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Authors

Sailer, Anne
Ghanouni, Pejman
Schade, George
et al.

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Anne Sailer, MD
Pejman Ghanouni, MD, PhD
George R. Schade, MD
Alessandro Napoli, MD, PhD
Joan Vidal-Jove, MD, PhD
Steven S. Raman, MD
Mishal Mendiratta-Lala, MD
Sangeet Ghai, MD
Andre Abreu, MD
Karthik M. Sundaram, MD, PhD
Antonio Westphalen, MD
Sandeep Arora, MBBS

Abbreviation: TUS = therapeutic US

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From the Section of Interventional Radiology, Dept of Radiology and Biomedical Imaging, Yale School of Medicine, 333 Cedar St, PO Box 208042, Room TE-2, New Haven, CT 06520 (A.S., S.A.); Dept of Rad/Body MRI, Dept of Radiology, Stanford Univ, Lucas Ctr, Stanford, Calif (P.G.); Dept of Urology, Univ of Washington School of Medicine, Seattle, Wash (G.R.S., A.W.); Dept of Radiological Sciences, MRgFUS and Cardiovascular Imaging Unit, Sapienza Univ of Rome, School of Medicine, Rome, Italy (A.N.); Institut Khuab for Interventional Oncology, Comprehensive Tumor Ctr Barcelona, Barcelona, Spain (J.V.J.); Dept of Interventional and Diagnostic Radiology, Univ of California Los Angeles, Los Angeles, Calif (S.S.R.); Abdominal and Cross-Sectional Interventional Radiology, Dept of Radiology, Univ of Michigan School of Medicine, Ann Arbor, Mich (M.M.L.); Dept of Medical Imaging, Univ Health Network–Mount Sinai Hosp–Women's College Hosp, Univ of Toronto, Toronto, Canada (S.G.); Inst of Urology, Univ of Southern California–USC School of Medicine, Los Angeles, Calif (A.A.); and Dept of Radiology, Hosp of the Univ of Pennsylvania, Philadelphia, Pa (K.M.S.). Presented as an education exhibit at the 2021 RSNA Annual Meeting. Received March 7, 2022; revision requested June 6 and received July 22; accepted July 28. The authors P.G., G.R.S., J.V.J., A.A., A.W., and S.A. have provided disclosures (see end of article); all other authors, the editor, and the reviewers have disclosed no relevant relationships. **Address correspondence to** S.A. (email: *sandeep.arora@yale.edu*).

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The full digital presentation is available online.

Therapeutic uses of US predate the use of US for medical imaging. Therapeutic US (TUS) can produce various effects on human tissues without the use of ionizing radiation, depending on the mode of sonic energy used. The three major mechanisms of action of TUS are thermal ablation, histotripsy, and hyperthermia. Thermal ablation is the most-used type of TUS. Focal heating occurs owing to absorption of focused acoustic energy: temperatures rapidly rise to 60°C or higher, leading to denaturation of proteins and cell death. The thermal dose required to produce irreversible damage and coagulative necrosis depends on the cell type, temperature, and duration of exposure. Histotripsy uses high-amplitude ultrasound pulses to generate microbubbles in target cells, which leads to increased cell surface tension and strain on cell membranes, eventually leading to the mechanical destruction of cells (Fig 1). Human trials using histotripsy are ongoing. Focused US can also be used to cause hyperthermia (ie, mild heating to around 42°C), with the primary aim of increasing perfusion to the heated tissue. Increased perfusion to heated tissue can be used for drug delivery.

TUS has been U.S. Food and Drug Administration (FDA)–approved for the treatment of many diseases including bone metastases, osteoid osteomas, essential tremor, Parkinson disease tremor, prostate cancer, benign prostatic hyperplasia, and fibroids. Outside the United States, there are many additional approved applications for focused US applications (eg, liver, renal, and pancreatic cancer treatment).

This online presentation reviews the history of TUS and describes various TUS modes, bioeffects, MRI versus US imaging guidance and monitoring, and current regulatory and reimbursement status. We describe abdominopelvic applications of TUS and detail the patient selection process, contraindications, treatment planning, intraprocedural monitoring, and follow-up imaging. Various trademarked systems (Fig 2) used in organs like the prostate are discussed, including the nuances and efficacy evidence associated with these devices. We also discuss new potential applications of TUS in experimental and clinical trial settings for renal cancer and desmoid tumor ablation. We also pay homage to the late Ferenc Jolesz, MD, who is considered a true pioneer of TUS.

US and MRI-guided TUS are gaining acceptance in the treatment of prostate, liver, and pancreatic cancers, as well as bone metastases and uterine fibroids. Understanding the mechanism of action of focused US, available devices, selection and optimization of treatment

TEACHING POINTS

- TUS is a novel noninvasive technology without any dose limitations.
- The three major mechanisms of action of TUS are thermal ablation, histotripsy, and hyperthermia.
- TUS has many applications in the abdomen and pelvis and is FDA approved for prostate ablation, bone metastasis treatment, and uterine fibroid ablation in the United States.

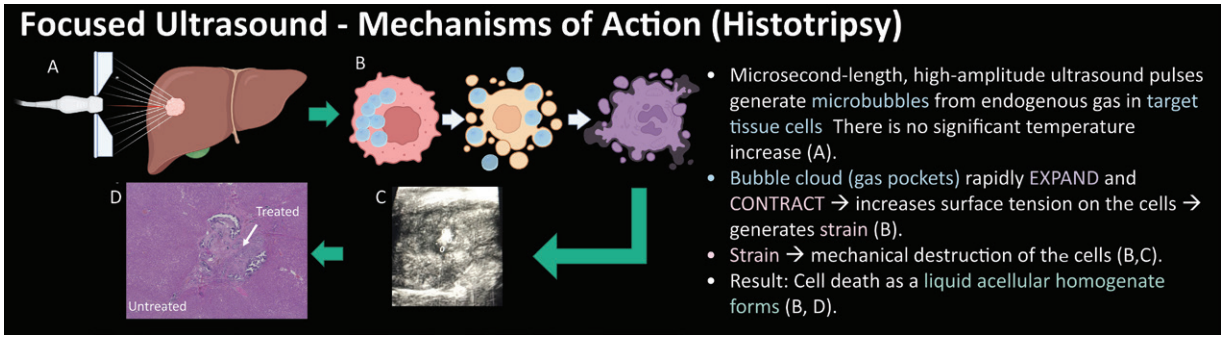

Figure 1. Chart shows the mechanism of action of histotripsy.

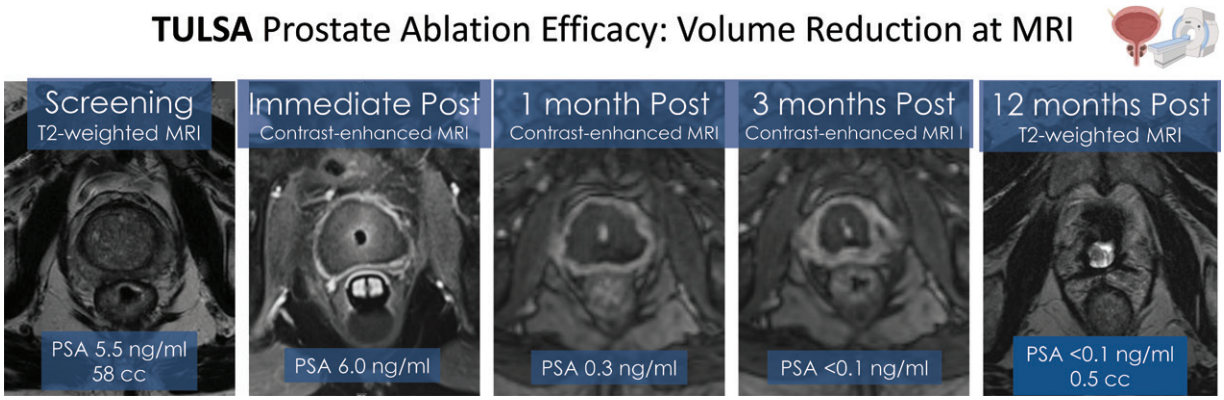

Figure 2. Axial MR images show decreased prostate volume 1 year after transurethral US ablation *(TULSA)* (TULSA-PRO; Profound Medical). There was a 92% negative predictive value for absence of disease at 1 year. Follow-up prostate MRI helps predict clinically significant disease at biopsy. The absence of a lesion with a Prostate Imaging Reporting and Data System (PI-RADS) score of 3 or greater at 1-year multiparametric MRI has a 92% negative predictive value for absence of grade group 2 disease at 1-year biopsy. The multivariate predictors of persistent grade group 2 disease at 12 months include intraprostatic calcifications at screening, suboptimal thermal coverage of the target volume, and a PI-RADS 3 or greater lesion at 12-month MRI ($P < 0.05$). *Post* = posttreatment, *PSA* = prostate-specific antigen.

strategies, and current literature is essential for furthering TUS advances and applications.

***Disclosures of conflicts of interest.*—P.G.** Consultant for Histosonics, stockholder in SonALASense. **G.R.S.** Royalties for intellectual property licensed to Global Cancer Technology, patents/patents pending (US10694974B2, US20200222728A1, US20170072228A1, US20200353293A1). **J.V.J.** Consultant to Histosonics, recipient of a Comprehensive Tumor Center Barcelona grant, honoraria from Chongqing HAIFU, stockholder in Advanced Microbubbles. **A.A.** Consultant for Koelis. **A.W.** Shareholder in Bot Image; member of committees at SAR, RSNA, ARRS. **S.A.** Principal investigator for TACT and CAPTAIN clinical trials (Profound Inc–Yale), patent pending for MR-guided focused US applications.

Suggested Readings

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