ULTRASONIC THERAPY AND IMAGING IN OPHTHALMOLOGY

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I. INTRODUCTION

The term "medical ultrasound" usually brings to mind the diagnostic ultrasonography systems that have become an internationally accepted modality for examining virtually all organs of the body. However, some of the earliest research with medical ultrasound was directed at studying how intense ultrasound could be used to modify tissue structures for possible therapy. For example, early work, reviewed by Kremkau (1), investigated how ultrasound might be used to treat cancer, and pioneering efforts in the laboratories of Fry, Dunn, and Lele (2,3) showed how focused ultrasound could be used to produce focal lesions for treating brain tumors and other disorders. Recently, there has been a renewed interest in therapeutic ultrasound, especially as a modality for inducing hyperthermia for cancer therapy (4).

Our interest in therapeutic ultrasound for treating diseases of the eye started in the late 1960s (5). In addition to therapeutic applications, we were motivated to examine ultrasonically induced lesions to provide background data relating to the safety of the high frequencies applied in ophthalmic diagnostic systems (6-8). Our research has continued to the present and has identified a variety of conditions that can benefit from ultrasonic therapy (7-14). After collecting animal data related to safety and efficacy, clinical trials have started in a number of areas, and equipment and procedures have been refined to support applications in the clinical setting. A key feature of our system (15-17) is the incorporation of diagnostic ultrasonography as an adjunct for aiming the treatment beam and, with new tissue characterization images (19), for planning tumor treatments and monitoring therapeutic results over time.

In ophthalmology, ablative and hyperthermia modes of applying therapeutic ultrasound are possible. In the ablative mode, a tightly focused beam is aimed at the tissue to be treated and a short (e.g., 1-sec), high-intensity (e.g., 2000 W/cm²) exposure is used to destroy or modify tissue within a well-defined region. The ablative mode causes brief, intense heating within a tissue volume whose size is comparable to the dimensions of the focal zone of the beam. The ablative use of ultrasound is similar to that employed with therapeutic lasers. However, ultrasound does not require an optically transparent path to the target tissue, and it is not
affected by optical properties that limit most laser treatments to the surface layers of tissues. In certain applications (e.g., vitreous membrane treatments) the ablative mode can be employed to produce mechanical effects that are useful for therapy.

The hyperthermia mode uses broader beams, lower intensities (e.g., on the order of 1 W/cm²), and longer exposure times (e.g., 10 min) to achieve sustained, lower-level heating (e.g., to 45 deg C). This mode is being investigated for tumor treatments in the eye and in other organs. We have emphasized its conjoint use with radiotherapy to treat a variety of ocular tumors: here, the synergism between hyperthermia and radiotherapy is exploited so that radiation doses can be lowered while still achieving successful tumor therapy.

Thus far, most of our clinical trials have involved treatments of glaucoma, a disease that elevates pressure in the eye and can thereby induce blindness. To treat glaucoma, an ablative mode is used to produce a series of lesions in the sclera and underlying ciliary body. These lesions promote the diffusion of excess aqueous humor (through the modified sclera and under the overlying, intact conjunctiva) and they also suppress aqueous humor production (in the treated ciliary body segments). The treatments have now been applied to approximately 150 patients and have proven effective in lowering intra-ocular pressure, even in cases that had proven resistant to drugs, lasers, and surgery.

In another clinical series, we have treated ocular tumors with a hyperthermia mode used with conjoint radiotherapy. Preliminary findings indicate that this approach may offer a welcome alternative to surgical removal of the eye in cases that resist conventional techniques.

This report describes portions of the research we have conducted into the nature and applications of ultrasonically induced lesions and discusses some of the design considerations that pertain to practical systems. First, it describes a therapeutic system that permits precise aiming and control of the therapeutic beam. Second, it briefly summarizes a mathematical simulation for ultrasonic treatments that guides experimental studies and treatment planning. Third, it describes a number of animal and clinical studies related to the safe and effective treatment of specific diseases.

The role of diagnostic ultrasound in practical applications of therapeutic ultrasound is also briefly outlined in the paper. We have found that high-resolution A- and B-mode techniques are important for precision lesion placement. Furthermore, new techniques in tissue characterization offer an important means of detecting subtle changes induced within treated tissues. This information can be useful for treatment monitoring and adjustment. As experience grows, this combined use of diagnostic and therapeutic ultrasound is expected to become particularly valuable.

II. THERAPEUTIC ULTRASOUND SYSTEM

The therapeutic ultrasound system has provisions for delivering a controlled amount of ultrasonic energy to a well-defined tissue volume. The key element in the system is the therapeutic transducer assembly shown in Fig. 1. The assembly houses a therapeutic piezoelectric transducer which is a spherically curved ceramic segment; typically, the diameter of the transducer is 80 mm, its focal length is 90 mm, and it is operated at a harmonic frequency between 4 and 10 MHz. For adjusting stand-off distances, a coaxial diagnostic ultrasound transducer is situated within a central aperture in the therapeutic transducer. Additionally, for