancreatic Cancer*

Research Project Inventory

Clinical Trials

Magnetic Resonance-guided High-intensity Focused Ultrasound Treatment of Locally Advanced Pancreatic Cancer (A Napoli, University of Roma La Sapienza, Italy)

*Focused Ultrasound for the Treatment of Pancreatic Cancer - an International Registry [ARRAY];

Treatment sites:

European Institute of Oncology, Italy (F Orsi)

^Hospital Universitari Mutua Terrassa, Spain (J Vidal-Jové)

^Oxford University Hospital, UK (S Reddy)

^National Taiwan University Hospital, Taiwan (KW Huang)

^Stanford University Medical Center (JH Hwang)

^University of Cologne, Ger (D Waldschmidt)

* The Focused Ultrasound Foundation is fully or partially funding these projects

^ These sites are not yet recruiting patients

Focused Ultrasound *for Pancreatic Cancer*

Research Sites

Preclinical laboratories

Asan Medical Center (Seoul, South Korea)
Centre Léon Bérard (Lyon, France)
Columbia University (New York, NY, United States)
Deutsches Krebsforschungszentrum (Heidelberg, Germany)
Drexel University (Philadelphia, PA, United States)
HistoSonics, Inc. (Ann Arbor, MI, United States)
Hôpital Cochin (Paris, France)
Inserm LabTAU (Lyon, France)
Institute of Cancer Research (Sutton, United Kingdom)
MD Anderson Cancer Center (Houston, TX, United States)
Methodist Hospital (Houston, TX, United States)
Rostov Scientific Research Institute of Oncology (Rostov-on-Don, Russian Federation)
Samsung Medical Center (Seoul, South Korea)
Scuola Superiore di Studi Universitari e di Perfezionamento Sant'Anna (Pontedera, Italy)
Seoul National University Hospital (Seoul, South Korea)
Stanford University School of Medicine (Stanford, CA, United States)
Tianjin Medical University (Heping, China)
Universitair Medisch Centrum Utrecht (Utrecht, Netherlands)
Universitätsklinik Köln (Cologne, Germany)
University of California, San Francisco (San Francisco, CA, United States)
University of Michigan (Ann Arbor, MI, United States)
University of Oxford (Oxford, United Kingdom)
University of Virginia Health System (Charlottesville, VA, United States)
University of Washington (Seattle, WA, United States)
Verasonics, Inc. (Kirkland, WA, United States)
Virginia Polytechnic Institute and State University (Blacksburg, VA, United States)

Focused Ultrasound *for Pancreatic Cancer*

Research Sites

Clinical trials

Azienda Ospedaliero - Universitaria Careggi (Florence, Italy)
Chinese People's Liberation Army, 2nd Artillery General Hospital (Beijing, China)
Hospital Universitario Mútua de Tarrasa (Terrassa, Spain)
Istituto Europeo di Oncologia (Milan, Italy)
National Taiwan University Hospital (Taipei City, Taiwan)
Seoul National University Hospital (Seoul, South Korea)
Shihezi University School of Medicine First Affiliated Hospital (Shihezi City, China)
Stanford University School of Medicine (Palo Alto, CA, United States)
Tenth People's Hospital of Shanghai (Shanghai, China)
Tokyo Medical University (Tokyo, Japan)
Università degli Studi di Roma 'La Sapienza' (Rome, Italy)
Universitätsklinik Bonn (Bonn, Germany)
Universitätsklinik Köln (Cologne, Germany)
University of Oxford, Churchill Hospital (Oxford, United Kingdom)
Zhejiang University, Second Affiliated Hospital (Hangzhou, China)

Commercial Treatment Sites

Chularat 9 Airport Hospital (Bang Phli District, Samut Prakan, Thailand)
Clinica Santa Elena (Madrid, Spain)
Hospital Universitario Mútua de Tarrasa (Terrassa, Spain)
Kobe Saisei Mirai Clinic (Kobe-shi, Hyogo-ken, Japan)
University Hospital Saint Marina, Pleven (Pleven, Bulgaria)

Manufacturers

Alpinion Medical Systems Co. Ltd | Seoul, South Korea, www.alpinion.com
Beijing Yuande Bio-Medical Engineering Co., Ltd. | Beijing, China, www.yuande.com
Chongqing Haifu Medical Technology Co., Ltd. | Chongqing, China, www.haifu.com.cn/en_index.asp
EpiSonica Corp. | Hsichu City, Taiwan, www.episonica.com
INSIGHTEC LTD | Tirat Carmel, Israel, www.insightec.com
Profound Medical Corp. | Mississauga, Ont. Canada, www.profoundmedical.com
Shanghai A&S Science Technology Development Co., Ltd. | Shanghai, China, www.aishen.com.cn

Focused Ultrasound *for Pancreatic Cancer*

Key Publications

- Focused Ultrasound Foundation Workshop. The Role of Focused Ultrasound in Pancreatic Cancer, 2019. https://www.fusfoundation.org/images/pdf/FUSF_Pancreatic_cancer_-3_pages_web.pdf
- Ning Z, Zhu Z, Wang H, et al. High-intensity focused ultrasound enhances the effect of bufalin by inducing apoptosis in pancreatic cancer cells. *Onco Targets Ther* 2019;12:1161-1170.
- Saccomandi P, Lapergola A, Longo F, Schena E, Quero G. Thermal ablation of pancreatic cancer: A systematic literature review of clinical practice and pre-clinical studies. *Int J Hyperthermia* 2018;14:1-21.
- Nabavizadeh A, Payen T, Saharkhiz N, McGarry M, Olive KP, Konofagou EE. Technical Note: Feasibility of the In vivo Young's modulus visualization of pancreatic ductal adenocarcinoma during HIFU ablation Using Harmonic Motion Elastography (HME) in vivo. *Med Phys* 2018;45(11):5244-5250.
- Marinova M, Huxold HC, Henseler J, et al. Clinical Effectiveness and Potential Survival Benefit of US-Guided High-Intensity Focused Ultrasound Therapy in Patients with Advanced-Stage Pancreatic Cancer. *Ultraschall Med* 2018; ePub.
- Park EJ, Ahn YD, Lee JY. In vivo study of enhanced chemotherapy combined with ultrasound image-guided focused ultrasound (USgFUS) treatment for pancreatic cancer in a xenograft mouse model. *Eur Radiol*. 2018; 28(9):3710-3718.
- Strunk HM, Lützwow C, Henseler J, et al. Mesenteric Vessel Patency Following HIFU Therapy in Patients with Locally Invasive Pancreatic Cancer. *Panc ca Ultraschall Med* 2018; 39(6):650-658.
- Maeda M, Muragaki Y, Okamoto J, et al. Sonodynamic Therapy Based on Combined Use of Low Dose Administration of Epirubicin-Incorporating Drug Delivery System and Focused Ultrasound. *Ultrasound in Med & Biol* 2017;43(10):2295-2301.
- Maloney E, Khokhlova T, Pillarisetty VG, et al. Focused ultrasound for immuno-adjuvant treatment of pancreatic cancer: An emerging clinical paradigm in the era of personalized oncotherapy. *Int Rev Immunol* 2017; 36(6):338-351.
- Farr N, Wang YN, D'Andrea S, et al. Hyperthermia-enhanced targeted drug delivery using magnetic resonance-guided focussed ultrasound: a pre-clinical study in a genetic model of pancreatic cancer. *Int J Hyperthermia* 2017; 34(3):284-291.
- Maeda M, Muragaki Y, Okamoto J, et al. Sonodynamic Therapy Based on Combined Use of Low Dose Administration of Epirubicin-Incorporating Drug Delivery System and Focused Ultrasound. *Ultrasound Med Biol* 2017;43(10):2295-2301.
- Shi Y, Ying X, Hu X, Shen H. Pain management of pancreatic cancer patients with high-intensity focused ultrasound therapy. *Pak J Pharm Sci* 2017;30:303-307.

Focused Ultrasound *for Pancreatic Cancer*

Key Publications

- Zhao J, Zhao F, Shi Y, Deng Y, Hu X, Shen H. The efficacy of a new high intensity focused ultrasound therapy for locally advanced pancreatic cancer. *J Cancer Res Clin Oncol* 2017;143(10):2105-2111.
- Dababou S, Marrocchio C, Rosenberg J, et al. A meta-analysis of palliative treatment of pancreatic cancer with high intensity focused ultrasound. *J Ther Ultrasound* 2017;5:9.
- Scott SJ, Adams MS, Salgaonkar V, Sommer FG, Diederich CJ. Theoretical investigation of transgastric and intraductal approaches for ultrasound-based thermal therapy of the pancreas. *J Ther Ultrasound* 2017;5:10. eCollection 2017.
- Hijnen N, Kneepkens E, de Smet M, Langereis S, Heijman E, Grüll H. Thermal combination therapies for local drug delivery by magnetic resonance-guided high-intensity focused ultrasound. *Proc Natl Acad Sci USA* 2017;114(24):E4802-E4811.
- Marinova M, Rauch M, Mücke M, et al. High-intensity focused ultrasound (HIFU) for pancreatic carcinoma: evaluation of feasibility, reduction of tumour volume and pain intensity. *Eur Radiol* 2016;26(11):4047-4056.
- Vidal-Jove J, Perich E, Del Castillo MA. Ultrasound Guided High Intensity Focused Ultrasound for malignant tumors: The Spanish experience of survival advantage in stage III and IV pancreatic cancer. *Ultrason Sonochem* 2015;27:703-706.
- Wu F. High intensity focused ultrasound: a noninvasive therapy for locally advanced pancreatic cancer. *World J Gastroenterol* 2014;20(44):16480-8.
- Sofuni A, Moriyasu F, Sano T, et al. Safety trial of high-intensity focused ultrasound therapy for pancreatic cancer. *World J Gastroenterol* 2014;20(28):9570-7.

Focused Ultrasound *for Pancreatic Cancer*

Media/News

[Ulster University scientists at the forefront of battle against pancreatic cancer](#)

Irish Times - November 21, 2018

"...by using ultrasound at a particular pressure and focusing that ultrasound at a solid tumour, such as a pancreatic tumour, we can control the explosion of [these] bubbles to release the drug payload and oxygen in a targeted manner."

- Professor John Callan, Norbrook Chair in Pharmaceutical Science at Ulster University

[Acoustic Cluster Therapy drives drug therapies to cancer cells](#)

European Pharmaceutical Review - March 21, 2018

"Ultrasound-mediated, targeted drug delivery is an emerging therapeutic approach with great potential and we are delighted to be in the forefront of this development."

- Rhim Sung Min, CEO of Humanscan

[Workshop Held to Define Roadmap for Focused Ultrasound and Pancreatic Cancer](#)

FUSF website - March 14, 2019

"The workshop provided an ideal setting for dialogue between the physicians and scientists who are beginning to use focused ultrasound to treat pancreatic cancer."

- Tim Meakem, MD, Chief Medical Officer at Focused Ultrasound Foundation

[Pancreatic Cancer Study Shows Potential Survival Benefit](#)

FUSF website - July 21, 2015

"We are very satisfied with these results. The work of our team proves that focused ultrasound helps patients with unresectable pancreatic cancer, improving their survival with a less aggressive approach."

- Joan Vidal-Jove, MD, Head of Surgical Oncology at Barcelona University Hospital