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HAL Authorization

Lithium niobate transducers for MRI-guided ultrasonic microsurgery

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Abstract

Focused ultrasound surgery (FUS) is usually based on frequencies below 5 MHz, typically around 1 MHz. Whilst this allows good penetration into tissue, it limits the minimum lesion dimensions that can be achieved. In the study reported here, we investigate devices to allow FUS at much higher frequencies, therefore in principle reducing the minimum lesion dimensions. **Furthermore, FUS can produce deep-sub-millimetre demarcation between viable and necrosed tissue; high frequency devices may allow this to be exploited in superficial applications which may include dermatology, ophthalmology, treatment of the vascular system, and treatment of early dysplasia in epithelial tissue. In this paper** we explain the methodology we have used to build high-frequency high-intensity transducers using Y-36° cut lithium niobate. This material was chosen as its low losses give it the potential to allow very high-frequency operation at harmonics of the fundamental operating frequency. A range of single element transducers with a centre frequency between 6.6 MHz and 20.0 MHz were built and the transducers' efficiency and acoustic power output were measured. A focused 6.6-MHz transducer was built with multiple elements operating together and tested using an ultrasound phantom and MRI scans. It was shown to increase phantom temperature by 32°C in a localised area of 2.5 mm × 3.4 mm in the plane of the MRI scan. Tests on poultry were also performed and shown to create lesions of similar dimensions. This study therefore demonstrates that it is feasible to produce high-frequency transducers capable of high-resolution FUS using lithium niobate.

Lithium niobate transducers for MRI-guided ultrasonic microsurgery

I. INTRODUCTION

Focused ultrasound surgery (FUS) is based on the application of high intensity focused ultrasound (HIFU) to heat tissue to a temperature that causes protein denaturation and coagulative necrosis [1]. The required temperature to generate lesions is between 56–60°C [2], [3]. The frequency of ultrasound used is generally around 1 MHz, generating characteristic ellipsoidal lesions on the order of 1 cm in length. Higher frequencies in the region of 4 MHz are also used where more precise treatment is needed, for example in the prostate where tumour sizes may be < 1 mm long [4]. At such frequencies, conventional piezoelectric transducers can be used, based on hard piezoceramic with high drive capability. The use of FUS is increasing as a non-invasive form of surgery and the need for even higher precision is increasing for example for use in aesthetic facial rejuvenation [5], ultrasonic thrombolysis [6] and treatment of malignant disease in breast [7] whilst helping maintain a patient's quality of life when compared to invasive surgery [8].

In this paper, we consider the type of device that could be used to apply HIFU at much higher frequencies, with our research ultimately targeting 50–100 MHz. A difficulty with FUS is to necrose a clinically significant volume quickly enough for financial viability within modern medical treatment systems. However, the exquisite precision of necrosis possible with HIFU must also be recognised. The interface region may be as thin as just a few cells, with deep sub-millimetre dimensions, offering interesting possibilities for precise intervention. These may include treatment of dermatological and ophthalmological conditions, of the walls of the digestive system, for example relating to pre-cancerous tissue dysplasia, and of the walls of the vascular system. The superficial nature of these applications, if necessary handled with intraluminal and intravascular devices, significantly eases the problem of penetration depth at high frequency. The formats of the devices we report here are not suitable for these applications directly but reports on transurethral and endocavitary devices [9], [10] point the way forward. In all cases, we would predict adoption of high frequency FUS for superficial treatments of small overall volumes. As the attenuation coefficient of human tissue has a near linear dependence on frequency [11] greater intensity fields are necessary at higher frequencies in order to be able to penetrate deep enough into human tissue even for superficial applications. Piezoceramic is expected to be incapable of sustaining sufficiently high-power operation at such frequencies because of mechanical fragility, losses, and electrical breakdown. Instead, we have based our investigation on lithium niobate, LiNbO_3 [12]. As a single crystal, this can be thinned easily without disintegrating

54 unlike ceramics. In addition LiNbO_3 can sustain high electric fields, and its low losses allow the use of harmonics.
 55 The use of single crystals and LiNbO_3 for high frequency ultrasound has been explored before, but only for
 56 high-resolution imaging [13], [14].

57 II. METHODOLOGY

58 A. *Lithium niobate*

59 As it was expected that piezoceramics would be unable to produce HIFU at high frequencies and harmonics
 60 due to de-poling or cracking, we have explored Y-36° LiNbO_3 . As well as its basic advantages, it has a high
 61 resonant frequency of 3.3 MHz mm^{-1} , thus allowing for thicker elements at higher frequencies for cost effective
 62 manufacturing compared to piezoceramics, and it has the highest electromechanical coupling coefficient compared
 63 to other LiNbO_3 cuts [15].

64 B. *Transducer manufacture*

65 Three transducer designs were prepared as shown in Fig.1: unfocused single elements with 17 mm square LiNbO_3
 66 plates (xDucer 1); a 2D faceted bowl with three pentagonal and four hexagonal plates to mimic a spherically-focused
 67 device (xDucer2); and a 1D faceted cylindrical section with five, $9 \times 30(\text{mm})^2$ rectangular plates to mimic a
 68 cylindrically focused device (xDucer3). The equivalent radii of curvature for xDucer2 and xDucer3 were 50 mm
 69 and 30 mm respectively. **The devices were manufactured as prototypes using a proof-of-concept approach; this**
 70 **limited their reliability and hence sometimes the completeness of the data that was recorded. Nevertheless, the**
 71 **manufacturing techniques and the principles of the devices could be taken forward to more robust examples.**

72 To prepare the plates for each transducer, Y-36° cut, 3-inch diameter, 0.5-mm thick LiNbO_3 wafers (Boston
 73 Piezo-Optics, Inc, Boston, MA) were obtained, polished on one side and lapped on the other. Figure 1 shows the
 74 position of each element from each wafer for each of the three transducer designs. Separation of the plates was
 75 performed with a programmable APD1 saw (Logitech Ltd, Glasgow, UK) with a spindle speed of 2900 rpm and a
 76 feed rate of 0.160 mm s^{-1} .

77 For the xDucer 1 devices, the 11 square elements cut from a single wafer were lapped individually in steps of
 78 $30 \mu\text{m}$ starting from $500 \mu\text{m}$ down to $200 \mu\text{m}$ using a PM5 precision lapping and polishing machine (Logitech Ltd,
 79 Glasgow, UK). The force applied during lapping was adjusted depending on the sample size, typically in the range
 80 $400\text{--}900 \text{ g}$. A slurry of $20\text{-}\mu\text{m}$ calcined Al_2O_3 powder in water was used as abrasive. Once the elements reached
 81 within $25 \mu\text{m}$ of the target thickness, $9\text{-}\mu\text{m}$ calcined Al_2O_3 powder was used to avoid scratching. The lapping
 82 machine was programmed to ensure maximum flatness.

83 The true thickness of the samples was measured and verified at regular intervals using a CG-10 Precision
 84 Electronic Measurement System (Logitech Ltd, Glasgow, UK). Once each element was flat at the desired thickness,

85 it was removed from the glass lapping plate and re-measured to verify the thickness. The elements were continuously
86 checked using a stereo microscope for flaws which could act to concentrate stress and lead to cracking.

87 An electrode was hand painted on to the lapped side using ELECTRODAG 1415 silver paint (Acheson Colloids
88 BV, Scheemda, Netherlands). Excess paint around the edges was removed using a scalpel and acetone. The polished
89 side of each element was then attached to the adhesive side of Adwill D-210 UV tape (Lintec of America, Inc.,
90 Phoenix, AZ). RG174A/U 50 Ω coaxial cable was used connected to the plates with Ag-loaded conductive epoxy,
91 curing taking place at 80°C for 10 min.

92 For xDucer 1 devices, Cu tubing with an internal diameter of 28 mm was cut into lengths of 50 mm and placed
93 over the LiNbO₃ plates onto the adhesive side of the UV tape. Epoxy was then introduced around the sides of the
94 LiNbO₃ plate to join it to the Cu tube. The case for the 2D faceted array, xDucer 2, had a height of 75 mm, outer
95 diameter of 70 mm and a wall thickness of 2 mm. The case for the curvilinear array, xDucer 3, had a height of
96 75 mm, outer diameter of 50 mm and wall thickness of 1.5 mm. For operation within a magnetic resonance imaging
97 (MRI) system, the cases of xDucer 2, and 3 were polyvinyl chloride (PVC) coated with a thin layer of Ag paint so
98 they could be used as the electrical ground connections to the front face of each transducer.

99 To support the fragile LiNbO₃, Epofix resin (Struers, Ballerup, Denmark) was mixed with S38 glass microballoons
100 (Lawrence Industries, Tamworth, UK) with a weight ratio of 65 : 35. The microballoon-epoxy mix was poured into
101 the transducer shell. The xDucer 1 devices were filled to a depth of 16 mm whereas xDucers 2 and 3 were filled to
102 a depth of 22 mm. It was found that the acoustic output with the backing material was reduced by 5 % compared
103 to devices made without backing. The backing was left to cure at room temperature. The earth cable was attached
104 to the shell using conductive Ag epoxy. The UV tape was then exposed to UV light and peeled off. Any remaining
105 adhesive residue was removed manually.

106 The exposed LiNbO₃ was cleaned using solvent then the front surfaces and part of each case were painted
107 with Ag paint. The cases were then filled with 5368 silicon (Henkel AG & Co. KGaA, Düsseldorf, Germany) to
108 waterproof the cables and 50- Ω BNC RG-174 plugs were connected to the coaxial cables.

109 *C. Acoustic pressure*

110 Each transducer was driven by a continuous wave at its fundamental frequency, generated by an AFG3102
111 waveform generator (Tektronix, Everett, WA). The signal was passed through a -20-dB attenuator before being
112 used as the input to a power amplifier. The single element transducers were tested using a 3100LA, +55-dB
113 RF amplifier (Electronics & Innovation, Rochester, NY). To test xDucer 2, the pentagonal elements were linked
114 and driven by a 2100L, +50-dB RF amplifier (Electronics & Innovation, Rochester, NY) and the hexagonal
115 elements were linked and driven by the 3100LA amplifier. This was done to give the ability to improve on the

116 alignment of the multiple sound fields by shifting the phase of each group of elements. The pressures outputs
117 were measured using a calibrated fibre-optic hydrophone (Precision Acoustics, Dorchester, UK) and verified using
118 an HGL-0200 piezoelectric hydrophone (Onda, Sunnyvale, CA). The curvilinear transducer, (xDucer 3), was tested
119 using a 150A250, 150W RF amplifier (Amplifier Research, Souderton, PA). The acoustic pressure was measured at
120 the acoustic focus, 13 mm from the transducer face using the HGL-0200 hydrophone. **The maximum peak-to-peak**
121 **acoustic pressure was defined at the acoustic focus of each transducer in a $25 \times 17 \times 12$ (cm)³, water filled, low-density**
122 **polyethylene container. For all measurements the free field was manually scanned to locate the acoustic focus of**
123 **each transducer using an M-652 *x-y-z* micro-translation stage (Newport, Didcot, Oxfordshire, UK).**

124 *D. LiNbO₃ Properties*

125 Data available for the properties of Y-36° LiNbO₃ were found to be limited and incomplete in the literature so
126 values for one-dimensional simulation were obtained using PRAP version 2.2 software (TASI Technical Software
127 Inc, Ontario, Canada) using electrical impedance data from a plate measured with a 4395A impedance analyser
128 (Agilent, Santa Clara, CA). Table I shows the measured properties for Y-36° cut LiNbO₃, with figures for Z-cut
129 material shown for comparison. The resonance frequencies of the transducers were also measured using the same
130 impedance analyser.

131 *E. Acoustic radiation*

132 The acoustic radiation force output of the transducers was measured using an EMS Model 67 ultrasound radiation
133 force balance (EMS Physio Ltd, Wantage, UK). The transducers were placed within 20 mm of the surface of the
134 ultrasound absorber in the balance to ensure that the total radiated flux was incident on it. The output voltage of
135 the waveform generator was increased and the amplifier forward and reflected power and the transducer acoustic
136 power were recorded.

137 *F. MRI temperature measurements*

138 MRI guidance is used for FUS [16] as it allows precise targeting of the HIFU field and direct temperature
139 measurement at the focus. For MRI-guided focused ultrasound surgery (MRgFUS) tests in the present work, xDucer 3
140 and a DQA Gel Phantom (ATS Laboratories, Bridgeport, CT) placed in a cylindrical perspex chamber filled with
141 tap water were placed in a GE Signa HDx 1.5T MRI system (GE Healthcare, Waukesha, WI). A gradient echo
142 planar image (EPI) was recorded with TE = 17.0 ms, ER = 230.0 ms and BW at 62.0 kHz to capture the temperature
143 increase of the phantom. The curvilinear transducer was turned on at t = 0 s with a pk-pk input voltage of 101 V,
144 equivalent to 8 W acoustic power and 32 W forward electrical power. The transducer was turned off after 55 s. The
145 size of the acoustic focus was determined by the area heated above the surrounding ambient temperature.

146 *G. Tissue sonication*

147 To test the effect of the HIFU field on tissue, two boneless, skinless chicken breasts (Tesco, Cheshunt, UK) were
 148 cut into 12, $2 \times 2 \times 8$ (cm)³ strips. The strips were placed in a $10 \times 15 \times 5$ (cm)³ container filled with tap water at
 149 room temperature and xDucer3 was clamped vertically with the acoustic focus on the surface of the tissue. Each
 150 sample was sonicated once. For tests beneath the surface of the tissue the transducer was lowered closer to the
 151 chicken. In all experiments it was ensured that the transducer surface was not in contact with the tissue. The chicken
 152 breast was sonicated using the same settings as in the MRgFUS measurements. Sonication time was increased in
 153 steps of 10 s. Lesion sizes were measured manually using ImageJ (National Institutes of Health, Bethesda, MD).

154

III. RESULTS AND DISCUSSION

155 *A. LiNbO₃ Properties*

156 The resonant frequency and third harmonic of the xDucer1 devices made with different LiNbO₃ thicknesses are
 157 compared to one-dimensional modelling (ODM) for both Z-cut and Y-36° cut LiNbO₃ in Fig. 2. Although the Z-cut
 158 material gives a higher frequency for a given material thickness, other key properties such as d_{33} and k_T are much
 159 lower, hence the preference for Y-36° cut material.

160 *B. Acoustic pressure*

161 The acoustic pressures generated by the three transducers is given in Table II. The xDucer2 device generated a
 162 modulated sound field. It was possible to improve the output and reduce the envelope frequency of the modulation
 163 by shifting the phase of each set of elements. The lowest modulation frequency of 550 kHz was achieved with a
 164 phase difference of 12°. **The modulated sound field was generated as a result of multiple interacting sound fields.**
 165 **This was due to misaligned elements in our proof of concept devices. To cancel out the modulation, the phase of**
 166 **each element would have to be controlled independently, or the faceted bowl must be manufactured to tolerances**
 167 **at $< \frac{1}{4}\lambda$ of the operating frequency. Higher harmonics of xDucer2 were not tested due to low reproducibility. The**
 168 **acoustic pressures generated were limited by the maximum outputs of the RF amplifiers used. From the fundamental**
 169 **pressure measurements, the design of xDucer2 would be the most logical to pursue.**

170 *C. Acoustic Radiation Power*

171 The acoustic power generated by the xDucer1 devices is shown in Fig. 3. Efficiency for these devices was found
 172 to be $33 \pm 5\%$ throughout the frequency spectrum. **Sustained operation of up to 5 minutes was possible without**
 173 **damaging the transducers at the resonance frequency, 3rd and 5th harmonic.** The output power is seen to drop as
 174 the element thickness decreases. This is due to the increasing electrical impedance mismatch shown in Fig. 4. For

175 maximum output power the impedance magnitude and phase should be 50Ω and 0° respectively. As the element
 176 thickness decreases the impedance magnitude also decreases. This is seen for both the fundamental resonance and
 177 3rd harmonic. The phase of the 3rd harmonic increases with element thickness due to the inductance generated
 178 by the cable. Factors such as amount of Ag-loaded epoxy and cable length were seen to affect the impedance of
 179 the transducers [17]. The xDucer3 device had an efficiency of $25\pm 2\%$ whereas a commercial 3.28-MHz, 58-mm
 180 diameter HIFU transducer made with piezoceramic (Precision Acoustics, Dorchester, UK) was found to have an
 181 efficiency of $20\pm 1\%$.

182 *D. MRI temperature measurements*

183 Figure 5 is an MRI image of xDucer3 positioned on the DQA gel phantom. Figure 6 shows the area heated by
 184 xDucer3 in the plane of the MRI scan, aligned with its focus. The surface area of heating after 55 s of sonication
 185 was $2.5\text{ mm} \times 3.4\text{ mm}$. Within 31 s the temperature in the acoustic focus of the transducer had increased 18°C above
 186 ambient to a temperature of 38°C . A peak temperature of 52°C was reached after 55 s of sonication, 32°C above
 187 ambient, as shown in Fig. 7. The acoustic intensity at the focus of the transducer was equivalent to 163 Wcm^{-2} .
 188 After sonication, cavitation related bubbles formed on the front surface of the transducer shown in Fig. 5. **These**
 189 **measurements demonstrate the viability of MRI ultrasonically-elevated temperature measurement with the devices**
 190 **reported here; it should be noted that at the 3rd and 5th harmonics (21.1 MHz and 35.2 MHz respectively), the**
 191 **ultrasound wavelength is substantially smaller than the spatial resolution of the 1.5T MRI system.**

192 *E. Tissue sonication*

193 Figure 8 shows the effect of xDucer3 on chicken breast. An increased sonication time was necessary in order
 194 to induce a lesion beneath the tissue surface, of similar size to the MRI measured results. This is partially due to
 195 scattering and gas content in the tissue. The lesions dimensions after 90 s of sonication at 6.6 MHz matched those
 196 measured with the MRI. In Fig. 8, the chicken has been sliced open to locate the region of sonication. The lesion
 197 was formed **60 mm** beneath the surface of the tissue without affecting the upper tissue boundary or the surrounding
 198 tissue. In further tests, after two minutes continuous sonication, when the transducer surface was in contact with
 199 the chicken tissue, sufficient heat was generated to cause protein denaturation on the chicken surface. **Thus, in a**
 200 **practical (clinical) setting, contact with tissue would have to be avoided. Impedance matching and better-attached**
 201 **electrodes might reduce element heating; water-cooling of commercial FUS transducers is also common.**

202 IV. CONCLUSIONS

203 In conclusion, we have shown that it is feasible to manufacture high-frequency, high-intensity, focused ultrasound
 204 transducers based on $Y-36^\circ$ cut LiNbO_3 . In a range of tests, we have demonstrated operating frequencies up to

205 more than 50 MHz using the 3rd harmonic of 200- μ m thick LiNbO₃, focal pressures of 4 MPa at 35 MHz, and
206 MI = 4.7 at 6.6 MHz. Two of the devices made, with faceted bowl and faceted cylindrical sections respectively, were
207 designed to be operated under MRI guidance. We have shown that this design was successful and have used one
208 of the devices to increase the temperature within a gel phantom, measured with MRI, to more than 50°C following
209 sonication of 55 s with an equivalent acoustic intensity of 163 Wcm⁻². We also created lesions within chicken tissue
210 after 90 s sonication.

211 Several aspects can be addressed in order to improve the performance of the transducers. At high acoustic
212 intensities the Ag-paint electrode was damaged. This is attributed to air pockets trapped between the electrode and
213 the LiNbO₃. The use of thin film Cr-Au, Ti-Pt or Al electrodes would be better acoustically and electrically as
214 electrodes compared to conductive Ag paint [18]. The cases of the devices for MRI guidance were made with PVC
215 tubing coated with Ag paint; using an alternative such as Cu-epoxy composite [19] would aid manufacture and
216 reliability and assist with shielding. The thin LiNbO₃ piezoelectric elements were supported by microballoon-filled
217 epoxy backing; this reduced the transducer output thus necessitating exploration of support materials with a lower
218 acoustic impedance or other methods to support the plates. Finally, electrical impedance matching was neglected.
219 However, as frequency increases electrical impedance decreases and sustained operation would be enhanced by
220 electrical impedance matching.

221 V. ACKNOWLEDGMENT

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LIST OF FIGURES

264
265
266
267
268
269
270
271
272
273
274
275
276
277
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1 Transducer manufacturing: (a) position of plates in single wafer used for each transducer, (b) dimensions of plates for each transducer, (c) computer-aided design representation of transducers, and (d) completed transducers. 11

2 Resonance frequency and third harmonic as a function of element thickness for single-element LiNbO₃ microballoon-backed transducers. The diamonds indicate the z-cut LiNbO₃ simulations, the circles indicate the experimental measurements, and the five-point stars indicate the Y-36° LiNbO₃ cut simulations. The grey data points show the 3rd harmonic. The error bars indicate the confidence interval for the LiNbO₃ thickness. 12

3 Acoustic power as a function of transducer input voltage for 17×17(mm)² single element LiNbO₃ transducers. 13

4 Minimum impedance magnitude and equivalent phase as a function of element thickness for single-element LiNbO₃ microballoon backed transducers. The black diamonds indicate the impedance magnitude whereas the grey circles indicate the phase. 14

5 (a) MRI side view of sonication setup where brightness indicates water content. Image is rotated 90° anticlockwise from true position. (b) Schematic representation of sonication setup (i) perspex water bath, (ii) xDucer 3, (iii) water, (iv) DQA gel phantom. The transducer generates negligible artefacts in the MRI image. The minor artefacts generated by the silver paint and coaxial cable are not in the acoustic path and thus do not affect the image or temperature measurement. 15

6 MRI view of sonication area. The focal region had a size of 2.5×3.4(mm)². The green areas represents pixels of equal temperature, the blue areas represent the acoustic field, whereas the red areas represent pixels of temperature > 70°C. The orange cross indicates the temperature measurement marker. . . . 16

7 Temperature increase as a function of time for xDucer 3 at the acoustic focus in ultrasonic phantom measured using MRI. The black diamonds indicates the temperature of the selected pixel, whereas the grey circles indicate average temperature of the eight surrounding pixels. 17

8 Photograph showing lesion formed on chicken tissue after 90 s sonication using xDucer 3. The acoustic focus was beneath tissue surface. The direction of acoustic propagation is into the image as indicated by the arrows. 18

LIST OF TABLES

292

293	I	Mechanical and piezoelectric properties for lithium niobate	19
294	II	Peak-to-peak acoustic pressures generated by xDucer 1, xDucer 2 and xDucer 3 at their fundamental	
295		frequency, 3 rd and 5 th harmonic.	20

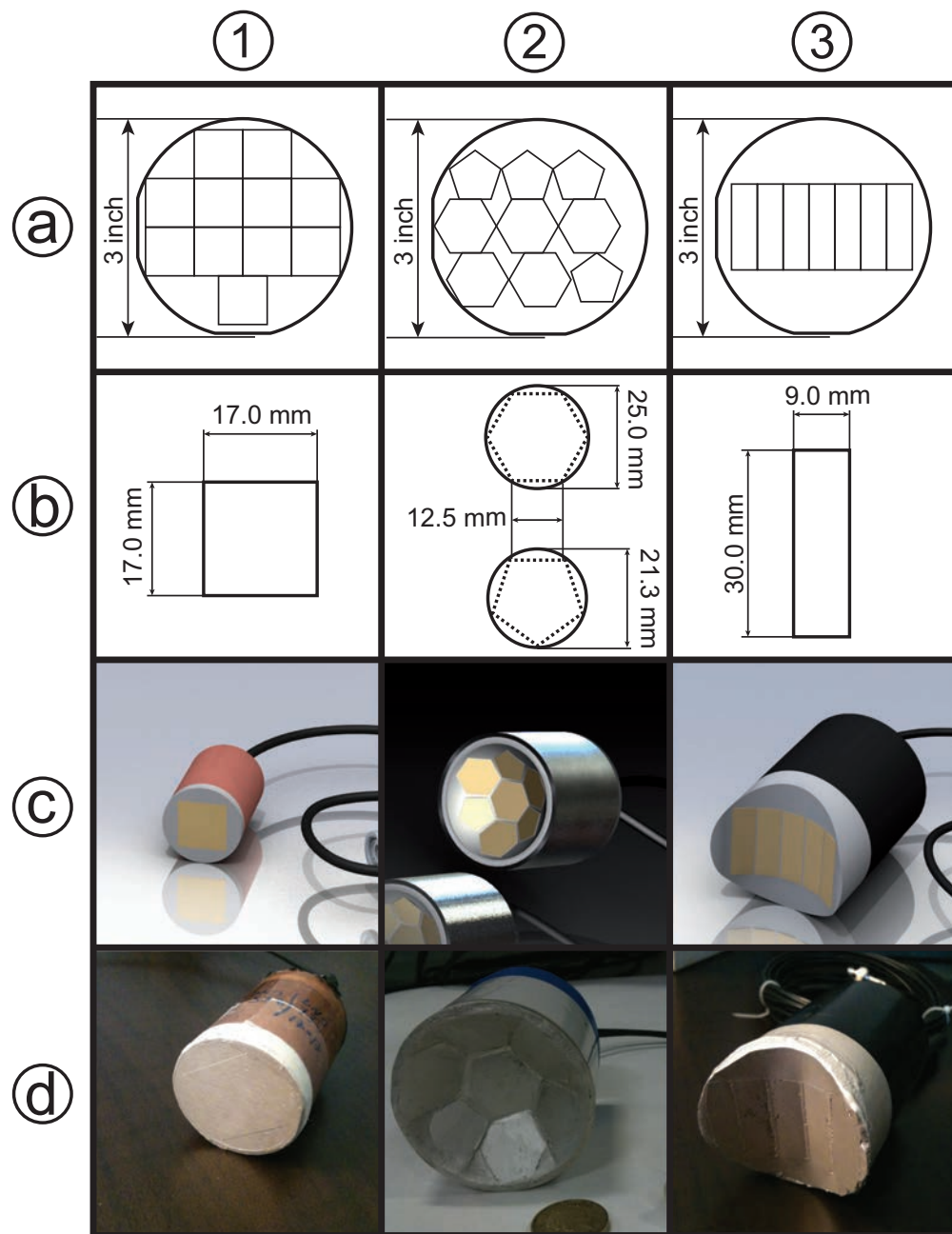


Fig. 1. Transducer manufacturing: (a) position of plates in single wafer used for each transducer, (b) dimensions of plates for each transducer, (c) computer-aided design representation of transducers, and (d) completed transducers.

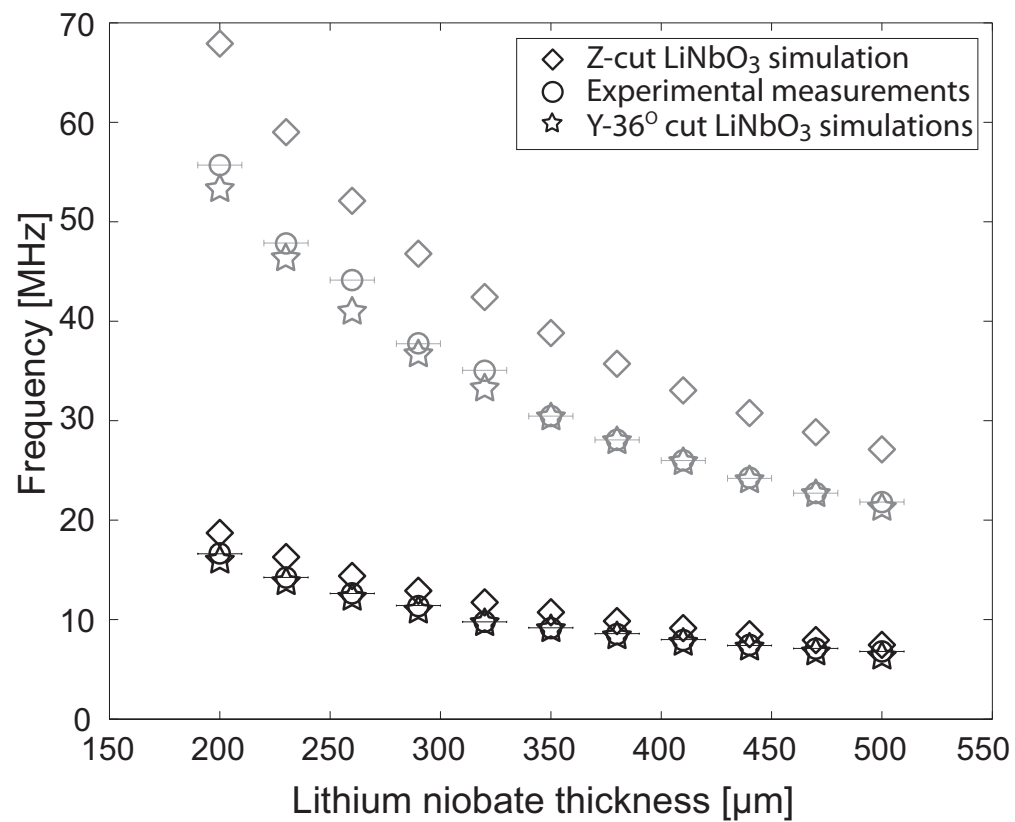


Fig. 2. Resonance frequency and third harmonic as a function of element thickness for single-element LiNbO_3 microballoon-backed transducers. The diamonds indicate the z-cut LiNbO_3 simulations, the circles indicate the experimental measurements, and the five-point stars indicate the Y- 36° LiNbO_3 cut simulations. The grey data points show the 3rd harmonic. The error bars indicate the confidence interval for the LiNbO_3 thickness.

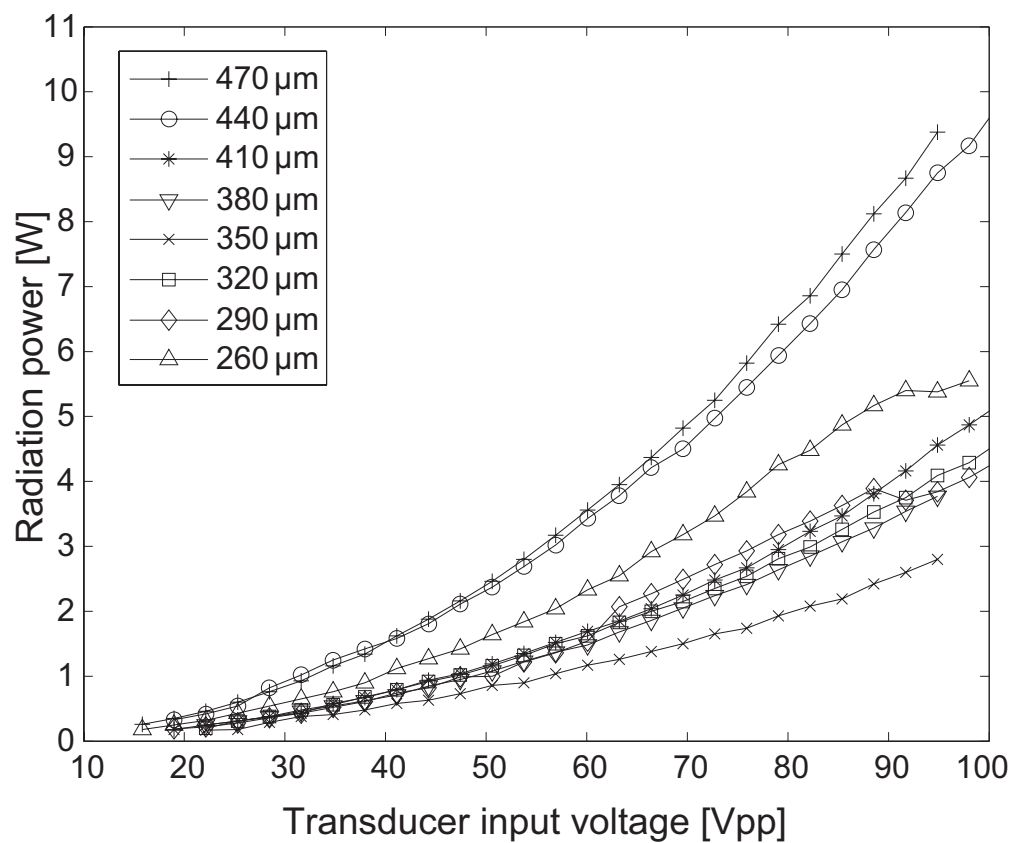


Fig. 3. Acoustic power as a function of transducer input voltage for 17×17 (mm)² single element LiNbO₃ transducers.

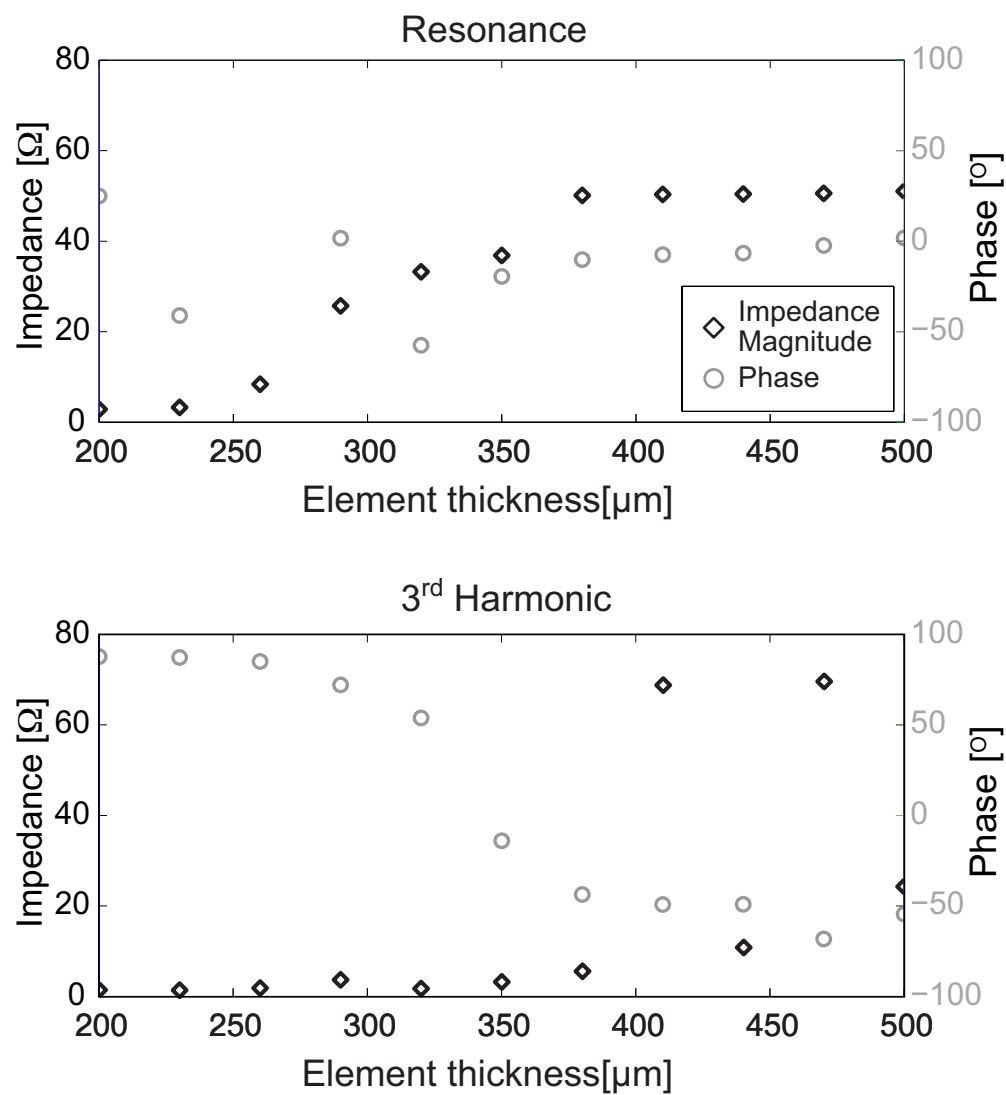


Fig. 4. Minimum impedance magnitude and equivalent phase as a function of element thickness for single-element LiNbO₃ microballoon backed transducers. The black diamonds indicate the impedance magnitude whereas the grey circles indicate the phase.

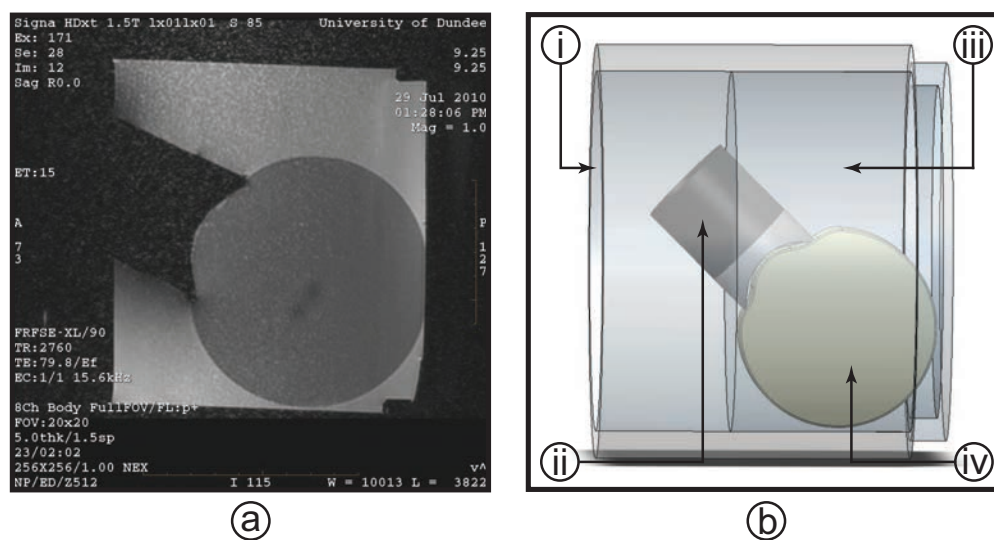


Fig. 5. (a) MRI side view of sonication setup where brightness indicates water content. Image is rotated 90° anticlockwise from true position. (b) Schematic representation of sonication setup (i) perspex water bath, (ii) xDucer 3, (iii) water, (iv) DQA gel phantom. The transducer generates negligible artefacts in the MRI image. The minor artefacts generated by the silver paint and coaxial cable are not in the acoustic path and thus do not affect the image or temperature measurement.

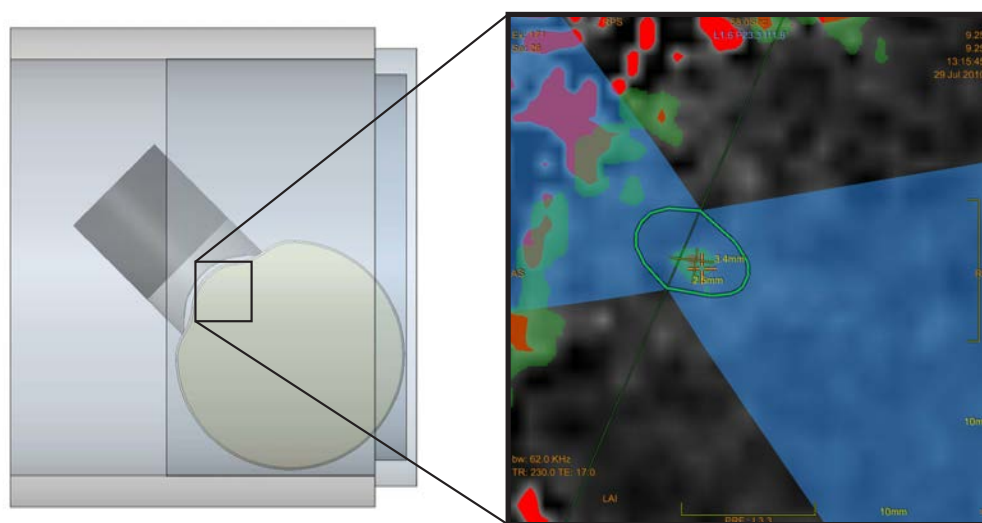


Fig. 6. MRI view of sonication area. The focal region had a size of $2.5 \times 3.4 \text{ (mm)}^2$. The green areas represents pixels of equal temperature, the blue areas represent the acoustic field, whereas the red areas represent pixels of temperature $> 70^\circ \text{C}$. The orange cross indicates the temperature measurement marker.

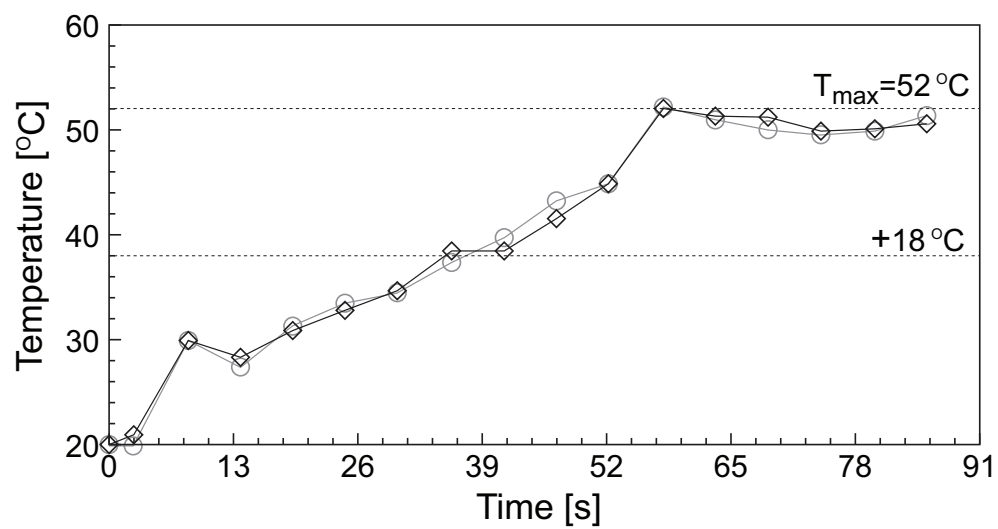


Fig. 7. Temperature increase as a function of time for xDucer3 at the acoustic focus in ultrasonic phantom measured using MRI. The black diamonds indicates the temperature of the selected pixel, whereas the grey circles indicate average temperature of the eight surrounding pixels.

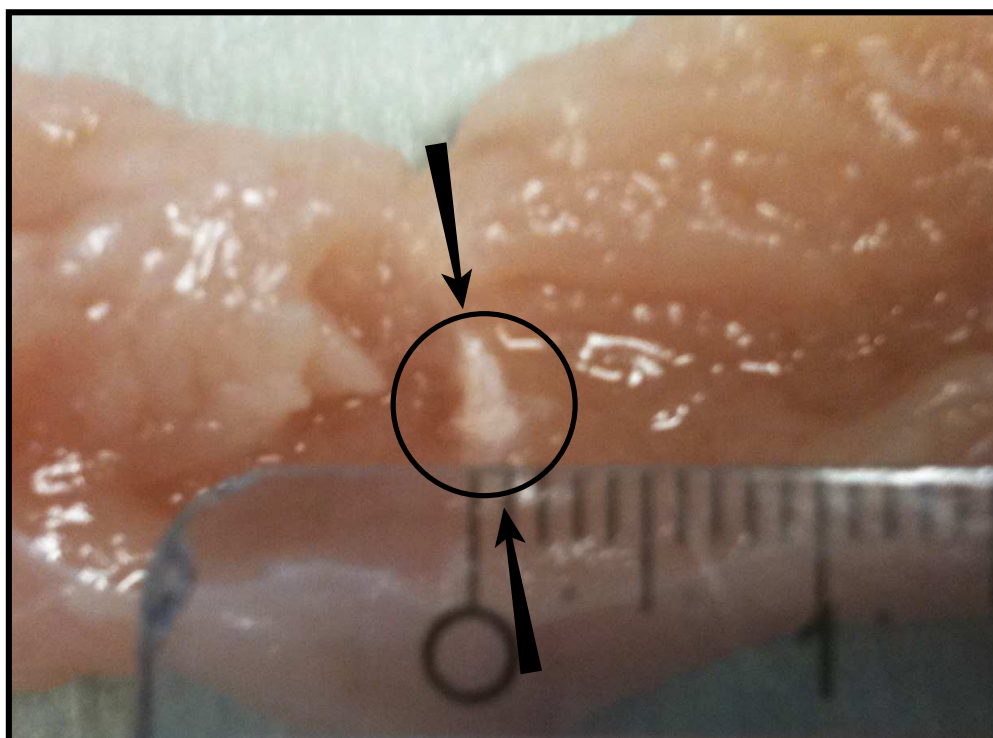


Fig. 8. Photograph showing lesion formed on chicken tissue after 90 s sonication using xDucer 3. The acoustic focus was beneath tissue surface. The direction of acoustic propagation is into the image as indicated by the arrows.

Property	Parameter (unit)	Z-cut	Y-36° cut
Density	ρ (kg m ⁻³)	4650	4650
Thickness mode velocity	v (m s ⁻¹)	7380	7260
Acoustic impedance	Z (MRayl)	34.2	33.8
Elastic constants	c_{11}^E (Nm ⁻²) $\times 10^9$	203	185
	c_{33}^E (Nm ⁻²) $\times 10^9$	245	185
	c_{33}^D (Nm ⁻²) $\times 10^9$	252	245
Dielectric constants	$\epsilon_{33}^T/\epsilon_0$	29.8	41.9
	$\epsilon_{33}^S/\epsilon_0$	25.7	37.6
Piezoelectric constants	e_{33} (C m ⁻²)	1.3	4.47
	h_{33} (V m ⁻¹) $\times 10^9$	5.71	13.4
	d_{33} (m V ⁻¹) $\times 10^{-12}$	5.15	18.2
Electromechanical coupling coefficient	k_T	0.171	0.495

TABLE I
MECHANICAL AND PIEZOELECTRIC PROPERTIES FOR LITHIUM NIOBATE

	Frequency (MHz)	Wavelength (μm)	Peak-to-peak acoustic pressure (MPa) Equivalent mechanical index [MI]		
			xDucer 1	xDucer 2	xDucer 3
Fundamental frequency	6.6	226	14.1 [2.7]	24.3 [4.7]	16.7 [3.3]
3 rd harmonic	21.1	77	6.6 [0.7]	-	10.5 [1.1]
5 th harmonic	35.2	44	4.3 [0.4]	-	5.4 [0.5]

TABLE II
PEAK-TO-PEAK ACOUSTIC PRESSURES GENERATED BY xDUCER 1, xDUCER 2 AND xDUCER 3 AT THEIR FUNDAMENTAL FREQUENCY, 3rd
AND 5th HARMONIC.

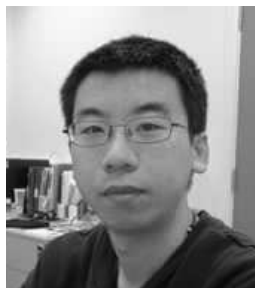
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VI. BIOSKETCHES



297 Spiros Kotopoulos (S'08) was born in Athens, Greece, in 1987. He received a first class B.Eng.(Hons) in
298 Mechanical Engineering from The University of Hull, England, in 2008. Mr. Kotopoulos is a member of the U.K.
299 Institute of Acoustics. He is currently pursuing a Ph.D. under the supervision of Professor Dr. Michiel Postema at
300 The University of Hull. His research interests include high-speed photography, microscopy, ultrasound transducer
301 manufacture and sonoporation.

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303 Han Wang was born in Tianjin, China, in 1986. He received his B.Eng. in Electronic Science and Technology
304 from Tianjin University, China, in 2009. He then gained an MSc with Distinction in Biomedical Engineering from
305 University of Dundee, Scotland, UK, in 2010. Mr. Han Wang is currently pursuing a Ph.D. under the supervision
306 of Dr. Christine E. M. Démoré at Institute for Medical Science and Technology, University of Dundee. His current
307 research interests are in ultrasonic device development for life sciences and electronics instrumentation for ultrasound
308 devices and system.

309



310 Sandy Cochran is Professor of Biophysical Science and Engineering, Deputy Director and Team Leader of
311 Medical Ultrasound in the Institute for Medical Science and Technology, University of Dundee, Scotland. He
312 received the B.Sc. degree in electronics and computing in 1986, the Ph.D. degree for work on ultrasonic arrays
313 in 1990, and the MBA for an investigation of universities as part of an enterprise network in 2001, all from the
314 University of Strathclyde. His present research interests are focused on medical ultrasound devices, with applications
315 in diagnosis, image-guidance and therapy. He also maintains interests in relevant materials, systems design and
316 applications issues, and in underwater sonar and industrial processing for medical and life sciences applications.
317 He has worked extensively with industry internationally and collaborates with several academic research groups.
318 His research income since 2009 as Principal Investigator has totalled more than \$4.5M. Outside work, he divides
319 his time between his homes in Dundee and Glasgow.

320



321 Michiel Postema (A'01–S'02–M'05–SM'08) was born in Brederwiede, Netherlands, in 1973. He received an
322 M.Sc. in Geophysics from Utrecht University, Netherlands, in 1996 and a Doctorate in the Physics of Fluids from
323 the University of Twente, Enschede, Netherlands, in 2004. Following a postdoctoral position at Ruhr-Universität
324 Bochum, Germany, between 2005 and 2007, he became Lecturer in Engineering at The University of Hull, England.
325 He was granted an Emmy Noether Research Group at Ruhr-Universität Bochum in 2009 and a Visiting Professorship
326 at the University of Orléans, France, in 2010. In the same year, he obtained the Chair in Experimental Acoustics at
327 the University of Bergen, Norway. Professor Dr. Postema is Associate Editor of Applied Acoustics (Elsevier) and

328 member of the editorial board of Bubble Science, Engineering and Technology (Maney). He is also Fellow of the UK
329 Institute of Acoustics (IOA), member of the IOA Research Coordination Committee and member of the Scientific
330 Committee of Revue des Sciences et Technologie (Université de Batna). He has written more than 70 scientific
331 publications on medical acoustics and cavitation, including 40 first-author papers and five co-authored textbooks. His
332 particular expertise lies in analysing medical microbubble behaviour under sonication and in high-speed photography.
333 He also explores non-medical applications of bubbles and droplets in sound fields. Since 2007, he has pulled in
334 more than US\$4.4 Million in research grants.