A History of the Sonocare CST-100: The First FDA-approved HIFU Device

Robert Muratore

Frederic L. Lizzi Center for Biomedical Engineering
Riverside Research Institute
156 William St Fl 9
New York NY 10038-2609 USA

Abstract. The Sonocare CST-100 Therapeutic Ultrasound System, designed for the treatment of glaucoma, was developed in the 1980s and became the first high intensity focused ultrasound (HIFU) device to receive Food and Drug Administration approval. The system arose from studies done by F.L. Lizzi, Eng.Sc.D., of Riverside Research Institute and D.J. Coleman, M.D., of Cornell Medical Center/New York Hospital on the safety of ultrasound diagnosis of the eye. As safety limits were probed, therapeutic regimes were discovered. Optimization of operational parameters, clinical experience, and engineering design came together through a spin-off company, Sonocare, Inc., formed to produce and market the ophthalmic device. Various precedents were set during the approval process, including the acceptance by the FDA of radiation momentum imparted to an absorber as a measure of acoustic power. Many devices were sold, but the laser industry, grandfathered into the therapeutic field, eventually out-marketed Sonocare. The CST-100 remains as a model of elegant industrial design, and existing units are used daily in HIFU laboratory experiments.

Keywords: HIFU, PMA, FDA, therapy, history
PACS: 43.58.Kr, 43.80.Qf, 43.80.Sh

INTRODUCTION

The Sonocare CST-100 was the first high intensity focused ultrasound (HIFU) device to receive United States Food and Drug Administration (FDA) Pre-Market Approval (PMA; see Table 1). It was used to treat thousands of patients with glaucoma, significantly reducing their intra-ocular pressure. It also served as a focal point in the intellectual affairs of the Biomedical Engineering Laboratories of Riverside Research Institute and the Cornell University Medical College ophthalmology lab during the 1980s.

THE DEVICE

The trade name of the device was the Sonocare CST-100 Therapeutic Ultrasound System for the Treatment of Glaucoma. In the Summary of Safety and Effectiveness Data filed with the FDA it was "indicated for the treatment of glaucoma of any type or etiology in phakic, aphakic or pseudophakic subjects of any age, gender or race."

CP829, *Therapeutic Ultrasound: 5th International Symposium on Therapeutic Ultrasound*
edited by G. T. Clement, N. J. McDannold, and K. Hynynen

The industrial design firm that designed the Sonocare CST-100 was also responsible for the Mobil Oil corporate makeover in 1965; they applied that same geometric simplicity to each of the CST-100 components: the transducer assembly (Fig. 2), the articulated support arm (Fig. 2) and the electronic control unit (Fig. 1). Many of the engineering ideas originally worked out in the development of the Sonocare transducer have become commonplace in HIFU systems worldwide.

The transducer assembly was composed of a focused ultrasound transducer for therapy, a central diagnostic transducer for biometry, and a fiber optics module for aiming. The therapeutic transducer was constructed from a 1.46 mm thick PZT-4 spherical shell, fabricated by Valpey-Fisher Corp. (Hopkinton MA USA). Designed with a fundamental frequency of 1.4 MHz, the transducer was operated near 4.2 MHz. The optimal operating frequency was determined heuristically for each unit based on Schlieren image clarity and maximum power output; a matching network was customized for the optimal frequency. The strategy of operating the transducer at its third harmonic resulted in a thicker, heavier, more robust device; many are still in operation after 20 years. This f/1.1 transducer was 80 mm in diameter with a focus of 90 mm, and a central 19.4 mm diameter hole designed to admit the coaxial confocal diagnostic transducer, a Panametrics (Waltham MA USA) model MD3657, modified with a central hole of its own to admit the fiber optics module. Because it had a focal length of 60 mm, the Panametrics diagnostic single-element A-mode transducer projected 30 mm in front of the therapeutic transducer surface. The fiber optics module was connected to a 150 W tungsten halogen light source and produced a small bulls-eye pattern near the transducer focus. The front of the transducer assembly was an acrylic resin cone, open at the distal end. Before operation, the cone was to be filled with degassed water. A small external ridge secured a latex condom stretched over the opening, forming a membrane which dammed the degassed water. The dimensions of the cone were such that the focus was 1 inch beyond the latex membrane. The back of the transducer assembly contained a semi-kinematic mount, adjusted for confocality during manufacturing.

The heavy articulated support arm was secured to a table with a built-in clamp. There were provisions for coarse, fine, and superfine height adjustments, as well as multi-axis rotations.

The electronic control unit was constructed of ready-made subunits (such as a Sonometrics Systems, Inc. (New York NY USA) A-mode display and an ENI (Rochester NY USA) 2100L Broadband Power Amplifier) bolted inside a cabinet and connected mostly with 50 Ω coaxial cables and BNC connectors. Custom circuitry was confined to a single board. This arrangement meant low development costs, quick assembly, robust operation, and easy field repair.

TABLE 1. Sonocare by the Numbers

US Patents	4 350 917, 4 484 569, 4 561 019, 4 858 124
IDE	G810076
Trademark Registration	1496652
PMA (CST-100)	P860046, notice date August 10, 1988
Frequency (MHz)	4.2 nominal
Power (W)	0, 11, 23, 33, 42, 48, 55, 56, 57, 59, 60 typical
Duration (s)	0, 1, 2, 3, 4, 5

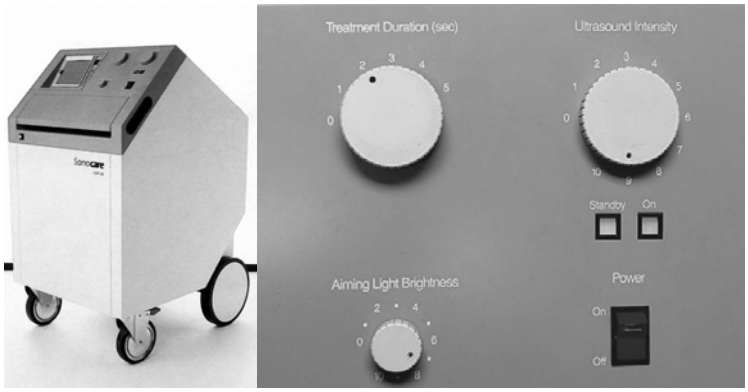

FIGURE 1. (Left) Sonocare CST-100 electronic control unit. (Right) Close-up of user interface.

The control panel on the face of the electronic control unit was a masterpiece of user interface design. As seen in Fig. 1, a 2 in. dial on the left was labeled "Treatment Duration (sec)" with indents at 0 through 5. A similar dial on the right was labeled "Ultrasound Intensity" with indents at 0 through 10 (Table 1). Below these were an infinitely adjustable dial labeled "Aiming Light Brightness" and a large red illuminated rocker switch labeled "Power On Off."

In operation, a Steri-Drape (3M Co., St. Paul MN USA) was placed around the eye and filled with warm sterile normal saline. The transducer was aimed at the appropriate scleral region, a foot pedal was depressed and held down, and a soft red rubber button on the side of the transducer housing was pressed to fire a HIFU burst.

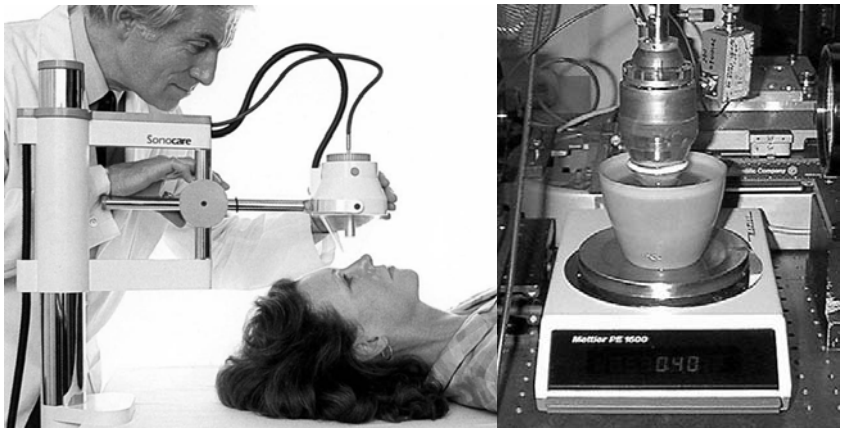

FIGURE 2. (Left) Sonocare CST-100 transducer assembly and articulated support arm are shown in this publicity picture from the product brochure. The required water bath is not shown. (Right) Flat absorbing target wattmeter in use with an alternative Sonocare prototype transducer.

FLAT ABSORBING TARGET WATTMETER

Proper transducer output was to be checked periodically by the practitioner. Until the 1980s, typical momentum based acoustic power measurement devices utilized acoustic reflection which required elaborate equipment to minimize pointing errors,

streaming, and stray beams. As part of the CST-100 development process, an easy-to-use inelastic technique was developed that used a saturated sponge (open-cell packing foam) as an absorber and a Mettler (Columbus Ohio USA) balance as a measurement device. In this process, the tip of the transducer cone was immersed in a small cup of water with the sponge, sitting on the balance (Fig. 2). The transducer was excited, and the number of grams displayed was multiplied by 14.7 to yield the acoustic output power in watts. Because small angle error varies as the cosine of the angle relative to the normal, aiming is not critical; small angle variations have less than 1% measurable effect. Total error is on the order of 5% (for an f/1.1 transducer), mostly from numerical approximations that act as a constant. The FDA accepted the new device, called the "flat absorbing target wattmeter," and it has become the standard for acoustic power output measurements that do not require spatial resolution.

HISTORY AS A HISTOGRAM OF DOCUMENTS

My approach to the history of the Sonocare system was to create a histogram[1] of the documents housed at Riverside Research Institute relevant to the Sonocare.

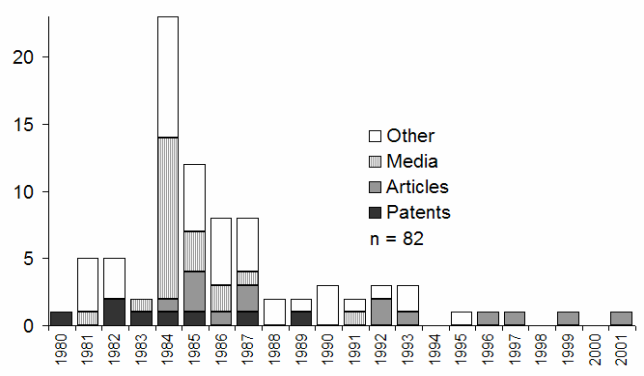

FIGURE 3. History as a histogram of documents. 82 Sonocare documents were sorted into 4 categories and year-long bins, from 1980 through 2001. Sonocare, Inc. was founded in the peak year, 1984.

Figure 3 shows the histogram, from 82 documents, sorted into year-long bins and 4 categories: Patents (applications and awards) (Table 1), Articles (published in the technical literature) [1-13], Media (press releases, newspaper articles, etc.), and Other (correspondence with the FDA, internal memoranda, etc.). Of note are the 4 patent applications that proceed the peak year of activity (1984) when the company was formed that would develop and market the device for ocular therapy. Sonocare, Inc., was founded in 1984 with Dr. Udo W. Drews as president and headquarters at 21 Industrial Ave., Upper Saddle River NJ 07458-2301 USA. The peak was caused mostly by press releases and newspaper articles. Journal and proceedings articles

[1] The word "histogram" is from the Greek ιστοσ (mast), but Karl Pearson, who coined the term, must have been aware of the overtone of "history", albeit from a different Greek root. (Ioannidis, Y., "The History of Histograms (abridged)," in *Proceedings 2003 VLDB Conference: 29th International Conference on Very Large Databases (VLDB)*, edited by J. C. Freytag et al., Berlin: Morgan Kaufmann, 2003.)

followed this peak. In 1985, the sales backlog was 21 units with a total value of US$1.5M. The PMA application was submitted in 1986, and the FDA issued a PMA notification in 1988. In 1992, an award-winning video, "Visualization of Simulated Treatment of an Ocular Tumor," was produced at the Cornell Supercomputer Center demonstrating HIFU for uveal melanomas, an extension to the original idea of glaucoma therapy. Despite the vigorous activity, by 1993 accountants were tallying the assets of Sonocare, Inc., and shortly thereafter the company was dissolved.

Today, glaucoma is typically treated with drug therapy. HIFU has grown enormously in the past 2 decades, and many practitioners are currently shepherding their devices through the FDA approval process. A few Sonocare CST-100 units remain in various labs, still used for HIFU research work, seen in the long tail of the document distribution.

ACKNOWLEDGMENTS

The author gratefully acknowledges the contributions of Dr. Ronald H. Silverman, Dr. Ernest J. Feleppa, Mr. Andrew Kalisz, Dr. D. Jackson Coleman, Dr. Richard Bernardi, Mr. Mark Rondeau, and Dr. Frederic L. Lizzi in manuscript preparation.

REFERENCES

1. Lizzi, F. L., Coleman, D. J., Driller, J., Ostromogilsky, M., Chang, S., and Greenall, P.; *IEEE Trans Sonics Ultrason* **SU-31**, 473-481 (1984).
2. Lizzi, F. L., Coleman, D. J., and Driller, J., "Ultrasonic Therapy and Imaging in Ophthalmology," in *Acoustical Imaging*, edited by A.J. Berkhout et al., Plenum, New York, 1985, pp. 1-17.
3. Coleman, D. J., Lizzi, F. L., Driller, J., Rosado, A. L., Chang, S., Iwamoto, T., and Rosenthal, D., *Ophthalmology* **92**, 339-346 (1985).
4. Coleman, D. J., Lizzi, F. L., Burgess, S. E., Silverman, R. H., Smith, M. E., Driller, J., Rosado, A., Ellsworth, R. M., Haik, B. G., Abramson, D. H., and McCormick, B., *Am J Ophthalmology* **101**, 635-642 (1986).
5. Coleman, D. J., Rondeau, M. J., Silverman, R. H., and Lizzi, F. L., *Trans Am Ophthalmol Soc* **85**, 49-81 (1987).
6. Driller, J., and Lizzi, F. L., *IEEE Eng Med Biol Mag* **6**, 33-40 (1987).
7. Lizzi, F. L., Driller, J., Kalisz, A., and Coleman, D. J., *Acta Ophthalmol* **S204**, 40-45 (1992).
8. Lizzi, F. L., Driller, J., Lunzer, B., Kalisz, A., and Coleman, D. J., *Ultrasound Med Biol* **18**, 59-73 (1992).
9. Lizzi, F. L., *Eur Urol*, **23S1**, 23-28 (1993).
10. Lizzi, F. L., Astor, M., Deng, C., Rosado, A., Coleman, D. J., and Silverman, R., “Asymmetric focussed arrays for ultrasonic tumor therapy” in *Proceedings of the 1996 IEEE Ultrasonics Symposium*, edited by M. Levy, S. C. Schneider, and B. R. McAvoy, New York: Institute of Electrical and Electronics Engineers, 1997 (filed as 1996), pp. 1281-1284.
11. Lizzi, F. L., Astor, M., Deng, C. X., Rosado, A., Coleman, D. J., and Silverman, R., “Strip-electrode ultrasonic arrays for production of asymmetric therapeutic thermal lesions” in *Proceedings of the 1997 IEEE Ultrasonics Symposium*, edited by S. C. Schneider, M. Levy, and B. R. McAvoy, New York: Institute of Electrical and Electronics Engineers, 1998 (filed as 1997), pp. 1331-1336.
12. Lizzi, F. L., Deng, C. X., Lee, P., Rosado, A., Silverman, R. H., and Coleman, D. J., *Eur J Ultrasound* **9**, 71-78 (1999).
13. Silverman, R. H., Lizzi, F. L., Ursea, B. G., Cozzarelli, L., Ketterling, J. A., Deng, C. X., Folberg, R., and Coleman, D. J., *J Ultrasound Med* **20**, 979-986 (2001).