

FUS Treatment Approaches in the Prostate

(Data as of January 2016)

EDAP's Ablatherm HIFU

Transrectal Approach, Ultrasound Guidance

Regulatory/Research Status	# Patients Treated	Countries Where Approved	Key Publications/Trials
<p>Ablatherm Maxis: CE marked in 2000</p> <p>Ablatherm Integrated Imaging: CE marked in 2005</p> <p>510(k) cleared by FDA; sales started in the US in November 2015</p> <p>"Several research projects in progress"; sites confidential</p>	<p>More than 45,000 patients treated via more than 300 sites</p>	<p>Ablatherm Integrated Imaging approved for sales in Canada, Korea, Brazil and Taiwan</p> <p>Approved in Europe for prostate cancer (T1, T2) as first choice therapy for non-candidates to surgery and as salvage therapy for local recurrence after radiotherapy, brachytherapy, radical prostatectomy and HIFU</p> <p>Approved in the US for Prostate Tissue Ablation</p>	<p>Thüroff S et al., Evolution and outcomes of 3 MHz High intensity focused ultrasound therapy for localized prostate cancer over 15 years.</p> <p>Ganzer R et al., Fourteen-year oncological and functional outcomes of high-intensity focused ultrasound in localized prostate cancer.</p> <p>Crouzet S et al., Whole-gland ablation of localized prostate cancer with high-intensity focused ultrasound: oncologic outcomes and morbidity in 1002 patients.</p> <p>Feijoo, et. al, Focal High-Intensity Focused Ultrasound Targeted Hemiablation for Unilateral Prostate Cancer: A Prospective Evaluation of Oncologic and Functional Outcomes.</p>

EDAP's Focal One

Ultrasound with MRI-elastic Fusion Guidance

Regulatory/Research Status	# Patients Treated	Countries Where Approved	Key Publications/Trials
<p>CE marked in 2013</p>	<p>3,000</p>	<p>Approved for sales in Canada</p> <p>Approved in Europe for local treatment of prostate cancer</p>	

Histosonics' Vortx Rx

Transperineal Approach, Image Guided via Transrectal Ultrasound

Regulatory/Research Status	# Patients Treated	Countries Where Approved	Key Publications/Trials
<p>IDE approval from FDA; ITA approval from Health Canada (both for BPH safety study)</p> <p>FDA also approved IDE supplement after system modifications were made to the Vortx Rx; second safety study was set to begin Oct 2015 to test modifications</p>	<p>25 patients treated</p>	<p>None</p>	<p>BPH trial (enrolling): https://clinicaltrials.gov/ct2/show/NCT01896973?term=Histosonics+prostate&rank=1</p> <p>Note: "Histotripsy is a platform technology and the Company is currently exploring clinical applications of histotripsy outside of BPH (solid tumor ablation, brain, cardiovascular)"</p>

Profound Medical Corp.'s TULSA-PRO

Transurethral Approach, MRI Guided with Transurethral Ultrasound

Regulatory/Research Status	# Patients Treated	Countries Where Approved	Key Publications/Trials
Not yet approved; 3 sites participated in Phase 1 trial in Canada, Germany, and US; Pivotal trial to begin in 2016	30 patients treated in Phase 1 trial 110 patients planned for 2016 Pivotal trial via 10+ sites in Canada, Germany and U.S.	None; anticipate CE mark/IDE approval in early 2016; FDA approval late 2017	<p>Chin et al. "Magnetic Resonance Imaging-Guided Transurethral Ultrasound Ablation of Prostate Cancer: A Prospective Phase I Clinical Trial". European Urology (submitted 2015, pending revisions). Midterm results of the Phase I trial have been presented at several meetings and conferences, for example at the 2014 FUS Symposium</p> <p>Burtnyk et al. "Magnetic Resonance Image Guided Transurethral Ultrasound Prostate Ablation: A Preclinical Safety and Feasibility Study with 28-Day Follow-up".</p> <p>Chopra et al. "MR imaging-controlled transurethral ultrasound therapy for conformal treatment of prostate tissue: initial feasibility in humans".</p>

InSightec's ExAblate

Transrectal Approach, MR Guidance

Regulatory/ Research Status	# Patients Treated	Countries Where Approved	Key Publications/Trials
<p>InSightec is now involved in two main trials:</p> <ul style="list-style-type: none"> Feasibility study in the US (5 of 40 patients have been treated to date) Phase III trial out of the US is pending to start in Europe, Canada and Korea 	57 patients under various feasibility trials	None; investigational	<p>Zini, Chiara et al. "Ultrasound- and MR-guided focused ultrasound surgery for prostate cancer."</p> <p>Linder, Uri et al. "Focal magnetic resonance guided focused ultrasound for prostate cancer: Initial North American experience."</p> <p>Woodrum, David et al. "Magnetic Resonance-Guided Thermal Therapy for Localized and Recurrent Prostate Cancer."</p> <p>Napoli, Alessandro et al. "Real-time Magnetic Resonance-guided High-intensity Focused Ultrasound Focal Therapy for Localised Prostate Cancer: Preliminary Experience."</p> <p>Cheng, C.W.S. et al. "Initial Experience with MR-guided Focused Ultrasound Ablation for Localized Low-Risk Prostate Cancer." European Society of Radiology (www.myESR.org). ECR 2011.</p>

SonaCare Medical's Sonablate

Transrectal Approach, Ultrasound and MRI Fusion Guidance

Regulatory/Research Status	# Patients Treated	Countries Where Approved	Key Publications/Trials
<p>Sonablate® has 510(K) clearance in the U.S. under a De Novo regulatory Classification</p> <p>Sonablate® 500, which has CE Marking and has obtained regulatory authorization in more than 49 countries outside the U.S.</p>	<p>15,000 patients treated worldwide (includes 4,000 US men who travelled outside the US)</p>	<p>Sonablate® is authorized for sale in the United States.</p> <p>Sonablate® 500 is approved for sale in the following countries:</p> <p>Europe: for soft tissue ablation including treatment of prostate.</p> <p>Argentina: Ultrasound surgery</p> <p>Australia: Prostate treatment</p> <p>Bahamas: Prostate cancer</p> <p>Bermuda: Prostate cancer</p> <p>Brazil: Prostate treatment</p> <p>Canada: Treatment of prostate including BPH, localized prostate cancer, recurrent prostate cancer</p> <p>Costa Rica: BPH and prostate cancer</p> <p>Dominican Republic: BPH and prostate cancer</p> <p>Ecuador: Ultrasound therapy</p> <p>India: Ultrasound therapy</p> <p>Israel: Prostate treatment</p> <p>Japan: BPH</p> <p>Mexico: Prostate treatment</p> <p>Pakistan: Prostate treatment</p> <p>Russia: prostate treatment</p> <p>Trinidad: Prostate treatment</p> <p>Uzbekistan: Treatment of prostate gland</p> <p>Vietnam: Ultrasound treatment</p>	<p>Ahmed, Hashim U. et al. "Focal Ablation Targeted to the Index Lesion in Multifocal Localised Prostate Cancer: A Prospective Development Study."</p> <p>Ahmed, Hashim U, Richard G Hindley, Louise Dickinson, Alex Freeman, Alex P Kirkham, Mahua Sahu, Rebecca Scott, Clare Allen, Jan Van der Meulen, and Mark Emberton. "FocalTherapy for Localised Unifocal and Multifocal Prostate Cancer: a Prospective Development Study."</p> <p>Uchida, Toyoaki et al. "Improved Outcomes with Advancements in High Intensity Focused Ultrasound Devices for the Treatment of Localized Prostate Cancer."</p>