

IMAGING AND THERAPY DEVICE FOR MECHANICAL LINE ABLATION**CROSS-REFERENCE TO RELATED APPLICATIONS**

[0001] This application claims priority to U.S. Provisional Patent Application No. 63/538,163, titled "IMAGING AND THERAPY DEVICE FOR MECHANICAL LINE ABLATION" and filed on September 13, 2023, the entire contents of which is incorporated herein by reference.

BACKGROUND

[0002] The present disclosure relates to therapeutic ultrasound. More particularly, the present disclosure relates to devices for performing tissue ablation via histotripsy.

[0003] There are numerous tools specifically designed for minimally invasive surgical procedures, represented by a broad range of sizes and mechanism of action for tissual removal. These include more traditional resection tools such as micro-cutters, micro-forceps and micro-graspers that can be employed using endoscopes or laparoscopic form factors. There are also many endoscopic thermal ablation-based instruments using a variety of technologies to remove tumor tissue using hyperthermic injury, including RF, microwave, focused ultrasound or laser ablation, as well as cryoablation which uses liquified gasses to improve the efficacy of RF ablation. Almost all current endoscopic ablation tools are thermoablative, which has the disadvantage of substantial damage to neighbouring tissue outside of the treatment zone, and leaving scarred tissue in place within the ablation zone.

[0004] One of the only examples of non-thermal endoscopic ablation tools is ultrasonic surgical aspirators, which act like miniature vibration saws. These

instruments, while effectively ablating tissue without heating, lack precision in the targeted ablation site. However, the most significant shortcoming of these traditional endoscopic ablation tools is the ablation zone being in contact with the tip of the endoscope. This means that when ablating superficial pathologies just below the surface of skin (or tongue), an open wound must be created to access the pathology leading to complications such as bleeding and infection.

[0005] While it is known that cavitation can be employed for tissue ablation, the state of the art in ultrasound cavitation-based ablation (histotripsy) involves transducers that are very large designed for ablating tissue from a far distance. This means that the transducers are required to be large in size and operate at low frequencies.

[0006] There has been some recent work in developing small higher frequency endoscopic histotripsy transducers with more precision. These have been developed for minimally invasive and small access surgeries. These devices, however, have been based on using single element piezoelectric transducers with a passive, fixed-focus acoustic lens applied to the front face for passively focusing the ultrasound beam (e.g. J. K. Woodacre and J. Brown, "TRANSDUCER ASSEMBLY FOR GENERATING FOCUSED ULTRASOUND," US 2020/0346044 A1, 2020, T. G. Landry et al., "Endoscopic Coregistered Ultrasound Imaging and Precision Histotripsy: Initial In Vivo Evaluation," BME Front., vol. 2022, 2022, doi: 10.34133/2022/9794321, and Maxwell, R. Hsi, T. Lendvay, P. Casale, and M. Bailey, "FOCUSED ULTRASOUND APPARATUS AND METHODS OF USE," US 2016/0287909 A1, 2016).

[0007] A disadvantage to such lens-based designs is that due to the strong curvature of the fixed-focus lens, acoustic coupling to tissue can be difficult because

the region between the curved lens surface and the tissue to be ablated needs to be completely filled with coupling material. Another disadvantage to such lens-based histotripsy endoscopes is that the ablation zone is limited by the fixed focus of the lens. This can limit the ablation rate since increasing the ablation zone requires relatively slow mechanical translation of the transducer.

SUMMARY

[0008] An ultrasound-based surgical system is provided for image guidance and mechanical ablation for minimally invasive procedures, particularly procedures which require the removal of tissue. The system includes a device having an elongate body portion that supports a therapeutic ultrasound transducer assembly containing a piezoelectric composite and an annular array of electrodes. The electrodes can be driven to generate focused ultrasound pulses for ablating tissue via cavitation. The device can be controlled to scan the focused ultrasound pulses within an elongate axial region for performing line ablation. An electrical isolation layer is formed over an annular array of electrodes to prevent arcing within a backing when high-voltage electrical pulses are delivered to the annular array of electrodes to generate ultrasound pulses for cavitation. The elongate body may support an imaging transducer assembly within a central aperture of the therapeutic ultrasound transducer assembly to facilitate image guidance during ablative procedures.

[0009] Accordingly, in a first aspect, there is provided a therapeutic ultrasound system for performing tissue ablation via cavitation, the therapeutic ultrasound system comprising:

a therapeutic ultrasound transducer assembly comprising:

a piezoelectric composite layer having a proximal surface and a distal surface;

an annular array of electrodes disposed on the proximal surface of the piezoelectric composite layer;

a common electrode disposed on the distal surface of the piezoelectric composite layer;

an electrical isolation layer disposed on the annular array of electrodes on the proximal surface of the piezoelectric composite layer;

an elongate body, wherein the therapeutic ultrasound transducer assembly is supported at a location remote from a proximal end of the elongate body;

an electrical signal delivery assembly disposed along at least a portion of the elongate body, wherein the electrical signal delivery assembly is operatively connected to the therapeutic ultrasound transducer assembly such that electrodes of the annular array of electrodes are in electrical communication with respective electrical channels of the electrical signal delivery assembly, and such that the common electrode is in electrical communication with a common electrical channel of the electrical signal delivery assembly; and

control and processing circuitry operatively coupled to the therapeutic ultrasound transducer assembly through the electrical signal delivery assembly, the control and processing circuitry configured to generate electrical pulses that are delivered, through the electrical signal delivery assembly, to the annular array of electrodes for generating focused ultrasound pulses suitable for generating cavitation in water; and

wherein a thickness of the electrical isolation layer is less than a wavelength of the focused ultrasound pulses within the electrically insulating layer; and

wherein the thickness of the electrical isolation layer and a dielectric breakdown strength of the electrical isolation layer are sufficiently high to prevent arcing, within a backing of the therapeutic ultrasound transducer assembly, among adjacent electrodes of the annular array of electrodes, during generation of the focused ultrasound pulses for cavitation.

[0010] In some example implementations of the system, the piezoelectric composite layer is configured such that between at least one pair of adjacent electrodes of the annular array of electrodes, an annular kerf extends from the proximal surface into the piezoelectric composite layer, and wherein an electrical insulating material forming the electrical isolation layer resides within each annular kerf.

[0011] In some example implementations of the system, at least one annular kerf extends from the proximal surface to the distal surface. Each annular kerf may extend from the proximal surface to the distal surface. At least one annular kerf is may be a partial kerf that extends from the proximal surface into the piezoelectric composite layer without extending to the distal surface. Each annular kerf may be a partial kerf that extends from the proximal surface into the piezoelectric composite layer without extending to the distal surface. The partial kerf may have a depth between 5% and 95% of the thickness of the piezoelectric composite layer. The partial kerf may have a depth between 5% and 90% of the thickness of the piezoelectric composite layer. The partial kerf may have a depth between 5% and 75% of the thickness of the piezoelectric composite layer. The partial kerf may have a depth between 50% and 95% of the thickness of the piezoelectric composite layer. The partial kerf may have a depth between 50% and 90% of the thickness of the

piezoelectric composite layer. The partial kerf may have a depth between 50% and 75% of the thickness of the piezoelectric composite layer.

[0012] In some example implementations of the system, the thickness of the electrical isolation layer residing on each electrode of the annular array of electrodes exceeds a width of the annular kerf.

[0013] In some example implementations of the system, the piezoelectric composite layer comprises an array of piezoelectric pillars embedded in a matrix, the piezoelectric pillars extending from the proximal surface to the distal surface, and wherein the piezoelectric pillars are arranged in a segmented annular array comprising a plurality of concentric arrays of piezoelectric pillars, such that each electrode of the annular array of electrodes is capable of electrically actuating one or more radially consecutive arrays of piezoelectric pillars, and such that each annular kerf is aligned with, and extends into, an annular matrix region residing between a respective pair of radially adjacent concentric arrays of piezoelectric pillars.

[0014] In some example implementations of the system, the electrical isolation layer has a dielectric breakdown strength between 10 and 280 kV/mm.

[0015] In some example implementations of the system, the therapeutic ultrasound transducer assembly is air-backed.

[0016] In some example implementations of the system, the therapeutic ultrasound transducer assembly comprises a backing layer embedded with microballoons.

[0017] In some example implementations of the system, the annular array of electrodes are defined such that a lateral inter-electrode spacing is between 20 and 80 microns.

[0018] In some example implementations of the system, an outer diameter of the annular array of electrodes is between 10 and 25 mm, and a number of electrodes forming the annular array of electrodes is between 8 and 64.

[0019] In some example implementations of the system, the piezoelectric composite layer comprises an array of piezoelectric pillars embedded in a matrix, the piezoelectric pillars extending from the proximal surface to the distal surface, and wherein the piezoelectric pillars are arranged in a segmented annular array comprising a plurality of concentric arrays of piezoelectric pillars, such that each electrode of the annular array of electrodes is capable of electrically actuating one or more radially consecutive arrays of piezoelectric pillars, and such that and such that each annular inter-electrode gap is aligned with an annular matrix region residing between a respective pair of radially adjacent concentric arrays of piezoelectric pillars.

[0020] In some example implementations of the system, the electrical signal delivery assembly is operatively connected to the therapeutic ultrasound transducer assembly via a plurality of wire bonds. Each wire bond may electrically connect a respective electrode of the annular array of electrodes with a corresponding conductive channel of the electrical signal delivery assembly through an aperture formed in the electrical isolation layer.

[0021] In some example implementations of the system, the common electrode is electrically connected to the electrical signal delivery assembly via a ground ring extending along at least a portion of an outer circumferential edge of the piezoelectric composite layer.

[0022] In some example implementations of the system, the electrical signal delivery assembly comprises a flexible printed circuit board. The flexible printed

circuit board may be operatively connected to the therapeutic ultrasound transducer assembly via direct bonding of a distal region of the flexible printed circuit board to the therapeutic ultrasound transducer assembly through an aperture formed in the electrical isolation layer.

[0023] In some example implementations of the system, the thickness of the electrical isolation layer is equal to a quarter of the wavelength of the focused ultrasound pulses within the electrical isolation layer.

[0024] In some example implementations of the system, the thickness of the electrical isolation layer is equal to a half of the wavelength of the focused ultrasound pulses within the electrical isolation layer.

[0025] In some example implementations of the system, the therapeutic ultrasound transducer assembly further comprises a fixed acoustic lens.

[0026] In some example implementations of the system, the fixed acoustic lens has a f-number between 0.5 and 3.

[0027] In some example implementations of the system, the control and processing circuitry is configured to control the therapeutic ultrasound transducer assembly to scan the focused ultrasound pulses within an elongate axial region residing distalward from a distal energy emitting surface of the therapeutic ultrasound transducer assembly. The control and processing circuitry may be configured to unidirectionally scan the focused ultrasound pulses within the elongate axial region. The control and processing circuitry may be configured to scan the focused ultrasound pulses at a scan rate between 0.3-1.3 m/s.

[0028] In some example implementations, the system further comprises an imaging transducer assembly supported by the elongate body such that a distal surface of the imaging transducer assembly resides within a central aperture defined

within the therapeutic ultrasound transducer assembly, and wherein the control and processing circuitry is operatively coupled to the imaging transducer assembly through the electrical signal delivery assembly, wherein the control and processing circuitry is configured to control the imaging transducer assembly to acquire ultrasound image data and to process the ultrasound image data to generate one or more ultrasound images characterizing an imaging region that spatially overlaps with the elongate axial region.

[0029] In some example implementations of the system, the control and processing circuitry is further configured to control the therapeutic ultrasound transducer assembly and the imaging transducer assembly such that scanning of the focused ultrasound pulses to perform line ablation is only initiated after detection of cavitation in the ultrasound images. The control and processing circuitry may be further configured to control the therapeutic ultrasound transducer assembly and the imaging transducer assembly such that collection of the ultrasound image data by the imaging transducer assembly is interleaved with delivery of the focused ultrasound pulses.

[0030] In some example implementations of the system, the control and processing circuitry is configured such that the ultrasound image data collected between successively generated focused ultrasound pulses represents a subset of a full image frame of a B-mode image. The control and processing circuitry may be configured such that ultrasound image data corresponding to a selected subset of a full B-mode image frame is collected before and after generation of a given focused ultrasound pulse, thereby obtaining first ultrasound image data and second ultrasound image data characterizing the selected subset of the full B-mode image frame, and wherein the control and processing circuitry is configured to process the

first ultrasound image data and the second ultrasound image data to generate a subtraction image characterizing a temporal change within the selected subset of the full B-mode image frame. The control and processing circuitry may be configured to display the full B-mode image frame and to annotate the full B-mode image frame based on the subtraction image.

[0031] In some example implementations of the system, the central aperture has a shape that results in segmentation of an inner electrode of the annular array of electrodes, and wherein the segmented portions of the inner electrode are electrically connected to facilitate actuation of the segmented portions by a single channel of the electrical signal delivery assembly.

[0032] In another aspect, there is provided a method of performing tissue ablation via cavitation, the method comprising:

bringing a distal, energy-emitting surface of a therapeutic ultrasound transducer assembly into acoustic contact with tissue, the therapeutic ultrasound transducer assembly comprising:

a piezoelectric composite layer having a proximal surface and a distal surface;

an annular array of electrodes disposed on the proximal surface of the piezoelectric composite layer;

a common electrode disposed on the distal surface of the piezoelectric composite layer;

an electrical isolation layer disposed on the annular array of electrodes on the proximal surface of the composite piezoelectric layer; and

generating and delivering electrical pulses to the annular array of electrodes to generating focused ultrasound pulses suitable for generating cavitation within a subsurface focal region;

wherein a thickness of the electrical isolation layer is less than a wavelength of the focused ultrasound pulses within the electrically isolation layer; and

wherein the thickness of the electrical isolation layer and a dielectric breakdown strength of the electrical isolation layer are sufficiently high to prevent arcing, within a backing of the therapeutic ultrasound transducer assembly, among adjacent electrodes of the annular array of electrodes, during generation of the focused ultrasound pulses for cavitation.

[0033] In some example implementations, the method further comprises controlling a delay between the electrical pulses delivered to the annular array of electrodes such the subsurface focal region is scanned to perform line ablation of the tissue.

[0034] In another aspect, there is provided a therapeutic ultrasound device for performing tissue ablation via cavitation, the therapeutic ultrasound device comprising:

a therapeutic ultrasound transducer assembly comprising:

a piezoelectric composite layer having a proximal surface and a distal surface;

an annular array of electrodes disposed on the proximal surface of the piezoelectric composite layer;

a common electrode disposed on the distal surface of the piezoelectric composite layer;

an electrical isolation layer disposed on the annular array of electrodes on the proximal surface of the piezoelectric composite layer;

an elongate body, wherein the therapeutic ultrasound transducer assembly is supported at a location remote from a proximal end of the elongate body;

wherein the piezoelectric composite layer is configured such that between at least one pair of adjacent electrodes of the annular array of electrodes, an annular kerf extends from the proximal surface into the piezoelectric composite layer, and wherein an electrical isolation material forming the electrical isolation layer resides within each annular kerf.

[0035] In some example implementations of the device, at least one annular kerf is a partial kerf that extends from the proximal surface into the piezoelectric composite layer without extending to the distal surface.

[0036] A further understanding of the functional and advantageous aspects of the disclosure can be realized by reference to the following detailed description and drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0037] Embodiments are described with reference to the accompanying drawings. In the drawings, like reference numbers can indicate identical or functionally similar elements.

[0038] **FIG. 1A** shows a non-limiting example embodiment of the imaging and therapy device for performing tissue ablation via cavitation.

[0039] **FIG. 1B** shows a cross-section view of the example embodiment in FIG. 1A to highlight internal details.

[0040] FIG. 1C shows a cross-section view of the example embodiment in FIG. 1A, with a representative ultrasound image field of view and therapy transducer treatment zone shown.

[0041] FIG. 1D shows an example of a piezoelectric composite layer kerfed to define an annular electrode array.

[0042] FIG. 2A illustrates the conditions for dielectric breakdown through the low density backing when no electrical isolation layer is applied.

[0043] FIG. 2B illustrates how an electrical isolation layer is applied between the piezoelectric composite substrate and the low density backing can prevent dielectric breakdown in the backing.

[0044] FIG. 2C shows a 2D cross section of the therapeutic ultrasound transducer assembly with only the electrode etched.

[0045] FIG. 2D shows a 2D cross section of the therapeutic ultrasound transducer assembly with shallow partial kerfs.

[0046] FIG. 2E shows a 2D cross section of the therapeutic ultrasound transducer assembly with deep partial kerfs.

[0047] FIG. 2F shows a 2D cross section of the therapeutic ultrasound transducer assembly with the composite fully kerfed.

[0048] FIG. 3A illustrates the fabrication of an example therapeutic ultrasound transducer assembly, showing a sectioned isometric view of a ring shaped piezoelectric composite material before applying electrodes.

[0049] FIG. 3B illustrates the fabrication of an example therapeutic ultrasound transducer assembly, showing the device in FIG. 3A with electrodes on the top and bottom surface.

[0050] FIG. 3C illustrates the fabrication of an example therapeutic ultrasound transducer assembly, showing the device in FIG. 3B creating partial kerfs in the composite material to define the array elements.

[0051] FIG. 3D illustrates the fabrication of an example therapeutic ultrasound transducer assembly, showing the device in FIG. 3C after applying the isolation layer, with a strip masked off to allow for the electrical connections to the array elements.

[0052] FIG. 3E illustrates the fabrication of an example therapeutic ultrasound transducer assembly, showing the device in FIG. 3D after applying the low-density backing layer on top of the electrical isolation layer.

[0053] FIG. 3F illustrates the fabrication of an example therapeutic ultrasound transducer assembly, showing the device in FIG. 3E after applying the acoustic matching layer on the bottom face of the piezoelectric composite.

[0054] FIG. 4A shows an example dice-and-fill 1-3 piezoelectric composite material substrate.

[0055] FIG. 4B shows the example composite material from FIG. 4A after creating partial kerfs to define the array elements.

[0056] FIG. 4C shows the piezoelectric pillars for an example 1-3 piezoelectric composite material substrate with radially defined pillars.

[0057] FIG. 4D shows an example 1-3 piezoelectric composite material substrate with radially defined pillars without the fill material.

[0058] FIG. 4E shows an example 1-3 piezoelectric composite material substrate with radially defined pillars after creating partial kerfs to define the array elements.

[0059] FIG. 5 shows an example system for performing tissue ablation via cavitation.

- [0060] FIG. 6A is a block diagram of imaging and therapy system.
- [0061] FIG. 6B is a block diagram of therapy electronics system forming part of the therapy system.
- [0062] FIG. 7A is a photograph showing a pulse generator connected to cable bundle.
- [0063] FIG. 7B is a plot of voltage versus time showing a pulse from a single channel during operation.
- [0064] FIG. 7C shows a typical delay profile across a 16 element array.
- [0065] FIG. 8 shows a bubble cloud tested in a tissue phantom with individual ablation regions compared to rastered line ablation (far right).
- [0066] FIG. 9 shows a non-limiting example embodiment of the imaging and therapy device form factor.
- [0067] FIG. 10 is a representative image obtained in vivo during treatment (left) and after tissue ablation (right), the arrow is annotating the line of mechanically ablated tissue.
- [0068] FIG. 11A, 11B, 11C and 11D show the steps involved in fabricating a first example method of interconnecting the therapy array to an interposer PCB.
- [0069] FIGS. 12A, 12B, 12C, 12D, and 12E show the steps involved in fabricating a second example method of interconnecting the therapy array to an interposer PCB.
- [0070] FIG. 13A shows an example embodiment in which the four inner elements are discontinuous around the square hole in the center.
- [0071] FIG. 13B shows a first example method of electrically connecting to the four sections of the disconnected elements.

[0072] FIG. 13C shows a second example method of electrically connecting to the four sections of the disconnected elements.

[0073] FIG. 14 shows a series photos of a fabricated design showing a) the array and interconnect mounted co-planar to each other, b) the electrical connections between the array elements and exposed pads on the interconnect, c) the connections protected with potting epoxy, d) a zoomed in view of the electrical connections and e) a zoomed in view of the PCB section used to rejoin elements disconnected by the hole for the imaging array.

[0074] FIG. 15 is a photo of a side-looking therapy array with imaging array in the center.

[0075] FIG. 16 shows radial composite pre-electrode patterning (left) and post-electrode patterning (right).

DETAILED DESCRIPTION

[0076] Various embodiments and aspects of the disclosure will be described with reference to details discussed below. The following description and drawings are illustrative of the disclosure and are not to be construed as limiting the disclosure. Numerous specific details are described to provide a thorough understanding of various embodiments of the present disclosure. However, in certain instances, well-known or conventional details are not described in order to provide a concise discussion of embodiments of the present disclosure.

[0077] As used herein, the terms “comprises” and “comprising” are to be construed as being inclusive and open ended, and not exclusive. Specifically, when used in the specification and claims, the terms “comprises” and “comprising” and variations thereof mean the specified features, steps or components are included.

These terms are not to be interpreted to exclude the presence of other features, steps or components.

[0078] As used herein, the term “exemplary” means “serving as an example, instance, or illustration,” and should not be construed as preferred or advantageous over other configurations disclosed herein.

[0079] As used herein, the terms “about” and “approximately” are meant to cover variations that may exist in the upper and lower limits of the ranges of values, such as variations in properties, parameters, and dimensions. Unless otherwise specified, the terms “about” and “approximately” mean plus or minus 25 percent or less.

[0080] It is to be understood that unless otherwise specified, any specified range or group is as a shorthand way of referring to each and every member of a range or group individually, as well as each and every possible sub-range or sub-group encompassed therein and similarly with respect to any sub-ranges or sub-groups therein. Unless otherwise specified, the present disclosure relates to and explicitly incorporates each and every specific member and combination of sub-ranges or sub-groups.

[0081] As used herein, the term “on the order of”, when used in conjunction with a quantity or parameter, refers to a range spanning approximately one tenth to ten times the stated quantity or parameter.

[0082] Unless defined otherwise, all technical and scientific terms used herein are intended to have the same meaning as commonly understood to one of ordinary skill in the art. Unless otherwise indicated, such as through context, as used herein, the following terms are intended to have the following meanings:

[0083] The present disclosure provides a tools capable of performing image guidance and mechanical ablation during minimally invasive procedures, particularly

procedures which require the removal of tissue. The systems, devices and methods disclosed herein may be employed for non-contact, non-thermal endoscopic line ablation procedures, with the advantage of providing imaging feedback to monitor the treatment and target the treated pathology. Unlike conventional and known devices for ultrasound-based tissue ablation, the embodiments described herein enables mechanical ablation, adjustable in depth, combined with real-time, co-registered (co-aligned) ultrasound image guidance in a form factor conducive to minimally invasive procedures.

[0084] Referring now to FIG. 1A, an example therapeutic ultrasound device 100 is shown for performing line ablation via ultrasound-induced cavitation. The example device includes a therapeutic ultrasound transducer assembly 200 that houses an annular ultrasound transducer array capable of generating focused ultrasound pulses. An elongate body 120 supports the therapeutic ultrasound transducer assembly 200 at location remote from a proximal end 121 of the elongate body 120. The therapeutic ultrasound transducer assembly 200 may be supported, relative to the elongate body 120, such that a distal functional axis associated with the therapeutic ultrasound transducer assembly 200 (such as an ultrasound beam delivery axis) is angled relative to a longitudinal axis of the elongate body 120 (either rigidly or with a flexible tip), for example, to facilitate placement and ease of access to the target tissue.

[0085] As shown in the figure, the elongate body 120 may have a narrow cross-section that expands within a distal region to accommodate the radial extent of the therapeutic ultrasound transducer assembly 200. In some example implementations, the body portion may be employed as a handle (e.g. employed, for example, as a pinch-grip handle) that is manually supported and positioned by a user, or may

alternatively be supported and manipulated by a robotic positioning system, either user-controlled, autonomously controlled, or semi-autonomously controlled.

[0086] Furthermore, in some example implementations, such as the present example embodiment illustrated in FIG. 1A, the device 100 also includes a centrally disposed imaging transducer assembly 300 that facilitates imaging during a tissue ablation procedure, for example, to provide image guidance that facilitates image-based monitoring and/or feedback. Accordingly, the device includes a set of annular ultrasound elements capable of mechanical ablation over a range of focal depths (a therapy array), and a second set of ultrasound elements configured for high frequency, high resolution ultrasound imaging (an imaging array).

[0087] Although not shown in FIG. 1A, an electrical signal delivery assembly, such as a printed circuit board or one or more cables, is disposed along or within at least a portion of the elongate body 120, and the electrical signal delivery assembly is operatively connected to the therapeutic ultrasound transducer assembly 200 (and the imaging transducer assembly 300 if included). A proximal portion of the electrical signal delivery assembly is connected to or connectable to control and processing circuitry for delivering electrical pulses to the therapeutic ultrasound transducer assembly 200 and optionally controlling the imaging transducer assembly 300 to acquire ultrasound image data.

[0088] FIG. 1B shows a detailed isometric view of a distal region of the device that includes the therapeutic ultrasound transducer assembly 200, shown with a cross-sectional cut through a central longitudinal plane. The therapeutic ultrasound transducer assembly 200 includes a piezoelectric composite layer (e.g. disc) 210, shown in the present example implementation with a backing layer 215 and matching layer 220, with an outer energy emitting surface shown at 225. As shown in

the figure, the elongate body 120 may also include a centrally-disposed elongate support 122 for the imaging transducer assembly 300. The region 124 between the elongate body 120, the centrally-disposed elongate support 122, and the lateral portion of the imaging transducer assembly 300 may be filled in with a material such as an epoxy, or a rigid spacer. The imaging transducer assembly 300 may be axially aligned with the therapeutic ultrasound transducer assembly and epoxied in place or compression fit into the space made by the aperture in the therapy array and the housing.

[0089] It will be understood that the backing material 215 may be a solid backing material or, in some example implementations, may be air or an inert gas. In some example implementations, the backing material is made from a low acoustic impedance material. The low acoustic impedance material, such as, for example, epoxy loaded with a low-density filler (microballoons). Epoxy loaded with a low-density filler provides rigidity to the device and enables a very thin form factor. The backing layer may be on the order of millimeters in thickness and does not require a casing like an air backed array would include.

[0090] FIG. 1B illustrates an example implementation in which an interconnect ring 230 circumferentially surrounds, at least in part, an outer portion of the piezoelectric composite layer 210. The interconnect ring 230 facilitates the formation of a common (ground) connection between a common electrical path within the electrical signal delivery assembly and a common electrode residing on a distal surface of the piezoelectric composite layer 210, and can facilitate ease of fabrication of the device. The interconnect ring may include features to fit and seal into a casing for the device. This example implementation illustrated one or many possible implementations for forming an electrical connection with a common

electrode of the therapeutic ultrasound transducer assembly 200, and other example implementations are described in further detail below.

[0091] As illustrated in the figure, the therapeutic ultrasound transducer assembly 200 is circular-shaped and has a square aperture (hole) 235 in the center to accommodate the imaging transducer assembly 300. It will be understood, however, that the shapes illustrated in the figures are meant to be illustrative only and not limiting. For example, therapeutic ultrasound transducer assembly 200, and its annular elements, need not have a circular shape (for example, an elliptical shape can be employed in the alternative) and the aperture 235 (and the shape of the imaging transducer assembly 300) can take on a wide variety of shapes other than square, including, for example, rectangular, circular and elliptical.

[0092] FIG. 1C schematically illustrates the spatial co-registration and spatial overlap between a two-dimensional image slice 320 obtained from the central imaging transducer assembly 300 and an elongate axial region 240 over which focused ultrasound pulses are scanned by the therapeutic ultrasound transducer assembly 200. The elongate axial region 240 that corresponds to a therapy transducer treatment zone represents the region that can be ablated by electronically steering the therapy transducer focus to achieve cavitation in tissue, as will be described in further detail below. In some example implementations, the elongate axial region 240 shares axial-symmetry with the therapeutic ultrasound transducer assembly 200.

[0093] The imaging transducer assembly 300 may be a 1D, 1.5D, 2D, or annular imaging transducer, provided that its imaging volume spatially overlaps with the elongate axial region 240 associated with treatment by the therapeutic ultrasound transducer assembly 200. An example implementation of a suitable imaging

ultrasound assembly for integration into the device is described in US Patent No. 10,149,660, which is incorporated herein by reference in its entirety.

[0094] FIG. 1D illustrates an example embodiment of an annular piezoelectric array, formed from a piezoelectric composite material, that resides within the therapeutic ultrasound transducer assembly 200. The figure shows the piezoelectric composite layer 210, with an annular array of electrodes 260 disposed on a first surface of the piezoelectric composite layer 210, the electrodes 260 formed by metal layer 250. A common electrode 255 is disposed on a second surface of the piezoelectric composite layer 210. The annular piezoelectric array is integrated into the therapeutic ultrasound transducer assembly 200 such that the first surface, on which the annular array of electrodes 260 reside, is a proximal surface (facing towards the proximal portion of the device) and the second surface, on which the common electrode 255 resides, is a distal surface facing the tissue region to be ablated during use. The figure also illustrates an example case in which the central aperture 235 is circular in shape.

[0095] In the example annular piezoelectric array shown in FIG. 1D, the annular electrodes are shown as being separated by kerfs 270 that extend from the proximal surface of the piezoelectric composite layer 210, into the piezoelectric composite layer 210, toward the distal surface of the piezoelectric composite layer 210 (for example, as described further below, during fabrication, the piezoelectric composite elements may be separated with a cut through the top electrode and partially or completely through the piezoelectric composite layer/substrate). The present inventors found that the inclusion of the kerfs 270 can be beneficial in enhancing the mechanical isolation of the piezocomposite material residing beneath the annular electrodes. As explained in further detail below, the kerfed configuration shown in

FIG. 1D is not intended to be limiting, and that in other example embodiments, the piezoelectric composite layer 210 may be absent of kerfs, may include one or more partial kerfs, and/or may include one or more full kerfs extending from the proximal surface to the distal surface of the piezoelectric composite layer 210. The kerf width can, in some example implementations, range between 5 and 15% of the thickness of the piezoelectric composite. The volume fraction of the piezoelectric composite, when kerfed, may be, for example, in the range of 30 to 90%.

[0096] While the annular piezoelectric array shown in FIG. 1D is beneficial in providing a compact configuration, with a distal-facing flat surface, the present inventors encountered a significant challenge when incorporating such a structure into the therapeutic ultrasound transducer assembly 200 and operating the device to perform histotripsy for tissue ablation. It was found that due to the high voltage pulses that are applied to adjacent electrodes of the annular electrode array to generate focused ultrasound pulses, very high potential differences are typically applied between adjacent electrodes, especially when the voltage pulses that are delivered to adjacent annular electrodes are out of phase. This is a result of the high pulse voltages necessary to produce the acoustic pressures required for cavitation, as well as the relatively large delays between elements required to focus to low f-numbers, such that neighboring electrodes have a high voltage difference during pulsing. This can lead to arcing between adjacent electrodes when the electric field within the backing exceeds the dielectric breakdown strength of the backing layer material (for example, a solid material or a gas, such as air in the case of air backing).

[0097] Indeed, to achieve focusing with an annular piezoelectric composite array, more than 8 elements are typically employed to reach cavitation thresholds. When

the array is divided into annular element rings (e.g. by the presence of annular electrodes), the elements become increasingly narrow toward the edge to maintain equal element area. The narrow elements impede the option of widening the kerf to prevent arcing between them. For example, in an example device with a 15 mm diameter annular array and 16 elements, the outer element is only 120 μm when using a 60 μm kerf between elements. The electrical breakdown in air (or microballoon loaded epoxy) is 3kV/mm, limiting the drive voltage to 180V, which is insufficient for mechanical cavitation.

[0098] This problem is illustrated in FIG. 2A, which shows a cross-sectional view through the piezoelectric composite layer 210 and the application of voltages to two adjacent annular electrodes 260A and 260B, relative to the common electrode 250, that results in a high inter-electrode voltage ΔV between the adjacent annular electrodes 260A and 260B. When the resulting electric field in the backing 215, within region 280 near the two adjacent electrodes 260A and 260B, exceeds the dielectric breakdown strength of the backing, dielectric breakdown (arcing) 285 occurs between the electrodes, potentially leading to damage of the array. Moreover, if kerfs 270 are included in the piezoelectric composite layer 210, arcing can also occur across the kerfs, especially if the kerfs are air filled or filled with a material or gas having a low dielectric breakdown strength. This problem is exacerbated for miniaturized device designs in which the inter-electrode spacing, and/or the kerf gap, is desired to be as small as possible to achieve a high volumetric fill factor in the piezoelectric composite layer 210.

[0099] To mitigate or avoid the problem of dielectric breakdown and arcing in the backing, the present inventors realized that this problem could be solved by the inclusion of a thin layer of electrically insulating material. The electrical isolation layer

is provided with a thickness that reduces the penetration of the electric field into the backing such that the electric field in the backing region proximal to the electrodes is below the dielectric breakdown strength of the backing. Moreover, the electrical isolation layer formed from a material with a sufficiently high dielectric breakdown strength to avoid dielectric breakdown within the insulating material. In some example embodiments, the electrical isolation layer may be an epoxy resin, which increases the electrical breakdown by a factor of 6.6 to 20kV/mm.

[0100] In some example implementations, the electrical isolation layer has a subwavelength thickness to avoid or reduce an impact on the acoustic performance of the device. Moreover, in some example implementations, the electrical isolation layer may have a quarter-wavelength or half-wavelength thickness, as per a wavelength of the ultrasound pulses within the electrical isolation layer.

[0101] In some example implementations, the electrical isolation layer has a dielectric strength of 20 kV/mm, 10 to 225 kV/mm (e.g. parylene C), 10 to 280 kV/mm (e.g. including parylene N), and may be formed from parylene.

[0102] As illustrated in FIG. 2B, the inclusion of the electrical isolation layer 290 prevents dielectric breakdown due to the thickness of the electrical isolation layer 290, which reduces the intensity of the electric field penetrating into the backing region 280, and due to the high dielectric breakdown strength of the electrical isolation layer that prevents dielectric breakdown in the electrical isolation layer 290. Moreover, in example implementations involving a kerf 270, as illustrated in FIG. 2B, the electrically insulating material forming the electrical isolation layer 290 extends into and substantially fills the kerf 270, and the high dielectric breakdown strength of the electrically insulating material forming the electrical isolation layer 290 prevents

dielectric breakdown in the kerf 270 during the application of electrical pulses to the device for the generation of ultrasound pulses sufficient for cavitation.

[0103] Accordingly, in various example implementations of the present disclosure, the therapeutic ultrasound device, configured for performing line ablation via ultrasound-induced cavitation, includes a therapeutic ultrasound transducer assembly that houses an annular ultrasound transducer array based on a piezoelectric composite. The annular ultrasound transducer array is formed by a piezoelectric composite layer having a proximal surface and a distal surface, an annular array of electrodes disposed the said proximal surface, a common electrode disposed on the distal surface of said piezoelectric composite layer, and an electrical isolation layer disposed on the annular array of electrodes on the proximal surface. The thickness of the electrical isolation layer and a dielectric breakdown strength of the electrical isolation layer are sufficiently high to prevent arcing, within a backing of the therapeutic ultrasound transducer assembly, among adjacent electrodes of the annular array of electrodes, during generation of the focused ultrasound pulses for performing cavitation in water, or for example, in tissue such as tumoral tissue, adipose tissue, or soft tissue pathologies. The thickness of the electrical isolation layer may also be less than a wavelength of the focused ultrasound pulses within the electrical isolation layer. The isolation layer may be configured to prevent arcing when the therapeutic ultrasound transducer assembly is employed to generate a -20 MPa peak negative pressure at the focus in water, to achieve shock scattering histotripsy (>3 cycles), typically greater than 80 MPa peak positive pressure.

[0104] In some example implementations, the piezoelectric composite layer may be configured such that between at least one pair of adjacent electrodes of the annular array of electrodes, an annular kerf extends from the proximal surface into

the piezoelectric composite layer. The electrically insulating material forming the electrical isolation layer extends into and resides within each annular kerf, thereby preventing arc within the kerf during the generation of focused ultrasound pulses sufficient for cavitation.

[0105] FIGS. 2C to 2F show various example implementations of the therapeutic ultrasound transducer assembly 200 in which the electrical isolation layer 290 is incorporated into the device structure to prevent dielectric breakdown in the backing 215 when generating focused ultrasound pulses for cavitation, with each figure showing a cross-sectional view. The figures also show the inclusion of a matching layer 295 defined on the common electrode 250. FIG. 2C shows an example implementation in which the electrodes 260 of the annular electrode array are defined on the proximal surface of the piezoelectric composite layer 210 in the absence of kerfs between adjacent electrodes. For example, in such an example implementation, the electrodes 260 can be photolithographically defined on the proximal surface. The electrical isolation layer 290, formed over the electrodes 260, prevents dielectric breakdown in the backing 215.

[0106] FIG. 2D shows an alternative example implementation in which the electrodes 260 of the annular electrode array are defined on the proximal surface of the piezoelectric composite layer 210 with shallow kerfs defined between adjacent electrodes, where the material forming the electrical isolation layer 290 extends into the kerfs. FIG. 2E shows an alternative example implementation in which the electrodes 260 of the annular electrode array are defined on the proximal surface of the piezoelectric composite layer 210 with deep kerfs defined between adjacent electrodes, with each kerf extending almost all of the way from the proximal surface

of the piezoelectric composite layer 210 to the distal surface. The material forming the electrical isolation layer 290 extends into the kerfs.

[0107] FIG. 2F shows another alternative example implementation in which the electrodes 260 of the annular electrode array are defined on the proximal surface of the piezoelectric composite layer 210 with full kerfs defined between adjacent electrodes, with each kerf extending fully across the piezoelectric composite layer 210, from the proximal surface to the distal surface. As in FIG. 2E, the material forming the electrical isolation layer 290 extends into the kerfs.

[0108] In some embodiments, the distal portion of the therapeutic ultrasound transducer assembly 200 may include an acoustic lens. The lens provides a focus at a fixed depth and the phase delay profile applied to the elements is chosen to bring the focal depth closer to the energy emitting face of the therapeutic ultrasound transducer assembly 200. In some example implementations, the lens is made of metal. In some embodiments the lens is integrated with the ground ring as one part with features to control the thickness of the bond layer between the lens and the therapy array. In some embodiments the lens has a f-number between 0.5 and 3..

[0109] Referring now to FIGS. 3A-3F, an example method of fabricating the therapeutic ultrasound transducer assembly 200 is illustrated. In FIG. 3A, a piezoelectric composite layer 210 disk is provided (the figure shows a half-portion of the disk with a cross-sectional cut along the midline). In FIG. 3B, electrode 260A (which will be processed to form the annular electrodes) is deposited on the proximal surface of the piezoelectric composite layer 210, and common electrode 250 is deposited on the distal surface. The electrodes could be deposited, for example, by evaporation, sputtering or other thin film deposition techniques. The electrode material is a conductive metal such as copper, aluminum, gold, silver, chrome, tin or

a combination thereof. The electrode thickness is commonly between 0.25 μm and 5 μm .

[0110] As shown in FIG. 3C, a set of annular kerfs 270 are cut into the electrode 260A and a first portion of the piezoelectric composite layer 210, such that the kerfs extend, partially, toward the distal surface of the piezoelectric composite layer 210. The kerfing of the electrode 260A creates the set of annular electrodes 260. As described above, in example implementations, the kerfs are just deep enough (e.g. $\leq 5 \mu\text{m}$) to remove the electrode 260A for segmenting the electrode 260A into the annular electrodes 260, while in other embodiments the partial kerfs extend partially through the piezoelectric composite layer 210, without extending to the distal surface, to reduce element mechanical coupling and improve element directivity ($\leq 90\%$ of the total thickness). The method of partially kerfing the piezoelectric composite layer 210 from the proximal surface provides the distinct advantage of leaving the electrode on the therapy transducer distal surface intact, which simplifies the electrical connection to the common (front, distal) electrode.

[0111] In an example embodiment in which the elements are defined with the partial kerfs and the composite is not kerfed, the patterning process can be completed with photolithography. In a positive photolithography process a mask is created by exposing photoresist to UV light in the areas of the electrode to be removed (kerfs) which causes the photoresist to be soluble by a developer. Then, an etchant is used to remove the electrode in the areas exposed by the photoresist mask.

[0112] In another example implementations, the kerfs can extend all the way from the proximal side of the piezoelectric composite layer 210 to the distal side. For example, this may be achieved by the example fabrication methods described below.

The kerfs can be formed according to a wide range of processes, including, but not limited to, laser micromachining and photolithography. In other example implementations that are absent of kerfs, the array of annular electrodes 260 may be formed via photolithography. In laser micromachining, short duration, high power laser pulses are used to precisely remove material (e.g. electrode, ceramic, epoxy) with minimal local heating or damage.

[0113] In FIG. 3D, the electrical isolation layer 290 is formed over the proximal surface of the piezoelectric composite layer 210 and the annular electrodes 260, such that the material forming the electrical isolation layer 290 extends into each kerf, filling the kerfs and avoiding or reducing the likelihood of dielectric breakdown within the kerfs and within the backing (not yet included) when electrical pulses are delivered to the annular electrodes for generating focused ultrasound pulses suitable for achieving cavitation within tissue. Electrical access to a portion of each underlying annular electrode 260 is made possible by providing an aperture (window) 292 within the electrical isolation layer 290, enabling the formation of electrical connections between the annular electrodes 260 and conductive channels within the electrical signal delivery assembly that connects the therapeutic ultrasound transducer assembly 200 to external driving and beamforming electronics. For example, a small portion of the annular array may be masked off such that the array electrodes are accessible for electrical connection using a method such as ultrasonic wire bonding. After completing the electrical connections, the electrical isolation layer may be applied to this section to complete coverage of the electrodes.

[0114] In FIG. 3E, a backing 215 is optionally added on the proximal side, over the electrical isolation layer 290, and over a distal portion of the electrical signal

delivery assembly that makes electrical connection with the annular electrodes 260. Alternatively, device may be air-backed (or backed with an inert gas), as shown in FIG. 3D. As noted above, the backing 215 may be a low-density backing layer, forming a low acoustic impedance material (e.g. with an acoustic impedance ranging from 428 Rayls to 2 MRayls), such as epoxy loaded with a low-density filler (e.g. microballoons), which provides rigidity to the device and enables a very thin form factor. A solid backing layer 215 may have a thickness of 0.5 to 10 millimeters in thickness and does not require a casing, as in the case of an air-backed configuration.

[0115] FIG. 3F shows the inclusion of an acoustic impedance matching layer 295 on a distal surface of the therapeutic ultrasound transducer assembly 200, which will face the tissue and enhance coupling of the focused ultrasound pulses.

[0116] FIG. 4A shows a segment from a piezoelectric composite material 210 disk. The piezoelectric composite consists of ceramic (e.g. pillars or rods) embedded in an epoxy matrix. A composite material is designed to reduce the acoustic impedance of the material to more closely match tissue and to improve the electromechanical efficiency. In the example embodiment shown in FIG. 4A, a conventional 1-3 composite structure is used where kerfs are diced into the ceramic in the x and y direction. This creates a grid of square ceramic pillars 350 with a rectangular prism (cuboid) geometry. The pillars are embedded in an epoxy resin (e.g. Epotek 301) fill material. The ceramic material chosen can be hard (e.g. PZT-5A) or soft (e.g. PZT-5H) piezoelectric ceramics, electrostrictive ceramic (e.g. PMN38) or specialized ceramics developed for therapy applications (e.g. PZ54). Histotripsy uses low duty-cycles (<1%), and low time averaged power, so ceramic loss isn't a critical parameter. Therefore, a variety of ceramics materials are suitable

and will each have a corresponding drive voltage required for reaching the threshold for cavitation.

[0117] A composite structure has the added benefit of providing some mechanical separation between elements defined by the annular electrodes. However, this mechanical separation is not complete if the elongate linear channels of the epoxy matrix, seen in FIG. 4A at 355, do not spatially align with the gaps between the electrodes of the annular array that will be formed over the piezoelectric composite layer 210 during fabrication.

[0118] In embodiments in which the substrate is a solid, low acoustic impedance ceramic (e.g. such as PZ39 or PZ37), some degree of mechanical isolation can be achieved with kerfing alone. For example, FIG. 4B shows the piezoelectric composite material 210 from FIG. 4A with partial kerfs 270 cut into the material. As described above, these partial kerfs are filled with the electrical isolation material during fabrication to avoid arcing between adjacent electrodes of the annular array. The material used for the electrical isolation layer may be the same as the composite fill material, or may be a different material that can be independently selected as required, to select the preferred mechanical properties and dielectric breakdown strength of each material.

[0119] FIG. 4C shows a segment of a piezoelectric composite disk 210A having an alternative composite structure, prior to inclusion of the epoxy matrix, showing only the piezoelectric pillars. In this example embodiment, the pillars 350 are segments of an annular rings instead of rectangular prisms. Such a structure of the piezoelectric composite disk 210A enables a higher volume fraction of ceramic relative to the structure of FIG. 4B. Moreover, mechanical isolation between adjacent ultrasound elements (as defined by adjacent annular electrodes) is

increased by having the kerfs 360 that segment the piezoelectric composite (and form the spatially-separated piezoelectric pillars) aligned with the annular intra-element gaps after deposition of the annular electrodes (and optional additional kerfing). The structure shown in FIG. 4C can be fabricated, for example, by laser dicing to achieve the curved kerfs. FIG. 4D shows the completed piezoelectric composite material 210A after the piezoelectric material grid in is filled with the matrix fill material to form the composite structure. As can be seen in the figure, the matrix fill material (e.g. epoxy) forms both radial 355A and annular 355B continuous channels of fill material.

[0120] FIG. 4E shows the piezoelectric composite 210A from FIG. 4D with partial kerfs (the upper annular electrodes are not shown in this figure). The second annular array element 370 (which would be defined by an annular electrode) is shaded to show the spatial alignment between the array element and the underlying structure of the composite material. As described above, the kerfs 270 are filled with the electrical isolation layer material during subsequent steps of the fabrication process (the isolation layer would also cover the entire top surface of the piezoelectric composite material as shown in the previous figures).

[0121] As noted above, an electrical signal delivery assembly, such as a printed circuit board or one or more cables, is disposed along or within at least a portion of the elongate body 120, and the electrical signal delivery assembly is connected to the therapeutic ultrasound transducer assembly 200, such that each electrode of the annular array of electrodes 260 is in electrical communication with a respective electrical channel of the electrical signal delivery assembly, and such that the common electrode 250 is in electrical communication with a common electrical channel of the electrical signal delivery assembly. Likewise, the electrical signal

delivery assembly is connected to the imaging transducer assembly 300, such that each electrode of an array of electrodes associated with imaging ultrasound elements of the imaging transducer assembly 300 is in electrical communication with a respective electrical channel of the electrical signal delivery assembly.

[0122] A proximal end of the electrical signal delivery assembly is operable coupled to, or connectable to, control and processing circuitry for controlling the generation and delivery of focused ultrasound pulses by the therapeutic ultrasound transducer assembly 200 and the collection of ultrasound image data by the imaging transducer assembly 300. As described in further detail below, the processing and control circuitry includes supporting electronics for the generation of focused ultrasound pulses from the therapeutic ultrasound transducer assembly 200 and the acquisition of ultrasound image data from the imaging transducer assembly 300.

[0123] Referring now to FIG. 5, an example system is illustrated for performing mechanical line ablation with an ultrasound therapy device. The example system includes a therapeutic ultrasound device 100, as described above, that includes the therapeutic ultrasound transducer assembly 200 and the imaging transducer assembly 300, transmit circuitry 500 for delivering transmit voltage pulses to the annular electrode array of the therapeutic ultrasound transducer assembly 200, transmit circuitry 505 and receive circuitry 510 for delivering transmit voltage pulses to, and receiving ultrasound signals from, respectively, the imaging ultrasound array of the imaging transducer assembly 300, a transmitter-receiver switch 515, and control and processing circuitry 400 (e.g. a controller, computer, or other computing system). While not shown in the figure, the system also includes beamforming circuitry for beamforming the transmit signals delivered to the therapeutic ultrasound transducer assembly 400 and the imaging transducer assembly 300, and for

beamforming ultrasound signals received by the imaging transducer assembly 300, and this may be implemented for example, as a subcomponent of the control and processing circuitry 400, the transmit and receive circuitry, or as separate components.

[0124] Control and processing circuitry 400 is employed to control transmit and receive circuitry 500, 505, and 510, the Tx/Rx switch 515, and for processing the receive signals obtained from the imaging receive circuitry 510. As shown in FIG. 5, in one embodiment, control and processing circuitry 400 may include a processor 410, a memory 420, a system bus 405, one or more input/output devices 430, and a plurality of optional additional devices such as communications interface 460, display 440, external storage 450, and data acquisition interface 470.

[0125] The present example methods of performing ultrasound mechanical, cavitation-based line ablation and ultrasound image guidance can be implemented via processor 410 and/or memory 420. As shown in FIG. 5, the control of the delivery of electrical pulses to the annular electrodes for generating focused ultrasound pulses and scanning the focal location for line ablation may be implemented by control and processing circuitry 400, via executable instructions represented as focused ultrasound scanning module 480. The control and processing circuitry 400 may include and execute scan conversion software (e.g. real-time scan conversion software) or other image processing functionality as represented by image processing module 490.

[0126] The transmit circuitry 500 for controlling delivery of voltage pulses to the therapeutic ultrasound transducer assembly 200 may be capable of high voltage, uni- or bi-polar, multi-cycle excitations. Each annular electrode of the therapeutic

ultrasound transducer assembly 200 is connected to a respective channel of transmit circuitry 500 with a programmable phase delay.

[0127] The functionalities described herein can be partially implemented via hardware logic in processor 410 and partially using the instructions stored in memory 420. Some embodiments may be implemented using processor 410 without additional instructions stored in memory 420. Some embodiments are implemented using the instructions stored in memory 420 for execution by one or more general purpose microprocessors. In some example embodiments, customized processors, such as application specific integrated circuits (ASIC) or field programmable gate array (FPGA), may be employed. Thus, the disclosure is not limited to a specific configuration of hardware and/or software.

[0128] Referring again to FIG. 5, it is to be understood that the example system shown in the figure is not intended to be limited to the components that may be employed in a given implementation. For example, the system may include one or more additional processors. Furthermore, one or more components of control and processing circuitry 400 may be provided as an external component that is interfaced to a processing device. For example, as shown in the figure, any one or more of transmit/receive circuitry 500, 505 and 510, and Tx/Rx switch 515 may be included as a component of control and processing circuitry 400 (as shown within the dashed line), or may be provided as one or more external devices.

[0129] While some embodiments can be implemented in fully functioning computers and computer systems, various embodiments are capable of being distributed as a computing product in a variety of forms and are capable of being applied regardless of the particular type of machine or computer readable media used to actually effect the distribution.

[0130] At least some aspects disclosed herein can be embodied, at least in part, in software. That is, the techniques may be carried out in a computer system or other data processing system in response to its processor, such as a microprocessor, executing sequences of instructions contained in a memory, such as ROM, volatile RAM, non-volatile memory, cache or a remote storage device.

[0131] A computer readable storage medium can be used to store software and data which when executed by a data processing system causes the system to perform various methods. The executable software and data may be stored in various places including for example ROM, volatile RAM, nonvolatile memory and/or cache. Portions of this software and/or data may be stored in any one of these storage devices. As used herein, the phrases “computer readable material” and “computer readable storage medium” refers to all computer-readable media, except for a transitory propagating signal *per se*.

[0132] A block diagram of an example control subsystem for generating and providing electrical pulses to therapeutic ultrasound transducer assembly 200 and the imaging transducer assembly 300 is shown in FIG. 6A. The delay generator hardware is digitally synchronized with the imaging pulses using a firmware-based programmable microprocessor (e.g., FPGA) via a trigger pulse. The microprocessor splits the trigger pulse into ‘N’ channels corresponding to the number of elements in the therapy array. The microprocessor then delays the individual channel pulses creating a profile such that the wavefronts from each element will converge onto a focal location. This profile corresponds to the difference in time of flight from each element to the focal depth. The delayed pulses are then converted into a short series of trigger pulses that are separated by one wavelength, with a duty cycle of less than 50%. This corresponds to the desired number of cycles in the excitation pulse. The

delayed multicycle pulses for each channel are then split into a positive pulse train and copy of the pulse train, nominally separated by half a wavelength, for the negative pulse. The half wavelength separation between pulse trains can be adjusted to compensate for FET switching times to give the desired output duty cycle. The digital pulse trains (two for each channel) are then directed to the high voltage high peak power pulse generator. For each channel, one copy of the pulse train is used to drive the positive side of the high voltage pulse and one copy is used to drive the negative side of the high voltage pulse.

[0133] FIG. 6B shows a block diagram that illustrates an example system configuration for splitting the delayed pulse train into two for each channel and delaying them by $\frac{1}{2}$ wavelength in order to trigger the positive and negative side of the therapy pulse. The process is repeated for each incoming trigger pulse and the focal depth may be changed within the delay generator by changing the delay profile.

[0134] FIG. 7A shows a photograph of an example therapy pulse generator subsystem. FIG. 7B shows an electrical pulse generated from a single channel during operation. FIG. 7C shows a portion of a typical delay profile across a 16 element array during generation of a focused ultrasound pulse.

[0135] As described above, the annular electrodes are excited with respective phase delayed voltage signals such that the acoustic waves constructively interfere at a focus at a prescribed depth in front of the distal energy-emitting surface of the therapeutic ultrasound transducer assembly. The constructive combination of the pressure generated from each of the annular array elements enables the threshold for mechanical ablation or cavitation to be reached, and the control of the phase delays among the annular electrodes enables the focal region where cavitation can be sustained to be scanned over an elongate axial region for tissue ablation. The

pressure threshold for mechanical ablation (cavitation) is much higher than for thermal ablation however, the pulses are short in duration (duty cycle <1%) therefore tissue heating is substantially avoided with the peripheral region surrounding the ablation region.

[0136] Cavitation is typically initiated at a low f-number (i.e., at the minimum ablation depth) where the pressure will be highest. Once a bubble cloud is formed, it becomes easier to maintain the cavitation because the cloud itself is a strong reflector and constructive interference increases the pressure at the boundary of the cloud. Accordingly, cavitation can be maintained while rastering the focal depth despite lower pressures generated with higher f-number focuses. Similarly, cavitation can be initiated at a higher frequency, where the focal gain is higher, and then dropped in frequency to complete the line ablation at a lower operating frequency. This method of cavitation generation and line ablation could be used to increase the width of the ablation region but initiating cavitation at a lower threshold. To widen the range of operating frequencies, matching layers can be applied to the front planar face of the device.

[0137] The raster speed during line ablation is typically based on the number of pulses per focal point, pulse repetition frequency, and the focal point step resolution. For example, the raster speed can be determined according to the equation: raster speed = $(Z_{\text{step}} \times \text{PRF}) / N_{\text{pulses}}$, where Z_{step} is the focal point step resolution, PRF is the pulse repetition frequency, and N_{pulses} is the number of pulses per focal point.

[0138] It has been found that the number of pulses per focal point generally impacts the cavitation threshold and the efficiency of tissue erosion. If the focus is made to dwell, for example, for several cycles (e.g. 2, 3, 4 or 5 cycles) at a single focal location, this can, in some cases, improve the initiation of the bubble cloud in

tissue. Conversely, sweeping the focal point rapidly and dwelling for less time can in some cases increase the rate of tissue erosion.

[0139] In some non-limiting example implementations, a therapeutic ultrasound device according to the embodiments described herein may perform histotripsy in tissue with focused ultrasound parameters of PRF = 0.5 to 2 kHz, 1 to 2 kHz, or 0.5 to 5 kHz, with N_{pulses} between 1 and 16. For example, for a device operating within a PRF of 0.5-2 kHz, a frequency of 1.6-2.4 kHz with N_{pulses} between 1 and 16, and with an outer annular array diameter within the range of 20 to 25mm, a step size during ablative line scanning may be, for example, within the range of 0.4 and 0.6 mm, with a raster speed, for example, ranging between 0.7-1.3 m/s. An another example, for a device operating within a PRF = 0.5-2 kHz, a frequency of 2.4-3.6 kHz, with N_{pulses} between 1 and 16, and with an outer annular array diameter within the range of 13-17 mm, a step size during ablative line scanning may be, for example, within the range of 0.2-0.4 mm, with a raster speed, for example, ranging between 0.3-0.7 m/s.

[0140] In device embodiments that incorporate the imaging transducer assembly within the central portion of the therapeutic ultrasound transducer assembly, and where the imaging transducer assembly is controlled to acquire image data, within a spatial region overlapping with the scanned focal region of the focused therapeutic ultrasound pulses, mechanical ablation caused by cavitation can be confirmed by viewing the bubble cloud forming and collapsing in an ultrasound image presented on a user interface, such as an image guidance system. For example, the image data can be processed to generate one or more ultrasound images from image modalities such as, but not limited to, B-mode, power Doppler image or other

ultrasound image modalities, such as the sub-frame difference method described below.

[0141] As explained above, the phase delay profile of each the transmit excitations delivered to the annular electrode array of the therapeutic ultrasound transducer assembly may be controlled, during a tissue ablation procedure, to raster the focal location (e.g. focal depth) along a line (or axis), extending from a first location to a second more distal location relative to the energy-emitting surface of the therapeutic ultrasound transducer assembly. In some example implementations, the phase delay profile can be controlled by a control unit (e.g., FPGA, microcontroller) with a sufficiently fast rate to raster the ablation spot at a rate of >20 Hz (generally perceived as “real time”), with delays accurate to less than 1/20th of a wavelength.

[0142] The control and processing circuitry may be programmed to jointly (e.g. synchronously) control the transmit/beamforming electronics associated with the therapeutic ultrasound transducer assembly and the transmit/receive/beamformer electronics associated with the imaging transducer assembly to interleave therapy and imaging excitations, while avoiding interference to either process.

[0143] It will be understood that the therapy pulses may be interleaved with the imaging pulses according to a variety of implementations that are not restricted to collecting a full image frame between the delivery of therapy pulses. For example, a first subset of focused image lines (a subset of a full image frame) may be collected by the imaging transducer assembly between therapeutic sonications, and a second subset of focused image lines (a subset of a full image frame) may be collected between the next pair of therapeutic sonications. This sequence may continue until a full image frame is captured, the interleaved image acquisition sequence may then repeat. The ultrasound image (e.g. a full frame B-mode image) may be updated after

each full frame of image data is collected, or locally updated each time a respective subset of image data is collected. This method avoids limiting the therapy pulse repetition frequency by the imaging frame rate.

[0144] The acquisition of the image data and generation and display of guidance images provides pre-operative image guidance to the surgeon by making the tissue types (muscle, fat, blood vessels and nerves) visible prior to initiating the mechanical ablation. The image guidance allows the surgeon to assess the size and locations of the areas requiring treatment, including target depth ranges, and also to confirm that all sensitive tissues such as arteries, major vessels, and nerves are well outside of the treatment zone. Part of the surgical plan may include assessing for structures near the target tissue that are not to be damaged (i.e., blood vessels and nerves). When cavitation is started, the bubble cloud becomes visible in the imaging plane, e.g. in the B-mode image, and optionally in an image enhancement overlay. After cavitation, blood may fill the ablated region and pool, coagulate and becomes hyperechoic, and is therefore bright in the B-mode ultrasound image.

[0145] As noted above, the imaging array may be a linear array or phased array, providing a 2D slice co-aligned and co-registered with the ablation region. Alternatively, the high-resolution imaging array may be capable of 3D imaging. An embodiment of this device could include a 2D array or a 1D array on a mechanical tilt fixture, both capturing planes around the ablation region for additional context in the image guidance.

[0146] The ultrasound guidance images can be augmented according to several techniques. A conventional power Doppler approach may be employed to highlight

the cavitation bubble cloud. Additionally, Elastography could be used to highlight the difference in tissue elasticity between treated and untreated areas.

[0147] In one example embodiment, a subframe difference method may be employed to augment a B-mode image to provide image enhancement associated with time-dependent features of cavitation. In one example implementation of this method, two image subframes, or subframes, collected with low latency are subtracted on a line-by-line basis, and the resulting difference (subtraction) image is overlaid on the B-mode image. In some example implementations, the time delay between acquisition of successive images for subtraction is low because only a subset (subframe) of a full image frame is collected. The repeat imaging insonifications for such a subframe difference method can also be flexibly interleaved with the therapy pulses. For example, a subframe corresponding to 8 image lines is collected, then the same subframe is recollected, optionally after one or more therapeutic sonications (pulses), and subtracted to generate the subtraction image for image annotation. The sequence can be completed on differently sized subframes and differently sized time intervals for the therapy. In this way, the therapy pulse repetition frequency and interval between the subframe collections is not dependent on the time required to collect a full B-mode image. This improves the highlighting capabilities of the subframe difference method by capturing faster movements of the bubble cloud.

[0148] FIG. 8 shows the result of the sub-frame difference method overlaid over the B-mode image for single focal depth ablation at 3 mm, 5 mm and 7 mm and real-time, line ablation between 3 mm and 8 mm. The tissue is shown in a B-mode image and the bubble cloud is highlighted in bright white in this example, however, color mapping further distinguishes the cavitation.

[0149] It will be understood that cavitation thresholds vary by tissue type. For example, fat has a lower threshold than muscle, nerves, blood vessels, making the tool ideal for debulking procedures that target fat. A mechanically ablative device enables tissue selectivity which increases the level of safety for the procedure. Patient-specific thresholding may be possible with a mechanically ablative device coaligned with the imaging device. When beginning a procedure, a surgeon could confirm the minimum transmit voltage needed to ablate in an area of fat using the image for confirmation of cavitation. The ultrasound guidance images would facilitate the tuning of the threshold. The threshold could be set based on the excitation required to induce an incomplete line of ablation for a tissue debulking procedure.

[0150] An incomplete line of ablation, as observed in an ultrasound guidance image, means that the fat is being ablated while the muscle remains unharmed. Depending on the risks and neighboring structures, the procedure may be completed at a voltage a small margin (10-20%) above the established threshold. In one example embodiment, the system may be employed to autonomously monitor the bubble cloud during the procedure and notify the surgeon if the ablation stops unexpectedly, or if the guidance images satisfy (or fail to satisfy) pre-determined image criteria associated with an acceptable or desired spatial ablation profile (for example, by processing the image data according to pre-determined mask or surgical plan). The system may also interrupt the delivery therapy of focused ultrasound therapy pulses if the ablation line becomes a complete continuous line, triggering the surgeon to reestablish the cavitation threshold. The system may automatically increase the excitation voltage for the therapy array within a safe range to maintain the bubble cloud.

[0151] Design decisions regarding the transducer dimension, number of elements and operating frequency will be informed by the requirements of individual procedures, including the maximum probe diameter compatible with surgical access, the depth of relevant anatomical features, size of relevant anatomical features and size and type of tissue to ablate. It will be understood that the dual-modality, imaging and therapy ultrasound transducer according to the present disclosure can be provided in multiple configurations, such as, for example, in a forward-looking, side-looking or custom orientation tailored to the laparoscopic or endoscopic application. Similarly, the length of the elongated portion can be chosen to access the anatomy of interest.

[0152] An example embodiment of the form factor is shown in FIG 9. In the example implementation shown in the figure, the high frequency, high resolution ultrasound imaging array can operate at a frequency, for example, that lies within the range of 15 to 25 MHz . The diameter of the therapy array and dual-modality device is between 10 and 25 mm. The thickness of a side-looking device can be between 1 and 5 mm. The therapy array is capable of real time, mechanical, line ablation adjusted to raster the focal depth or ranges corresponding to a f-number of 0.3 - 1.2.

[0153] In some embodiments, the probe is rigid, and the handheld portion is connected to an elongated portion and an angled portion such that the probe is bent for better access to a desired anatomical region, such as the tongue. Additionally, the imaging and therapeutic ultrasound transducer assemblies may be oriented at an angle to further facilitate access to a desired anatomical region, such as the base of the tongue. In some example implementations, the first, elongated portion of the handle body between 5 and 15 cm in length and the angled portion is between 2 and 8 cm in length. The angled portion may reside at an angle between 15 and 45

degrees relative to the elongated portion. The imaging and therapy ultrasound transducer may be oriented at an angle of between 70 and 90 degrees from the angled portion of the probe.

[0154] In some example, embodiments the annular array, as defined by the outer diameter of the outer annular electrode, lies within a range of 8 mm to 50 mm and operates between range of frequencies of 600 kHz to 6 MHz. The therapeutic annular array is made of up range of element counts ($N = 8$ to $N = 64$) to scan and focus over range of depths (e.g. $f\#$ 0.4 to $f\#$ 1.5). The hole in the annular array is made to accommodate the imaging array. In some embodiments the hole is circular, with a diameter ranging from 3 mm to 10 mm, while in other embodiments, the hole is rectangular (with a width ranging from 3 mm to 10 mm). The imaging array might be a 1D, 1.5D, 2D or annular array, however, one or several imaging lines generated by the array overlap with the therapy focal line.

[0155] In one example embodiment, the dual modality imaging and therapy transducer is between 12 and 17 mm in diameter at the distal end. The therapy elements capable of mechanical ablation may be arranged in an annular array pattern and operate at between 2.5 and 3.5 MHz. The ablation region may be approximately 1 mm wide and can be varied over a depth of 5-15 mm. There is a hole in the center of the therapy elements where the imaging elements are co-aligned with the central axis of the therapy elements. The imaging elements may be operated at between 15 and 25 MHz and the imaging window has a maximum depth of 2.5-3.5 cm. The linear set of imaging elements are 4-5 mm in width and 4-5 mm in height, and focuses over range of f numbers (range of depths $f\#$ 0.4 to $f\#$ 1.5).

[0156] For 16 elements arrays with an outer diameter of between 8 and 23mm, and frequency of between 2 and 5 MHz, the outer element is typically between 60

and 230 μm , respectively. The narrow elements impede the option of widening the kerf to prevent arcing between them. With the isolation layer, the kerf width between elements typically lies within the range of 20 to 80 μm for the range of embodiments previously listed.

[0157] In the present example embodiment, the 2D imaging plane can be oriented in one of two directions, relative to the handpiece. First, the same plane as the elongated portion of the probe. In the case of tongue debulking, this would produce an image along the length of the tongue. In an alternate embodiment, the imaging array and corresponding plane would be rotated 90 degrees. Again, in the tongue debulking example, this would produce an image of the tongue in cross-section, making the lingual artery and nerves that run along either side of the tongue visible during the procedure.

[0158] The embodiments of the present disclosure can enable the non-invasive removal of tissue in minimally invasive procedures. The ablation region lies below the contact surface. Therefore, the procedures would be completed without creating an open wound. The non-invasive nature of the method removes the complications around wound healing and risks of infection. A non-limiting list of example applicable procedures includes superficial, endoscopic and laparoscopic procedures of the skin, nose, tongue, prostate, thyroid, brain, esophagus, stomach, and colon.

[0159] In one example implementation, the therapeutic ultrasound devices described above can be employed in a tissue debulking procedure is as follows. For ease of example, debulking of the tongue to treat sleep apnea is used as the example procedure. The probe is positioned on the tongue in imaging mode. The surgeon evaluates the tissue to be debulked and the structures to protect. Based on the size of the target tissue, the surgeon can plan the number, location, and depth

range of the set of non-overlapping ablation lines. When the surgical plan is completed, the surgeon uses the system to test the cavitation threshold in an area that includes fat. This procedure determines a safe range of excitation voltages for the therapy array.

[0160] The ablation can begin at the first location. While the bubble cloud is rastering, it is monitored in the image. A motion enhancing overlay may be laid on top of the B-mode to highlight the rapidly changing bubble cloud. After the therapy dose, blood will coagulate in the empty space. The coagulated blood is hyperechoic in the B-mode ultrasound image (shown in FIG. 10). Therefore, treated areas remain visible throughout the procedure. The surgeon would reposition the device for the next ablation line, using the image as guidance and initiate cavitation on the system. Because the rastering is happening in real time, each location takes only seconds for the cavitation to complete. This process is repeated until the surgical plan is complete.

[0161] FIG. 11A shows an example embodiment of illustrating an example of the interconnection of an electrical signal delivery assembly to the therapeutic ultrasound transducer assembly. In the present example embodiment, the electrical signal delivery assembly is implemented as a two-prong flexible interconnect PCB 600. The two prongs have exposed pads to electrically connect to the exposed annular electrodes 260 and the interconnect ring 230. FIG. 11B shows the details of the electrical interconnection. The end portions of the two outer prongs 610 are each bonded to the back of the array. An electrical connection, in the present example illustration implemented by wirebonds 630, is made between the interconnect PCB pads 620 and the exposed annular array elements 620 (accessible through the aperture formed within the electrical isolation layer 290), and between the ground

pads 640 and the interconnect ring 230 that is in electrical communication with the common electrode on the distal side of the piezoelectric composite layer. In some example embodiments, the front (distal) face electrical connection with the common electrode is achieved with physical metal-to-metal contact, thin metal deposition, conductive epoxy, soldering or wire bonding. FIG. 11C shows the electrical connections protected with potting epoxy and the isolation layer 192 cast across the remaining surface of the array. Finally, the low impedance backing layer 215 is cast on top of the isolation layer as shown in FIG. 11D. Depending on the desired form factor the interconnect (45) can remain flat or be bent up prior to casting the isolation (145) and backing layers (150).

[0162] FIGS. 12A-12E show a similar example embodiment of the interconnection between the electrical signal delivery assembly (the flexible printed circuit board 600) to the therapeutic ultrasound transducer assembly 200. In addition to the two outer prongs 610, an inner prong 640 is used to connect to the common electrode on the front (distal) surface of the piezoelectric composite instead of the ground ring. FIG. 12A and FIG. 12B show the distal portion of the flexible circuit board bonded to the array with electrical connections 630. The inner prong 640 is bent so that the end is perpendicular to the piezoelectric composite surface and an electrical connection is made from the thickness of the interconnect trace (cross section) to the common electrode residing on the distal (front) surface of the piezoelectric composite, creating the ground connection.

[0163] FIG. 12C shows the view from FIG. 12B after the potting, isolation and backing layers 215 are added. FIG. 12D shows the front view of the therapeutic device before backing layers are applied, to highlight the ground electrical connections 645 to the front of the therapy array before backing, and to show the

imaging transducer assembly 300 residing within the central aperture. FIG. 12E shows the front view after the potting 650, isolation and backing layers 215 are added.

[0164] In some cases, the aperture for the imaging transducer assembly interferes with the annular array pattern, creating discontinuous annular electrode elements near to the center of the annular array. FIG. 13A shows the therapeutic ultrasound transducer assembly 200 (an example case with an 8 mm diameter) with partial kerfs 270 and an example therapy element 700 shown as shaded. These elements can be joined to regain the active therapy area.

[0165] FIG. 13B illustrates one example implementation for connecting the segmented annular electrodes. A partial ring-shaped PCBs 720 with traces (not shown in the figure) is used to route the electrical connections to each quadrant. A backing 725 (for example, as shown in FIG. 3E) can be applied under the partial ring-shaped PCB prior to wire bonding to the elements as shown at 730. The remaining portion of the array can be coated with the electrical isolation layer and backed as previously discussed.

[0166] An alternative example solution involves the use of contact points with small (~0.5 mm square) sections of a PCB 750 with exposed pads or trace cross sections, as shown in FIG. 13C. The number of pads/traces per PCB segment corresponds to the number of elements that are divided by the aperture. The sections of PCB can be bonded to the annular, for example, near three inner corners of the annular array. Jumper connections 755 can be made from one section of the element to the PCB section to the next section of the element. The electrical connection could be completed with a wire bond. Using this approach, the electrical connections to the PCB would be completed from a single area as described.

EXAMPLES

[0167] The following examples are presented to enable those skilled in the art to understand and to practice embodiments of the present disclosure. They should not be considered as a limitation on the scope of the disclosure, but merely as being illustrative and representative thereof.

[0168] FIGS. 14-16 show photographs of various therapeutic devices fabricated according to the embodiments disclosed above.

[0169] FIG. 14 shows the detailed assembly of an example side looking therapy array, focusing on the electrical interconnection. FIG. 14a shows the array and interconnect PCB mounted co-planar to each other. FIG. 14b shows the electrical connections between the array elements and the exposed pads on the interconnect PCB as well as the PCB used to join the segments of the elements interrupted by the hole for the imaging array. In FIG. 14c, the connections are protected by potting with loaded epoxy. FIG. 14d provides a zoomed-in view of the electrical connections prior to potting or the isolation layer application. FIG. 14e highlights a PCB section used to rejoin elements that were disconnected due to the central hole made to accommodate the imaging array to maximize the active portion of the aperture.

[0170] FIG. 15 is a photo of a side-looking therapy array with imaging array in the center. In this example the imaging array is 3.5mm wide and operates at 30MHz. The therapy array is 8mm and focuses over a range of approximately 3 mm to 8 mm. The high frequency imaging array monitors throughout the therapy treatment.

[0171] FIG. 16 highlights the process of the annular electrode patterning and alignment on the radial composite. The image on the left shows the composite structure before electrode patterning, while the image on the right displays the

structure after electrode patterning. Aligning the composite pattern with the annular array element pattern maximizes the achievable volume fraction and mechanical separation of the array elements.

[0172] The specific embodiments described above have been shown by way of example, and it should be understood that these embodiments may be susceptible to various modifications and alternative forms. It should be further understood that the claims are not intended to be limited to the particular forms disclosed, but rather to cover all modifications, equivalents, and alternatives falling within the spirit and scope of this disclosure.

CLAIMS

1. A therapeutic ultrasound system for performing tissue ablation via cavitation, the therapeutic ultrasound system comprising:

a therapeutic ultrasound transducer assembly comprising:

a piezoelectric composite layer having a proximal surface and a distal surface;

an annular array of electrodes disposed on said proximal surface of said piezoelectric composite layer;

a common electrode disposed on said distal surface of said piezoelectric composite layer;

an electrical isolation layer disposed on said annular array of electrodes on said proximal surface of said piezoelectric composite layer;

an elongate body, wherein said therapeutic ultrasound transducer assembly is supported at a location remote from a proximal end of said elongate body;

an electrical signal delivery assembly disposed along at least a portion of said elongate body, wherein said electrical signal delivery assembly is operatively connected to said therapeutic ultrasound transducer assembly such that electrodes of said annular array of electrodes are in electrical communication with respective electrical channels of said electrical signal delivery assembly, and such that said common electrode is in electrical communication with a common electrical channel of said electrical signal delivery assembly; and

control and processing circuitry operatively coupled to said therapeutic ultrasound transducer assembly through said electrical signal delivery assembly, said control and processing circuitry configured to generate electrical pulses that are delivered, through said electrical signal delivery assembly, to said annular array of

electrodes for generating focused ultrasound pulses suitable for generating cavitation in water; and

wherein a thickness of said electrical isolation layer is less than a wavelength of the focused ultrasound pulses within said electrically insulating layer; and

wherein the thickness of said electrical isolation layer and a dielectric breakdown strength of said electrical isolation layer are sufficiently high to prevent arcing, within a backing of said therapeutic ultrasound transducer assembly, among adjacent electrodes of said annular array of electrodes, during generation of the focused ultrasound pulses for cavitation.

2. The therapeutic ultrasound system according to claim 1 wherein said piezoelectric composite layer is configured such that between at least one pair of adjacent electrodes of said annular array of electrodes, an annular kerf extends from said proximal surface into said piezoelectric composite layer, and wherein an electrical insulating material forming said electrical isolation layer resides within each annular kerf.

3. The therapeutic ultrasound system according to claim 2 wherein at least one annular kerf extends from said proximal surface to said distal surface.

4. The therapeutic ultrasound system according to claim 2 wherein each annular kerf extends from said proximal surface to said distal surface.

5. The therapeutic ultrasound system according to claim 2 wherein at least one annular kerf is a partial kerf that extends from said proximal surface into said piezoelectric composite layer without extending to said distal surface.
6. The therapeutic ultrasound system according to claim 2 wherein each annular kerf is a partial kerf that extends from said proximal surface into said piezoelectric composite layer without extending to said distal surface.
7. The therapeutic ultrasound system according to claim 5 or 6 wherein said partial kerf has a depth between 5% and 95% of the thickness of said piezoelectric composite layer.
8. The therapeutic ultrasound system according to claim 5 or 6 wherein said partial kerf has a depth between 5% and 90% of the thickness of said piezoelectric composite layer.
9. The therapeutic ultrasound system according to claim 5 or 6 wherein said partial kerf has a depth between 5% and 75% of the thickness of said piezoelectric composite layer.
10. The therapeutic ultrasound system according to claim 5 or 6 wherein said partial kerf has a depth between 50% and 95% of the thickness of said piezoelectric composite layer.

11. The therapeutic ultrasound system according to claim 5 or 6 wherein said partial kerf has a depth between 50% and 90% of the thickness of said piezoelectric composite layer.

12. The therapeutic ultrasound system according to claim 5 or 6 wherein said partial kerf has a depth between 50% and 75% of the thickness of said piezoelectric composite layer.

13. The therapeutic ultrasound system according to any one of claims 2 to 12 wherein the thickness of said electrical isolation layer residing on each electrode of said annular array of electrodes exceeds a width of said annular kerf.

14. The therapeutic ultrasound system according to any one of claims 2 to 13 wherein said piezoelectric composite layer comprises an array of piezoelectric pillars embedded in a matrix, said piezoelectric pillars extending from said proximal surface to said distal surface, and wherein said piezoelectric pillars are arranged in a segmented annular array comprising a plurality of concentric arrays of piezoelectric pillars, such that each electrode of said annular array of electrodes is capable of electrically actuating one or more radially consecutive arrays of piezoelectric pillars, and such that each annular kerf is aligned with, and extends into, an annular matrix region residing between a respective pair of radially adjacent concentric arrays of piezoelectric pillars.

15. The therapeutic ultrasound system according to any one of claims 1 to 14 wherein said electrical isolation layer has a dielectric breakdown strength between 10 and 280 kV/mm.
16. The therapeutic ultrasound system according to any one of claims 1 to 15 wherein said therapeutic ultrasound transducer assembly is air-backed.
17. The therapeutic ultrasound system according to any one of claims 1 to 15 wherein said therapeutic ultrasound transducer assembly comprises a backing layer embedded with microballoons.
18. The therapeutic ultrasound system according to any one of claims 1 to 17 wherein said annular array of electrodes are defined such that a lateral inter-electrode spacing is between 20 and 80 microns.
19. The therapeutic ultrasound system according to any one of claims 1 to 17 wherein an outer diameter of said annular array of electrodes is between 10 and 25 mm and wherein a number of electrodes forming said annular array of electrodes is between 8 and 64.
20. The therapeutic ultrasound system according to claim 1 wherein said piezoelectric composite layer comprises an array of piezoelectric pillars embedded in a matrix, said piezoelectric pillars extending from said proximal surface to said distal surface, and wherein said piezoelectric pillars are arranged in a segmented annular array comprising a plurality of concentric arrays of piezoelectric pillars, such that

each electrode of said annular array of electrodes is capable of electrically actuating one or more radially consecutive arrays of piezoelectric pillars, and such that and such that each annular inter-electrode gap is aligned with an annular matrix region residing between a respective pair of radially adjacent concentric arrays of piezoelectric pillars.

21. The therapeutic ultrasound system according to any one of claims 1 to 20 wherein said electrical signal delivery assembly is operatively connected to said therapeutic ultrasound transducer assembly via a plurality of wire bonds.

22. The therapeutic ultrasound system according to claim 21 wherein each wire bond electrically connects a respective electrode of said annular array of electrodes with a corresponding conductive channel of said electrical signal delivery assembly through an aperture formed in said electrical isolation layer.

23. The therapeutic ultrasound system according to any one of claims 1 to 20 wherein said common electrode is electrically connected to said electrical signal delivery assembly via a ground ring extending along at least a portion of an outer circumferential edge of said piezoelectric composite layer.

24. The therapeutic ultrasound system according to any one of claims 1 to 20 wherein said electrical signal delivery assembly comprises a flexible printed circuit board.

25. The therapeutic ultrasound system according to claim 24 wherein said flexible printed circuit board is operatively connected to said therapeutic ultrasound transducer assembly via direct bonding of a distal region of said flexible printed circuit board to said therapeutic ultrasound transducer assembly through an aperture formed in said electrical isolation layer.

26. The therapeutic ultrasound system according to any one of claims 1 to 25 wherein the thickness of said electrical isolation layer is equal to a quarter of the wavelength of the focused ultrasound pulses within said electrical isolation layer.

27. The therapeutic ultrasound system according to any one of claims 1 to 25 wherein the thickness of said electrical isolation layer is equal to a half of the wavelength of the focused ultrasound pulses within said electrically isolation layer.

28. The therapeutic ultrasound system according to any one of claims 1 to 27 wherein said therapeutic ultrasound transducer assembly further comprises a fixed acoustic lens.

29. The therapeutic ultrasound system according to claim 28 wherein said fixed acoustic lens has a f-number between 0.5 and 3.

30. The therapeutic ultrasound system according to any one of claims 1 to 29 wherein said control and processing circuitry is configured to control said therapeutic ultrasound transducer assembly to scan the focused ultrasound pulses within an

elongate axial region residing distalward from a distal energy emitting surface of said therapeutic ultrasound transducer assembly.

31. The therapeutic ultrasound system according to claim 30 wherein said control and processing circuitry is configured to unidirectionally scan the focused ultrasound pulses within the elongate axial region.

32. The therapeutic ultrasound system according to claim 30 or 31 wherein said control and processing circuitry is configured is configured to scan the focused ultrasound pulses at a scan rate between 0.3-1.3 m/s.

33. The therapeutic ultrasound system according to any one of claims 30 to 32 further comprising an imaging transducer assembly supported by said elongate body such that a distal surface of said imaging transducer assembly resides within a central aperture defined within said therapeutic ultrasound transducer assembly, and wherein said control and processing circuitry is operatively coupled to said imaging transducer assembly through said electrical signal delivery assembly; and

wherein said control and processing circuitry is configured to control said imaging transducer assembly to acquire ultrasound image data and to process the ultrasound image data to generate one or more ultrasound images characterizing an imaging region that spatially overlaps with the elongate axial region.

34. The therapeutic ultrasound system according to claim 33 wherein said control and processing circuitry is further configured to control said therapeutic ultrasound transducer assembly and said imaging transducer assembly such that scanning of

the focused ultrasound pulses to perform line ablation is only initiated after detection of cavitation in the ultrasound images.

35. The therapeutic ultrasound system according to claim 33 or 34 wherein said control and processing circuitry is further configured to control said therapeutic ultrasound transducer assembly and said imaging transducer assembly such that collection of the ultrasound image data by said imaging transducer assembly is interleaved with delivery of the focused ultrasound pulses.

36. The therapeutic ultrasound system according to claim 35 wherein said control and processing circuitry is configured such that the ultrasound image data collected between successively generated focused ultrasound pulses represents a subset of a full image frame of a B-mode image.

37. The therapeutic ultrasound system according to claim 36 wherein said control and processing circuitry is configured such that ultrasound image data corresponding to a selected subset of a full B-mode image frame is collected before and after generation of a given focused ultrasound pulse, thereby obtaining first ultrasound image data and second ultrasound image data characterizing the selected subset of the full B-mode image frame, and wherein said control and processing circuitry is configured to process the first ultrasound image data and the second ultrasound image data to generate a subtraction image characterizing a temporal change within the selected subset of the full B-mode image frame.

38. The therapeutic ultrasound system according to claim 37 wherein said control and processing circuitry is configured to display the full B-mode image frame and to annotate the full B-mode image frame based on the subtraction image.

39. The therapeutic ultrasound system according to any one of claims 33 to 38 wherein said central aperture has a shape that results in segmentation of an inner electrode of said annular array of electrodes, and wherein the segmented portions of said inner electrode are electrically connected to facilitate actuation of the segmented portions by a single channel of said electrical signal delivery assembly.

40. A method of performing tissue ablation via cavitation, the method comprising:

bringing a distal, energy-emitting surface of a therapeutic ultrasound transducer assembly into acoustic contact with tissue, the therapeutic ultrasound transducer assembly comprising:

a piezoelectric composite layer having a proximal surface and a distal surface;

an annular array of electrodes disposed on the proximal surface of the piezoelectric composite layer;

a common electrode disposed on the distal surface of the piezoelectric composite layer;

an electrical isolation layer disposed on the annular array of electrodes on the proximal surface of the composite piezoelectric layer; and

generating and delivering electrical pulses to the annular array of electrodes to generating focused ultrasound pulses suitable for generating cavitation within a subsurface focal region;

wherein a thickness of the electrical isolation layer is less than a wavelength of the focused ultrasound pulses within the electrically isolation layer; and

wherein the thickness of the electrical isolation layer and a dielectric breakdown strength of the electrical isolation layer are sufficiently high to prevent arcing, within a backing of the therapeutic ultrasound transducer assembly, among adjacent electrodes of the annular array of electrodes, during generation of the focused ultrasound pulses for cavitation.

41. The method according to claim 40 further comprising controlling a delay between the electrical pulses delivered to the annular array of electrodes such the subsurface focal region is scanned to perform line ablation of the tissue.

42. A therapeutic ultrasound device for performing tissue ablation via cavitation, the therapeutic ultrasound device comprising:

a therapeutic ultrasound transducer assembly comprising:

a piezoelectric composite layer having a proximal surface and a distal surface;

an annular array of electrodes disposed on said proximal surface of said piezoelectric composite layer;

a common electrode disposed on said distal surface of said piezoelectric composite layer;

an electrical isolation layer disposed on said annular array of electrodes on said proximal surface of said piezoelectric composite layer;

an elongate body, wherein said therapeutic ultrasound transducer assembly is supported at a location remote from a proximal end of said elongate body;

wherein said piezoelectric composite layer is configured such that between at least one pair of adjacent electrodes of said annular array of electrodes, an annular kerf extends from said proximal surface into said piezoelectric composite layer, and wherein an electrical isolation material forming said electrical isolation layer resides within each annular kerf.

43. The therapeutic ultrasound device according to claim 42 wherein at least one annular kerf is a partial kerf that extends from said proximal surface into said piezoelectric composite layer without extending to said distal surface.