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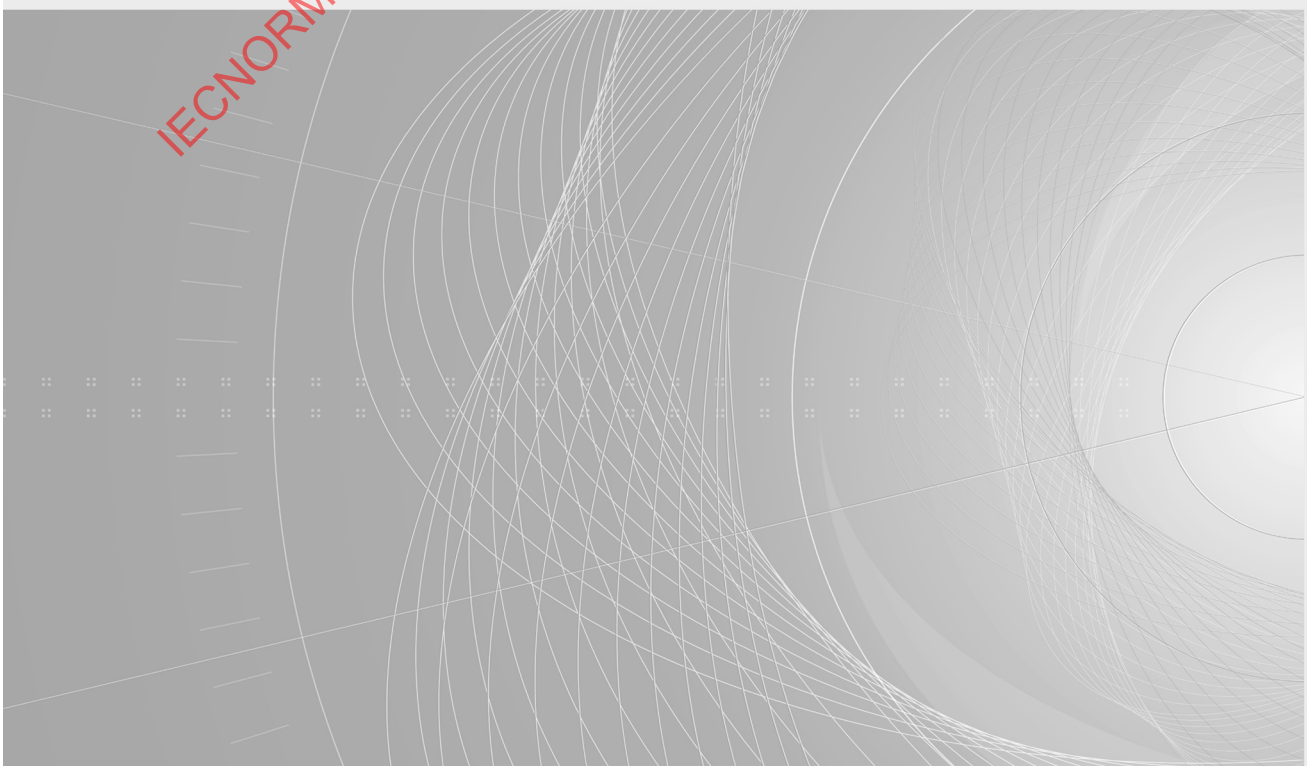
TECHNICAL REPORT

Requirements for measurement standards for high intensity therapeutic ultrasound (HITU) devices



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INTERNATIONAL ELECTROTECHNICAL COMMISSION

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INTERNATIONAL ELECTROTECHNICAL COMMISSION

REQUIREMENTS FOR MEASUREMENT STANDARDS FOR HIGH INTENSITY THERAPEUTIC ULTRASOUND (HITU) DEVICES

FOREWORD

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IEC 62649, which is a technical report, has been prepared by committee TC 87: Ultrasonics.

The text of this technical report is based on the following documents:

Enquiry draft	Report on voting
87/420/DTR	87/428/RVC

Full information on the voting for the approval of this technical report can be found in the report on voting indicated in the above table.

This publication has been drafted in accordance with the ISO/IEC Directives, Part 2.

The committee has decided that the contents of this publication will remain unchanged until the stability date indicated on the IEC web site under "http://webstore.iec.ch" in the data related to the specific publication. At this date, the publication will be

- reconfirmed,
- withdrawn,
- replaced by a revised edition, or
- amended.

A bilingual version of this publication may be issued at a later date.

INTRODUCTION

This Technical Report is concerned with standards for high intensity therapeutic ultrasound (HITU) and concentrates on applications that destroy tissue by heating which may or may not be accompanied by acoustic cavitation and other mechanisms. The purpose of the report is to identify topics where there is a consensus that the development of international standards would benefit the industries and/or patients involved with these forms of therapeutic ultrasound. The shortcomings of existing standards as they may be related to the applications of interest are reviewed. It is not its purpose to propose or evaluate specific alternative measurement methods which may be more reliably applied to HITU or other therapeutic equipment. Physiotherapy and lithotripsy are excluded as there are existing standards for these established uses. Lower intensity applications such as enhanced bone healing or ultrasound-induced gene therapy are not explicitly considered.

The use of HITU has advanced to the point where systems have achieved clinical approval for general use in several countries. Medical applications and product development are continuing rapidly. The corresponding products of many companies have been approved for marketing and clinical applications. Fast development in preclinical medicine, clinic medicine, and product manufacture has created an urgent need to standardize measurements of the basic acoustic parameters and the field characteristics of HITU. In order to promote the further development of HITU and to ensure its safe and effective use, international standards are required.

REQUIREMENTS FOR MEASUREMENT STANDARDS FOR HIGH INTENSITY THERAPEUTIC ULTRASOUND (HITU) DEVICES

1 Scope

This technical report is relevant to the measurement and specification of ultrasound fields intended for medical therapeutic purposes. Lithotripsy and physiotherapy are excluded, since there are existing International Standards for these applications.

It establishes:

- topics where there is a consensus that the development of International Standards would benefit the industries and/or patients;
- topics where the writing of standards should start immediately;
- topics where the writing of technical specifications should start immediately in order to gain practical experience and establish consensus prior to standardisation;
- topics which require future standardisation but where further research is required before initiating the writing of standards or technical specifications.

This report addresses primarily the requirements for measurement standards related to high intensity therapeutic ultrasound (HITU) [also known as high intensity focused ultrasound (HIFU)] fields which are both high intensity and focused and where the main mechanism for action is thermal. However, aspects of the discussion, conclusions and any resulting standards or technical specifications may also be relevant to therapeutic applications which are either focused or high intensity or where the main mechanism is not thermal.

Scientific literature has been reviewed and responses to a questionnaire which was sent to experts around the world are reported.

2 Background

Recent years have seen a dramatic rise in interest in using ultrasound as a surgical and therapeutic tool in its own right. Much of this growth has been due to the use of High Intensity Therapeutic Ultrasound (HITU) for tissue ablation in the treatment of cancers and conditions such as benign prostate hyperplasia (BPH). Here, ultrasound is brought to a focus within tissue with the intention of generating intensity levels sufficient to raise the local tissue temperature above 55 °C. Like so much in ultrasound, this technique was first tested many years ago (Lynn *et al*, 1942; Wall *et al*, 1951, Fry *et al*, 1954), but recent materials, computing and other technological advances have allowed it to come close to the medical mainstream. The ability to generate such high temperatures within tissue brings with it the absolute requirement to ensure that the treatment is delivered to the correct level and at the correct site. This in turn means that accurate methods of predicting the dose and monitoring performance are required. Consequently, reliable measurement and characterisation methods are needed for this application above all others.

However, HITU is not the only therapeutic application. Ultrasound physiotherapy, of course, has been widely used since the 1950s (Imig *et al*, 1954; Gersten, 1955) and lithotripsy since 1980 (Chaussy *et al*) for the destruction of kidney stones. More experimental applications include treatment of tendon injuries using lithotripter-like devices, stimulation of bone repair by low intensity ultrasound, ultrasound-induced haemostasis, and the targeted delivery of drugs through the localised destruction of carrier particles by ultrasound. Typical characteristics of ultrasound used for these different applications are described in general terms in Table 1.

Table 1 – General characteristics of ultrasound used for different therapeutic applications

Physiotherapy	1 MHz; 1 W cm^{-2}; <0,5 MPa
Lithotripsy	0,5 MHz; very low, >20 MPa
Soft tissue lithotripsy[a]	0,25 MHz; very low, 5 to 30 MPa
HITU[a]	0,5 MHz to 5 MHz; 1 000 W cm^{-2} to 10 000 W cm^{-2}; 10 MPa
Haemostasis[a]	1 MHz to 10 MHz; 100 W cm^{-2} to 5 000 W cm^{-2}
Bone growth stimulation	1,5 MHz; 30 mW cm^{-2}; 50 kPa
Drug delivery[a]	Up to 2 MHz; various; 0,2 MPa to 8 MPa
[a] Experimental techniques: limited information or wide range of characteristics under investigation. Acoustic parameters shown are a strong function of treatment duration or dose time and other factors.	

Medical ultrasound fields in the MHz frequency range are typically characterised in water by measuring the spatial and temporal distribution of pressure using a piezoelectric hydrophone, and by measuring the radiation force on a target which intercepts the entire field. International standards directly relevant to the measurement of medical ultrasound fields generally are given in Table 2; national standards are generally identical to international standards or specify parameters which are very similar. A range of terms defined in selected IEC standards (which are identical to the equivalently numbered British Standards) are given in Appendix B. Measurement aspects are also included in many textbooks on medical ultrasound and are the specific subject of Preston (1991), Ziskin and Lewin (1992), and Harris (2005), amongst others.

Table 2 – International standards and related documents for the measurement of medical ultrasound fields

Number	Title	Relevance
IEC 60500:1974	IEC standard hydrophone	L
IEC 60565:2006	Underwater acoustics – Hydrophones – Calibration in the frequency range 0,01 Hz to 1 MHz	L
IEC/TR 60854:1986	Methods of measuring the performance of ultrasonic pulse-echo diagnostic equipment	H
IEC 60866:1987 (withdrawn)	Characteristics and calibration of hydrophones for operation in the frequency range 0,5 MHz to 15 MHz	L
IEC 61101:1991 (withdrawn)	The absolute calibration of hydrophones using the planar scanning technique in the frequency range 0,5 MHz to 15 MHz	L
IEC 61102:1991 (withdrawn):	Measurement and characterisation of ultrasonic fields using hydrophones in the frequency range 0,5 MHz to 15 MHz	H
IEC 61102-am1:1993 (withdrawn)	Amendment 1 – Measurement and characterisation of ultrasonic fields using hydrophones in the frequency range 0,5 MHz to 15 MHz	H
IEC 61157:2007	Standard means for the reporting of the acoustic output of medical diagnostic ultrasonic equipment	M
IEC 61161:2006	Ultrasonics – Power measurement – Radiation force balances and performance requirements	H
IEC 61205:1993	Ultrasonics – Dental descaler systems – Measurement and declaration of the output characteristics	L
IEC/TR 61206:1993	Ultrasonics – Continuous-wave Doppler systems – Test procedures	L
IEC/TS 61220:1993 (withdrawn)	Ultrasonics – Fields – Guidance for the measurement and characterization of ultrasonic fields generated by medical ultrasonic equipment using hydrophones in the frequency range 0,5 to 15 MHz	H
IEC 61266:1994	Ultrasonics – Hand-held probe Doppler foetal heartbeat detectors – Performance requirements and methods of measurement and reporting	L
IEC/TS 61390:1996	Ultrasonics – Real-time pulse-echo systems – Test procedures to determine performance specifications	L
IEC 61685:2001	Ultrasonics – Flow measurement systems – Flow test object	L
IEC 61689:2007	Ultrasonics – Physiotherapy systems Field specifications and methods of measurement in the frequency range 0,5 MHz to 5 MHz	M
IEC 61828:2001	Ultrasonics – Focusing transducers – Definitions and measurement methods for the transmitted fields	H
IEC 61846:1998	Ultrasonics – Pressure pulse lithotripters – Characteristics of fields	M
IEC 61847:1998	Ultrasonics – Surgical systems – Measurement and declaration of the basic output characteristics	L
IEC/TS 61895:1999	Ultrasonics – Pulsed Doppler diagnostic systems – Test procedures to determine performance	L
IEC 61949:2007	Ultrasonics – Field characterization – In-situ exposure estimation in finite-amplitude ultrasonic beams	H
IEC 62092:2001 (withdrawn)	Ultrasonics – Hydrophones – Characteristics and calibration in the frequency range from 15 MHz to 40 MHz	H
IEC 62126 Ed. 1.0 (in preparation)	Ultrasonics – Fields: Methods for computing temperature rise in homogeneous soft tissue for diagnostic ultrasonic fields	H
IEC 62127-1:2007	Ultrasonics – Hydrophones – Part 1: Measurement and characterization of medical ultrasonic fields up to 40 MHz	H
IEC 62127-2:2007	Ultrasonics – Hydrophones – Part 2: Calibration for ultrasonic fields up to 40 MHz	H

Number	Title	Relevance
IEC 62127-3:2007	Ultrasonics – Hydrophones – Part 3: Properties of hydrophones for ultrasonic fields up to 40 MHz	H
IEC 62359:2005	Ultrasonics – Field characterization – Test methods for the determination of thermal and mechanical indices related to medical diagnostic ultrasonic fields	L
IEC/TS 62462:2007	Ultrasonics – Output test – Guide for the maintenance of ultrasound physiotherapy systems	L
IEC 60601-2-5:2009	Medical electrical equipment – Particular requirements for the basic safety and essential performance of ultrasonic physiotherapy equipment	H
IEC 60601-2-36:1997	Medical electrical equipment – Particular requirements for the safety of equipment for extracorporeally induced lithotripsy	M
IEC 60601-2-37:2007	Medical electrical equipment: Particular requirements for the basic safety and essential performance of ultrasonic medical diagnostic and monitoring equipment	H

In normal practice, no attempt is made to measure intensity (or the distribution of intensity) directly but it is derived from the measurement of pressure by assuming that the local pressure and particle velocity are in phase and therefore that the intensity is proportional to pressure squared (a 'plane-wave' assumption). Ultrasound power is not directly measured either but is derived either by integrating the derived intensity over a plane which intersects the field, or by measuring the radiation force experienced by a target and assuming that power is proportional to the radiation force and that the constant of proportionality can be determined from the acoustic and geometric properties of the target (another 'plane-wave' assumption). Geometric properties of the field (for example, focal distance and beamwidth) can be defined in terms of either pressure or derived intensity: most commonly, derived intensity (or, equivalently, pressure-squared integral) is used.

Although these measurement standards are well established and the measurement procedures laid down in them are widely practised, there are known limitations with both the measurement devices and the procedures. These limitations introduce uncertainties in attempting to characterise the true acoustic field. In addition, the existing defined terms may not be the most appropriate for characterising HITU fields, especially when attempting to compare their probable therapeutic effectiveness.

There is, however, a National Standard from China which relates specifically to characterisation of HITU transducers. An English translation of this standard is included in Appendix C. In brief, the approach is to characterise the field with a hydrophone at a low output setting using the techniques of the IEC standards for diagnostic fields. In addition, power is measured with a radiation force balance over a wider range of output settings. Some electrical characteristics of the transducer are also determined.

The standards listed in Table 2 have been reviewed for their relevance (L = Low, M = Medium, and H = High) as annotated above. It is possible that parts of relevant standards may be adapted for therapeutic applications; however, most standards are not directly applicable to HIFU and related applications. These shortcomings and limitations are the subject of the next section.

3 Limitations of existing standard methods

3.1 General

It can be difficult or inaccurate to apply many of the standard measurement methods to HITU fields, either due to fundamental measurement issues or to practical problems.

For radiation force balances, the major problems relate to:

- shielding by bubbles:
- thermal damage of target;
- force dependence on field geometry, not just on power;
- measurements away from the focal plane;
- extreme nonlinear effects including shock loss.

For hydrophone measurements, the major problems relate to:

- shielding by bubbles;
- thermal or cavitation damage;
- non-ideal frequency response;
- non-ideal directional response/spatial-averaging;
- high pressure levels;
- high harmonic content;
- off-axis measurements.

Some of the causes of these difficulties and inaccuracies are introduced in the following subsections.

3.2 Very high pressures

Pressures above the cavitation threshold for the measurement medium (usually water) can produce bubbles as dissolved gas is drawn out of solution. Three main problems may then arise: first, the bubbles formed may partly shield the sensor from the ultrasound field; secondly, violent bubble activity can damage or destroy the sensor. The occurrence of both of these effects can be minimised by removing dissolved gas and particulate matter from the measurement medium, but it may be difficult to maintain sufficient purity for a prolonged period. Thirdly, because of the high pressure levels involved, a proportionately larger fraction of the pressure spectrum is distributed into higher harmonics compared to a bubble-less medium.

There is also the risk of direct mechanical effects on the sensor itself due to large compressional and tensional forces. This is most likely to be a problem when there are weak points between different components of the sensor (for instance, if there is delamination of the glue layer in a bilaminar hydrophone).

3.3 Very high intensities

Energy absorbed from the ultrasound beam heats the sensor and this may affect its performance or even destroy it. For instance, the sensitivity of a membrane hydrophone can change if it is heated close to its Curie temperature. For polyvinylidenefluoride (pvdf), the most widely used hydrophone material, depolarisation occurs progressively with time at temperatures above about 70 °C and almost immediately at 110 °C. The thinness of membrane hydrophones will offer some protection against thermal damage because heat is very quickly lost to the surrounding medium. However, the sensitivity of pvdf hydrophones is temperature dependent and this change will be an additional source of uncertainty. Probe hydrophones may face greater risk and absorbing radiation force balance targets will certainly be damaged unless great care is taken to dissipate the absorbed energy. Heating can be reduced by generating low duty cycle toneburst ultrasound rather than continuous-wave. However, HITU transducers are generally only weakly damped and, consequently, may take many acoustic cycles for the pressure ‘ring-up’ at the start of the toneburst; there is an equivalent ‘ring-down’ at the end of the toneburst. This must be accounted for by scaling results from toneburst to the c.w. situation. In addition, since typically 30-50 % of the electrical energy is dissipated within the transducer, its temperature and properties will change with time during operation. Using toneburst mode will reduce this self-heating and may lead to significant differences in acoustic output compared to the c.w. case.

3.4 Strong focusing

In a focused field, two important plane-wave assumptions are not valid. Firstly, the particle velocity is not strictly in phase with the pressure, meaning that the local intensity is not truly proportional to the square of the pressure; hence, there is an increased uncertainty when deriving the intensity from a pressure measurement with a hydrophone. Secondly, the radiation force on a target placed in the field is no longer determined solely by the properties of the target and the total ultrasound power. The geometry of the field also plays a role, especially for the widely-used conical reflecting targets; absorbing targets are preferable provided that they are not damaged by excessive heating.

There is also a third effect which relates to the directional response of a hydrophone. In a plane wave, the hydrophone can be aligned so that the wave is incident in the preferred direction for the hydrophone (usually perpendicular to the plane of the sensing element). In a focused field, the pressure at the hydrophone can be considered as the superposition of wavelets with a relative phase and an angular distribution which are determined by the transducer geometry and its distance from the hydrophone. An ideal hydrophone would respond equally to wavelets from any direction and the output signal would be proportional to the sum of the wavelets. A real hydrophone, on the other hand, has a sensitivity which depends on the angle of incidence of the wavefront and the output voltage therefore depends on a **weighted** summation of the wavelets. This means that the output voltage waveform is different in magnitude and shape from the pressure waveform. This distortion increases with the large physical apertures and short focal lengths frequently used for therapeutic applications. Furthermore, the non-ideal nature of real transducers which have amplitude and phase variations across their apertures introduce additional complexities into the measurement process. There is no information available on the measurement uncertainties in cases where the field is generated by two or more widely separated transducers, or where the point of measurement lies within or close to the volume defined by the surface of the transducer or transducers.

In other therapeutic applications, the transducer is nonfocusing, or it operates over short distances or it has an unusual geometry. In these cases, existing measurement standards cannot be applied.

3.5 Nonlinear harmonics

Hydrophones have a frequency dependent amplitude and phase response. Consequently, in any ultrasound field where the acoustic spectrum at the point of measurement contains a significant spread of frequencies, the output voltage waveform (which is the acoustic spectrum convolved with the complex frequency response of the measurement system) will differ in shape from the true pressure waveform. In general, membrane hydrophones have a smoother frequency response (particularly in the low MHz region) and will give a closer representation of the pressure waveform. However, when the acoustic spectrum contains many high harmonics (as are generated by nonlinear propagation of high pressure fields), the output signal from the hydrophone can still be very different from the acoustic pressure waveform because the thickness resonance of the membrane typically results in a sensitivity which is 6 dB to 8 dB higher at the resonance frequency than at 1 MHz. Pulses of sufficiently high amplitude can achieve ‘full-shock’ conditions in which several hundred harmonics can be present with a relative amplitude proportional to 1/N, where N is the harmonic number. This problem is well recognised in the measurement of diagnostic ultrasound pulses and research is being carried out on the determination of the complex frequency response of hydrophones and the best method for deconvolving this response. So far, it seems that deconvolution to determine temporal-average intensity is relatively straightforward because it requires knowledge only of the amplitude response. The problem of determining peak negative and, particularly, peak positive pressures has not yet been solved with accuracy since it requires phase response data up to high frequencies.

3.6 Acoustic saturation and nonlinear loss

High amplitude acoustic pulses propagate nonlinearly in water, which results in a distortion of the wave and the generation of harmonics. Since the acoustic attenuation coefficient of water

is proportional to frequency squared, these harmonics are absorbed more quickly than the fundamental, leading to 'nonlinear loss' and eventually to 'acoustic saturation', where any change in the acoustic pressure generated at the transducer is not seen at the measurement point in the field. For radiation force balance measurements, nonlinear loss can mean that the incident power is strongly dependent on the distance at which the measurement is made. It can also mean that there is significant streaming in the water path and this also results in a force on the target. Determining the output power of the transducer is therefore subject to greater uncertainties.

For hydrophone measurements, acoustic saturation and nonlinear loss can be problematic when making measurements in water. Unlike diagnostic pressure levels measured in water, which fall within a prescribed range, the high pressures and extended pulse lengths for therapeutics can contain a significantly more extended and higher harmonic spectrum and this places a more stringent requirements on the frequency response of the measurement system.

NOTE The amplitude of a narrowband spectrum at the fundamental from a tone burst is proportional to the number of cycles; therefore, the harmonics also increase under high drive pressures. Acoustic saturation will be more pronounced at these levels. In addition, a problem arises when extrapolating from measurements in water to anticipated values in tissue, where the nonlinear properties and attenuation coefficients are significantly different. This is being addressed for diagnostic ultrasound by an IEC project which specifies a parameter and associated threshold that guarantees 'quasi-linear' conditions. To ensure quasi-linear conditions, the transducer output is reduced until nonlinear propagation processes transfer less than 10 % of the energy flux through any point in the field to the higher harmonics; it is believed that extrapolation from water values to tissue values can be better made by making measurements under these quasi-linear conditions.

3.7 Relevant parameters

Parameters for ultrasonic fields in existing standards have been defined primarily to compare fields propagating in water near the acoustic axis. A selection of these parameters taken from IEC standards current in 2005 is given in Annex B. Whilst these are still relevant to the description of HITU and other therapeutic fields, it may be possible to define a different set of parameters which can be related more closely either to therapeutic effect or to safety. For instance, it may be helpful to integrate intensity over a fixed area, to average pressure or intensity over a fixed area, or to determine a thermal dose or cavitation volume according to a specified protocol. While most previous measurements were near an acoustic axis, for therapeutic applications, a more complete regional measurement may be necessary to determine localized contributions to heating.

In addition, most existing defined parameters rely on either hydrophone or radiation force measurements. It may be possible to use alternative sensors to measure different quantities directly: for instance, intensity, temperature distribution, or cavitation activity.

4 Survey of experts

To establish the views of experts around the world as to where standards would be of benefit, a questionnaire was prepared and sent initially to attendees of the 2003 International Society of Therapeutic Ultrasound (ISTU) meeting which was held on Lyon, France. Further to this circulation, the questionnaire was handed out at the 2004 ISTU meeting in Kyoto, Japan, and at the 2004 meeting of Technical Committee 87 (Ultrasonics) of the International Electrotechnical Commission (IEC) held in Hangzhou, China.

The questions related to three different topics and are given with summarised responses in Table 3. A total of 26 replies were received and are given in full in Annex A.

Table 3 – Questions and summarised answers

A. YOUR APPLICATION		
A1	What is your current involvement in therapeutic ultrasound?	ESWL [3] Thermal ablation [7] Fundamental research [3] Equipment manufacturers [4] Haemostasis [2] Clinical [3]
A2	What is the therapeutic mechanism (eg cavitation, thermal…)?	Cavitation [8] Heat [14] Radiation force [1] Bubble mediated heating [1] “Other” [2]
A3	What ultrasonic power level range are you interested in?	Power 0 W – 500 W Intensity range “mW” – 2 500 W cm^{-2}
A4	What frequency range are you interested in?	0,2 MHz – 20 MHz
A5	What acoustic pressure range are you interested in?	40 Pa – 100 MPa
A6	What exposure mode are you interested in? E.g. pulse length, tone burst, cw.	Cw [12] “Pulse” [8] “Tone burst” [6] 1-20s
A7	What transducer size and f-number or focal length are you interested in?	Focal length 2 cm – 25 cm Transducer diameter 0,4 cm – 25 cm f-number 0,75 – 2
A8	Is there a particular exposure geometry that makes calibration difficult in your application?	No [3] Trans-rectal probes High pressure and intensity Multiple independent beams *In vivo [4]* “The small transducers are difficult to measure output power from. At lower frequencies the beam becomes divergent and it is difficult to achieve repeatable measurements.”

B. YOUR EXISTING MEASUREMENTS		
B1	How do you routinely test that your equipment is working properly?	Force balance [7] Pressure measurement [2] Hydrophone [4] Water fountain [2] Schlieren [1] Thermocouple [1] MR thermometry [2] Impedance spectrum [3] Cymometer [1] Melting a plastic cup [1] Not [1]
B2	How do you currently determine the effectiveness of the therapy in your	US imaging [3] MRI [4] Thermometry [2] Macroscopic visualisation [3]

B. YOUR EXISTING MEASUREMENTS		
	application?	Gels [3] *In vivo* [5] MR thermometry [1] SWR [2]
B3	Which parameters do you generally quote to describe your fields?	Pressure [5] Frequency [5] Intensity [8] Pulse parameters [4] Transducer dimensions [2] Exposure time [3] Power [5] Beam shape [5] Focal spot size [5] Transducer efficiency
B4	Do you currently use a phantom? If so, what type of phantom and for what purpose?	Stone model [1] Rubber [1] Abattoir liver [2] Gels [6] Liquid crystal [1] Acrylic [1] No [5]
B5	Briefly describe the equipment and method you use to measure pressure, intensity or power.	Needle hydrophone [11] Membrane hydrophone [6] Force balance [9] Extrapolation from theory [2] “The acoustic pressure cannot be measured directly by hydrophone under high power output. So we use a hydrophone to measure the acoustic pressure under the low power output to get the distribution of the acoustic field. A full-scale absorption method is used to measure the ultrasonic radiation force of the running transducer, and the acoustic power and intensity are drawn by theoretical deduction.” “We use a pvdf membrane hydrophone and short pulses (low duty cycle) in a water bath. We do not exceed a peak positive pressure of 3 MPa during calibration. We assume electromechanical linearity thereafter and use a propagation code to account for nonlinearity”
B6	Briefly describe the equipment and method you use to measure heating, cavitation or other relevant effect.	Microscope [2] Thermocouple [9] Liquid crystal [1] Thermal camera [1] MR [2] PCD [6] ACD [4 High speed cine [1] Hydrophone + frequency spectrum analyser [1] Sonochemistry [1] Luminescence [1] Force balance [1]

C. YOUR PERCEIVED NEEDS		
C1	What characteristics of the u/s field do you think is important for effective therapy in your application?	Frequency spectrum [1] Frequency [6] Intensity [6] Exposure time [5] Transducer dimensions [1] Pressure [3] Pulse parameters [4] Cavitation noise [1] Temperature as function of time [3] Beam shape [5] Power [2]
C2	Do you feel you are able to characterise	Non linear fields [2] Power measurement [2]

C. YOUR PERCEIVED NEEDS		
	your equipment or the u/s field satisfactorily? If not, what do you perceive to be the shortcomings of your existing measurement methods?	Absolute values [1] Yes can do it [2] “There are no standard methods and measures to test the acoustic field under high power. Normal hydrophone is unable to be used to directly measure the acoustic pressure under high power. We use normal hydrophone to test the acoustic field under low power, and calculate the theoretic focal intensity under high power, supposing the acoustic distribution keeps stable. Since we ignore the nonlinear influencing factors, we cannot evaluate the errors.” “Mostly yes, but transfer of water measurements to tissue needs work. Knowledge of expected temperature, finite amplitude effects and cavitation initiation would be valuable.” “Generally happy. The biggest shortcoming is with respect to our uncertainty in output power measurements (currently about 5 % – 10 %)” “Yes, but not from manufacturer's data. The most basic shortcoming is non-linearity in water. A measurement fluid in which non-linearity doesn't occur, or is repeatable and predictable up to very high intensities, would help.” “In the manufacturing site: OK In the field (clinical practice): Needs for transportable measurement equipment and methods, phantoms.... to measure acoustical transducer performance.”
C3	Do you have an opinion on how therapy fields/treatments should be measured or characterised?	Power [2] Intensity [2] Exposure time [1] Frequency [1] Acoustic efficiency [1] Acoustic power [1] Derating [1] “Research fields should give as much information as possible. Medical instruments should provide users with real time feedback on quantities like thermal and mechanical indices, and cavitation emissions.” “Acoustic efficiency is an important parameter, and acoustic power should be quoted more often instead of electrical power delivered to transducer.” “Hydrophone at low power levels, schlieren at low power levels, TAP, comparison with simulations, gel phantoms, in-vitro tissue exposure, in-vivo tissue exposure, thermometry arrays (if applicable), thermal dose.” “Yes, measure pressure as well as intensity. Measure both peak positive and peak negative pressure.” “1: Transducer calibration at the end of the manufacturing process (US beam measurement, transducer efficiency). 2: Transducer control during treatment (electrical power measurement, electrical matching control). 3: Any methods to measure and control the effectiveness of tissue destruction (????). 4: Periodic control of the transducer’s performance (before each treatment, every weeks or months …).”

C. YOUR PERCEIVED NEEDS		
C4	Do you feel aspects of your work would benefit from the widespread use of more standardised measurement or evaluation methods? If so, which aspects?	No [2] Yes [12] “It is hoped that methods and standards for measurement of acoustic field could be established, and an international language in such a field could be formed.” “For **publication** it would be helpful to have a set of standard parameters. This is a prerequisite to understand articles and to compare different publications. For patient therapy, we need a standard for **quality assurance** and to compare the performed studies at different times and places. In addition a standardized instruction on ’how to measure‘ these parameters would be helpful.” “Yes. Mainly, reports using transducer/field intensity are extremely misleading. Any reporting of intensity must also include: tissue depth, attenuation, cross-sectional area, spatial average? or time average?, and TAP values.” “If there were some standard physical characteristics or parameters to aim for, it would be relatively easy to make estimates.” “Power transducer temperature. PROBE temperature rise in °C per watt of input (not reflected) power, per second. And, probe cooling time-constant.” “It would be useful to have a table relating acoustic power levels measured in a water tank to intensities delivered to tissue as a function of frequency, organ type, depth, exposure time etc.” “Acoustical power measurement for highly focused transducers.”
C5	Would you be willing to participate in development of standards by providing written comments, drafting documents or attending committee meetings.?	Possibly [4] In writing only [2] Yes [8] No [1] “In an informal way, but not in one of those big, endless committees.”
C6	Please add any other comments or observations you would like to make.	“It is important to create standards and criteria for clinical treatment using focused ultrasound.” “Standardization is most important for clinical HIFU instruments now becoming available. Standardization could borrow from experience with diagnostic machines, but with much improved exposimetry and dosimetry available in real-time.” “I feel that there is a wide variation in the methods used for characterisation among groups as well as the preferred measurement/characterisation parameters quoted.” “Universal standards are needed for equipment performance – e.g. probe temperature rise per above; probe thermal and acoustic energy tolerance; and system parameters such as frequency, probe temperature, forward and reflected power, probe information keyed to equipment, and more. With respect to patient safety, standards are needed but it's hard to imagine what they will be, beyond the obvious. One needs to look outside the ultrasound discipline, e.g. electrosurgery, radiation therapy, etc.” “The need for non-invasive temperature measurement is acute. In addition, we need to develop techniques for sensing the onset of lesion formation and (preferably) imaging the lesion based on irreversible changes in tissue properties. It would be very helpful if we had a database of measured cavitation thresholds for various organs. This issue of registering images generated by a guidance device (MRI) and the therapy beam is a difficult problem. (Image registration has been extensively studied by other communities – maybe we could transfer some of their knowledge and expertise?) Finally, there is much work to be done *vis a vis* cavitation bubble dynamics in non-Newtonian media, as well as developing techniques for nucleating cavitation activity at safe pressure levels.”

5 Existing literature for measurement of HITU fields

Although there have been many papers published in the past 10 years on the use of HITU, most of these are understandably concerned primarily with the development of the application and deal only in passing with the methods used to characterise the acoustic properties of the fields. Of the measurement methods described, the two most commonly used are the radiation force balance to determine total output power and the pvdf hydrophone to determine focal position, peak pressure and beamwidth (typically these hydrophone measurements are made at much lower output levels than are used for clinical therapy to avoid damaging the hydrophone). It is noticeable that even important properties of the hydrophone (such as effective radius, film thickness and frequency response) are often not reported. Other methods that have been used or suggested include schlieren imaging, scanning a small embedded thermocouple through the field, and determination of total output power using the pyroelectric effect. This clause summarises the measurements reported in a selection of (mostly recent) papers. A review of a number of calibration issues relevant to HITU can also be found in Shaw and Hodnett (2008).

Hill *et al* (1994) identified deficiencies in existing practice for measuring and reporting acoustic exposures for focused ultrasound surgery. He proposed that the intensity spatially averaged over the area enclosed by the half-pressure-maximum contour in the focal plane, as determined under linear conditions (denoted as I_{SAL}) would be more satisfactory for both metrology and biophysical relevance. This quantity is used by a number of later authors and appears to have been adopted almost as a standard or reference quantity. Hill's calculations assume a Gaussian beam and the method of determining a value for I_{SAL} is to measure the –6dB beam diameter, D, with a hydrophone at a low (linear) drive level and to measure the power, P, with a radiation force balance at the relevant clinical (nonlinear) drive level. For a Gaussian beam, the intensity averaged over the –6dB beam-area has a fixed relationship to the total power in the beam and so I_{SAL} can be derived from measured quantities according to the relationship:

$$I_{SAL} = 0{,}867\ P / D^2.$$

The temporal-average intensity on the beam-axis, which Hill calls the spatial-peak intensity, I_{SP}, can also be calculated under the Gaussian assumption to be:

$$I_{SP} = 1{,}56\ P / D^2.$$

Hill showed correlation between lesion diameter and I_{SAL}. However, it is clear that, although the basic definition (intensity spatially averaged over the area enclosed by the half-pressure-maximum contour) may have a general applicability, the use of W and D to determine I_{SAL} and particularly I_{SP} is very questionable. Even if the main lobe of the beam is approximately Gaussian at low drive levels, any power in the sidelobes will contribute to P, but should not be included according to the definition. A strictly Gaussian beam of course would have no sidelobes, but no transducer is strictly Gaussian and phased arrays in particular may produce substantial sidelobes, especially when firing off-axis. Another major limitation comes in using the value of I_{SP} as if it were a real intensity which governs, for instance the rate of temperature increase on the beam-axis. The beam-profile is known to become more sharply peaked as the drive level increases due to nonlinear propagation, leading to substantial differences from the Gaussian assumption.

Chen *et al* (1993) varied the total acoustic power (measured using a radiation force balance in the focal plane) from 3,8 to 24 W. This resulted in *in situ* spatially averaged focal intensities, I_{SAL}, of 67 W cm^{-2} – 425 W cm^{-2} (corresponding to *in situ* spatial peak intensities of 121 W cm^{-2} – 765 W cm^{-2}). The acoustic field was mapped using a calibrated pvdf membrane hydrophone (GEC Marconi, Chelmsford, UK[1)]), and corresponding exposure

1) The manufacturers cited in this clause as the producers of equipment used in the various studies referenced here are identified for the convenience of users of this document. This does not constitute an endorsement by IEC of these products.

values were reported in terms of *in situ* spatially averaged focal intensity. It is not clear whether the mapping was carried out over the full range of output levels available, or at a single low output level. The high-intensity focal region was found to be cigar-shaped, with dimensions (defined as the full width at half pressure maximum) of 18 mm along the beam axis and 1,6 mm in the transverse direction.

Hynynen (1993) measured the power from a cylindrical applicator placed on the axis of a convex conical reflector to direct the ultrasound onto a radiation force balance target. He also mapped the intensity field using a 50 μm thermocouple (type not specified) embedded in a 0,5 mm diameter silastic sphere.

Fjield (1999) used a 0,2 mm diameter needle hydrophone (Precision Acoustics, UK) in degassed water. Stepper motors scanned the hydrophone through the focal region of the transducer with measurements taken every 1,0 mm in the axial direction and 0,25 mm in the radial direction. Output power was measured using a radiation force technique (Stewart 1982).

Rivens *et al* (1999), carried out a feasibility study of the occlusion of blood flow *in vivo* using an array of multiple single exposures of 1,7 MHz focused ultrasound. These were placed in two rows of four lesions at a focal depth of 5 mm. The 4 660 W cm^{-2} (free field spatial peak intensity), 2 s duration exposures were placed 2 mm apart. All intensities quoted in this paper are described as free field spatial peak values and were determined using radiation force balance measurements and pvdf hydrophone measured beam profiles (full width half maximum pressure dimensions of 1,8 cm long and 1,8 mm wide) using the method described by Hill (1994). The errors in the measurement are evaluated as being 9-10 %, which is optimistic since deriving a value for spatial-peak intensity using Hill's method relies strongly on the assumption that the beam in Gaussian in cross-section.

Graham *et al* (1999) used a calibrated bilaminar membrane hydrophone to determine a calibration curve of ultrasound intensity versus input voltage to the transducer. They recorded a –6 dB focal depth of field of 6,0 mm and a full-width at half-maximum (FWHM) of 1,0 mm at the ultrasound focus; during insonation of tissue samples, the range of intensity and heating duration were (40 to 150) W cm^{-2} spatial peak and (10 to 600) s, respectively.

Clement (2000) describes measurements carried out in a tank filled with degassed deionized water and padded with rubber to inhibit reflections from the tank walls. A 0,5 mm diameter (Precision Acoustics, UK) polyvinylidene difluoride (pvdf) hydrophone (presumably of a needle-type) was used in the evaluation of a 'virtual array' created by moving a single transducer around a section of a 16 cm diameter hemisphere. Hydrophone response was amplified by a Precision Acoustics pre-amp into a second amplifier (Preamble Instruments, Oregon, model 1820) and recorded by a digital oscilloscope (Tektronix, Oregon, model 680). For absolute pressure measurement in the relevant frequency range, the pvdf hydrophone was calibrated by the authors between 0,5 MHz and 2 MHz in a water bath against a calibrated Marconi type Y-34-3598 membrane hydrophone in combination with a matched amplifier (GEC-Marconi, Essex, UK).

Huber *et al* (2000) measured the pressure field with two calibrated needle hydrophones (SEA, Milpitas, CA, USA and Imotec, Wuerselen, Germany). At 1 MPa pressure amplitude, the focus (-6 dB full-width half-pressure maximum contour) in the water was ellipsoidal, 3 cm long in the ultrasound propagation direction and 3 mm wide. The spatial peak intensity in the focus during the burst was approximately 33 W cm^{-2} at 1 MPa peak pressure (p_+ or p_- is not specified) in the focus of the undisturbed sound field in water. The results from the two hydrophones are not compared in the paper.

McDannold *et al* (2000) used a 0,75-mm diameter hydrophone to scan the beam pattern created by a 'sector-vortex' phased-array transducer. The scan with a step size of 0,20 mm was obtained at the focal plane, perpendicular to the direction of the ultrasound beam. In this arrangement, adjacent sections of the array had alternating acoustic phase. It is interesting to

speculate whether this could cause spatial-averaging effects at the hydrophone which are different to those due to a source of smoothly varying phase distribution (eg Zeqiri *et al* 1992).

Edson (2001) measured the pressure at 1,1 MHz *in situ* in an agar/graphite phantom using a calibrated needle hydrophone (NP-4, 1,0 mm active element, Dapco, Branford, CT). Temperature was also measured in the same phantom with one or more type-E thermocouples (0,127-mm diameter bare wire, 40 ms response time, Omega Engineering Inc., Stamford, CT). Cavitation activity was monitored using a damped, spherically focused transducer (15 MHz center frequency, Panametrics, Waltham, MA) with a 1,9 cm focal length (in water) and a 0,64 cm aperture. Viscous heating and thermal conduction errors at the thermocouple are not discussed, and the hydrophone used has a resonance between 1 MHz and 3 MHz, which gives a 20 dB increase in sensitivity. Consequently, absolute values of pressure and temperature are unlikely to be reliable.

Konofagou *et al* (2001) studied an application which uses ultrasonic acoustic emission (USAE) where two focused ultrasound beams of frequencies (1 to 2) MHz with a difference in frequency of tens of kilohertz generate a localized vibration in tissues and produces an acoustic emission at the difference frequency. The acoustic power was calibrated by using a radiation force technique on an absorbing target and these measurements were used to obtain equal acoustic power from both transducers. A hydrophone detected the acoustic emission signal.

Mahoney *et al* (2001) describe measurements made by scanning (under stepper motor control in degassed water) a 0,2 mm diameter needle hydrophone (Precision Acoustics, UK) across a plane in the focal region of the transducer (perpendicular to the direction of the ultrasound beam). The scan area was 100 mm^2 with a 0,2 mm step size. Both magnitude and phase information was recorded at each point to allow back propagation of the wave front (Clement *et al,* 1998). They were also interested in transducer efficiency. The total acoustic power was measured as a function of RF power using a radiation force measurement system. The RF power (forward and reflected) and driving phase were monitored during each sonication by power meters integrated into the amplifier system. The transducer efficiencies were 70 % and 71 % for the two transducers concerned.

Chana *et al* (2002) measured the pressure amplitude distribution in degassed water using a pvdf needle hydrophone (NTR Systems Inc., Seattle, WA). The hydrophone was 0,5 mm in diameter and was moved using stepper motors. The acoustic power output was determined using a radiation force balance technique. In addition, the acoustic beam pattern was determined with a schlieren imaging system at three different acoustic power levels: 10 W, 30 W and 60 W. Further, a transparent tissue-mimicking gel phantom was used to determine if lesions could be formed at target locations and if these lesions could be visualized using ultrasound. The thermally sensitive gel consisted of bovine serum albumin and polyacrylamide. Lesion widths were compared at I_{spta} values of 3 600 W cm^{-2} and 1 200 W cm^{-2}.

Melodelima *et al* (2002) wanted to use an array of transducers to generate a pseudo-plane wave. Pressure measurements were carried out in a tank full of freshly degassed water in which the array was set up together with a needle hydrophone (SEA, Milpitas, CA, USA). The hydrophone was controlled by a motorized system which allowed micrometre displacements in all three directions. All pressure measurements were made using tone bursts which were long enough to reach a steady state excitation. After electrical matching, the electroacoustic efficiency of each of the 16 transducers was measured using a RFB.

Mesiwala *et al* (2002) created a map of the acoustic field by measuring the positive pressure distribution generated by the HITU device in degassed water, using a needle hydrophone (DNU-001A needle hydrophone, NTR Systems, Inc., Seattle, WA) mounted on a three-way positioner (APL). The peak positive pressure used was approximately 10 times lower than that applied therapeutically. Hydrophone movement and data acquisition were controlled by computer (PowerPC, Apple Computer, Cupertino, CA) via appropriate software (Labview, National Instruments Corporation, Austin, TX). During HITU application, cavitation was observed in a layer of coupling gel via scintillation of laser beams. To estimate the effect of

endogenous bubbles and cavitation within the gel on the transmission of US from the transducer to the brain, the acoustic field was also mapped after transmission through a layer of coupling gel placed on mylar sheet on the surface of a water bath. Distortion of the HITU field was observed.

Sokka *et al* (2003) measured the acoustic power output and the focal pressure amplitude as a function of applied RF power. Acoustic efficiency of two arrays was determined to be approximately 70 % (the details are not given), and acoustic power was calculated from this measurement and the transmitted RF power (measured by an in-house driving system). The intensity values were calculated from hydrophone pressure measurements performed in water at low pressure amplitudes and then extrapolated to higher powers based on the measured acoustic power. They note that this assumption is true only if the focal spot shape is kept constant and they claim that this was the case in these experiments, since no intentional change in the focusing was made. This claim must be considered dubious since it is known that nonlinear propagation effects change the spatial pressure distribution. The water intensity values were adjusted for attenuation through 10 mm – 20 mm of muscle with an attenuation coefficient of 5 Np m^{-1} MHz^{-1}.

Ishikawa *et al* (2003) measured the peak acoustic intensity of the transducer in degassed water with a needle-type calibrated reference hydrophone (Force Technology, Brøndby, Denmark). They were interested in heating occurring near the femoral artery of a rat. A real-time visual representation of blood flow within the target artery was obtained by applying color Doppler ultrasonography before and after HITU treatment. The HITU-induced temperature rise at the intensity of 4 300 W cm^{-2} was measured with a 0,25-mm diameter, sheathed chromel-alumel thermocouple (Sukegawa Electric, Ibaraki, Japan) inserted into the tissue. The thermocouple's tip was adjacent to the target artery. All exposures lasted 5 s and the maximum temperature at 4 300 W cm^{-2} was 98 °C. Temperatures at other intensities were assumed to be linearly proportional to the applied intensity, although this seems unlikely to be true over such a wide temperature range, especially as the temperature approaches the boiling point of water.

Sasaki *et al* (2003) measured the distribution of the acoustic pressure at 4,25 MHz in degassed water with a 0,5-mm diameter needle-type pvdf hydrophone (Imotec, Wurselen, Germany). The transducer was scanned on the focal plane over an area of 8 mm × 8 mm square, with a 0,1 mm mesh separation. These measurements were performed at a low acoustic-pressure level. The absolute acoustic power from the transducer was calibrated by measuring the radiation force on a hollow aluminium plate (although this target type is advised against even at much lower power levels in current standards) in degassed water. The profile of the acoustic field in degassed water was visualized using the schlieren technique.

Kennedy (2004) used a calibrated pvdf membrane hydrophone (GEC Marconi, Chelmsford, Essex, UK) with a 0,5 mm sensitive element in degassed water. The beam-profile was mapped using this hydrophone, and power was measured using a radiation force balance. These measurements were performed at low power, near-linear conditions in water. They therefore represent 'free-field' values, and were adjusted using an attenuation correction based on literature values to give an indication of the more clinically relevant *in situ* values conditions resulting from loss of energy in the tissue path. When possible for the hydrophone measurements, the transducer was driven in toneburst mode and the hydrophone tilted by approximately 10° to avoid standing waves. Beam-plotting measurements were also made of a 'JC-Tumor Therapy System' (Chongqing HAIFU™ Technology Company Limited, Chongqing, P.R. China) at low power setting. Here, the hydrophone was held stationary (but tilted) and the transducer was moved using the HITU positioning system. Two different designs of radiation force balance were used. One was a beam-balance with a small (approximately 2 cm × 4 cm) elliptical plane reflecting target mounted on a vertical arm. The target was placed approximately 1,5 cm in front of the focus and counterweights were moved along a horizontal arm until the balance was restored to its equilibrium position. The second was an absorbing rubber target suspended from a top-loading commercial balance (0,1 g resolution). This second balance and target was supplied by the HAIFU company. The transducers for the HAIFU system have a central hole where the ultrasound imaging probe is

situated. According to the operating procedure for this second balance, a correction factor was calculated for each transducer: this correction factor depends on the focal length, the diameter of the transducer and the diameter of the central hole. I_{SAL} and I_{SP} were calculated, although the Gaussian assumption does not appear to be justified from the beam-plots presented, which show sidelobes at about 20 % to 40 % of the on-axis pressure near the focus. Differences between the two balances were typically around 5 %.

Wang Wei *et al* (2004) investigated "practical, safe, easy-to-use, non-cytotoxic, and reliable" parameters to apply to an ultrasound (US) naked gene therapy system. The ultrasound pressure at the point of cell exposure was measured using a calibrated hydrophone and the intensity calculated. An acoustic power meter calibrated against a hydrophone by the planar scanning method was used to measure the power of the transducer. The ultrasound exposures of cells were characterised using a calibrated hydrophone (Reson, Goleta, CA). They found that the effect of US gene delivery and cell viability correlated as a fifth order polynomial with US intensity and exposure time and concluded that, with optimal parameters, US can safely deliver naked a gene into a cell without damage to cell function. They pointed out that the experimental conditions must be accurately specified in order to produce valid results (thus the calibration of acoustic power is important) and that the intensity to which the cells were exposed is not the same as that at the surface of the source.

Feng Wu *et al* (2004) have a set of 12-cm diameter PZT-4 ceramic transducers with a range of focal length and frequency. The focal lengths used in clinical applications are 90 mm, 130 mm, or 160 mm. The US frequencies used for treatment are 0,8 MHz, 1,6 MHz or 3,2 MHz. The focal region is claimed to be an ellipsoid, which was mapped using a membrane-type hydrophone at focal peak intensities from (200 to 300) W cm^{-2}. In clinical applications, the target tissue is exposed to focal peak intensities from (5,000 to 20,000) W cm^{-2}, depending on the focal depth.

Kun *et al* (2004) calibrated their transducer in deionized, degassed water with a needle hydrophone (0,05-mm diameter; Precision Acoustic, Dorset, UK). The half-pressure maximum focal beam length and width were 19,2 mm and 3 mm respectively: the "focal region" was here defined as the volume enclosing the full width half maximum (FWHM) dimensions. The "free field" focal peak was the position of the focal peak intensity in water at 21 °C, as determined using the hydrophone. Experiments were undertaken in a tank of degassed water maintained at 21 °C. When the position of a lesion is described, the front refers to the part closest to the transducer and the back to the part farthest away. Kun makes use of the term spatial average linear intensity, $I_{SAL,}$ given by Hill (1994). The values of incident power, input power, transducer acoustic power, spatial peak intensity (I_{SP}) and spatial average intensity (I_{SAL}) over the range used in this work were determined. Experiments were performed in the intensity range (2 000 to 4 000) W cm^{-2} (I_{SP} or I_{SAL} is not clear). *In situ* intensities were calculated assuming a 2 cm path through muscle. The rest of the axial path was water, for which losses were neglected. Thermal measurements and US imaging were performed during the HITU application with a chromega-alomega thermocouple of 0,5-mm diameter (calibrated in hot, 85 °C, and cold, 22 °C, water) inserted into the muscle. Viscous heating and conduction artefacts in the temperature measurements are not discussed.

Deng *et al* (2004) generated HITU exposures (described as 'tone-bursts' but actually c.w. excitation for a specified period) with durations (10 to 75) s to achieve thermal coagulation. The HITU beam profile (operated at lower output levels) was measured using a calibrated hydrophone system (Precision Acoustics, Dorchester, UK). The effective ultrasound output powers were characterized using an ultrasound power meter (UPM-DT-10, Ohmic Instrument Co, Easton, MD).

Damianou (2004) obtained the size of the focal region produced by his transducer by mapping the acoustic pressure field with a needle hydrophone (Specialty Engineering Associates, San Jose, CA), having an active element 1 mm. The transducer was driven by a pulse/receiver (Panametrics 5050R, Waltham, MA). The hydrophone was connected to the receiver input of the pulse/receiver. The output of the pulser/receiver was connected through an A/D card (CS1250, A/D 12-bit, 50-MHz; GAGE, Lachine, Montreal, Canada) to the PC for signal processing. The transducer was moved automatically by a positioning system (MD-2, Arrick

Robotics). The full width at half-maximum intensity (D) of the transducer was measured and the spatial average intensity was estimated using I_{SAL} = 0,87 P/D^2. Total power was measured using an ultrasound power meter UPM-DT-100N (Ohmic Instruments, Easton, USA). An uncertainty of 2 % is quoted for power measurements (which is probably a manufacturer-supplied value but is excessively optimistic).

Foley *et al* (2004) characterised a 3,2 MHz single-element HITU transducer with a focal length of 3,5 cm and an F-number of 1. Specially moulded polyacrylamide gels were used with the device to provide efficient coupling of the HITU energy into tissue, enabling formation of a lesion encompassing a targeted nerve in rabbit leg muscle. The lateral and axial dimensions of the HITU beam were measured by mapping the pressure field of the transducer with a needle hydrophone (TNU001A, NTR Systems, Inc., Seattle, WA). The hydrophone had a spatial resolution of 0,6 mm and was moved using stepper motors. The acoustic power output of the HITU transducer at electrical powers ranging from (5 to 60) P was measured using a radiation force balance with an absorbing target. It was known that significant attenuation would take place in the polyacrylamide gel and that heating would occur in it during prolonged HITU applications. Therefore, the attenuation through the polyacrylamide coupler was measured using an acoustic transmission technique. This technique was also used to measure the attenuation through fresh rabbit hamstring muscle. Allowing for a 55 % duty cycle of the HITU pulsing and the attenuation of the beam as it propagated through the gel coupler and the muscle of the rabbit leg, the HITU focal intensity (I_{sata}, spatial-average temporal-average intensity) at the site of the nerve was calculated.

Maruvada *et al* (2004) used two focused air-backed PZT transducers of fundamental frequencies 0,747 MHz and 1,091 MHz. The 0,747 MHz transducer has a diameter of 4 cm and a focal distance of 7 cm, and the 1,091 MHz transducer has a diameter of 5 cm and a focal distance of 10 cm. Utilizing the third harmonic frequencies of both transducers, the following frequencies were used in these experiments: 0,747 MHz, 1,091 MHz, 2,279 MHz and 3,273 MHz. The acoustic power output and the focal pressure amplitude as a function of applied radiofrequency power was measured in water with a radiation force method and a calibrated membrane hydrophone (spot diameter 0,5 mm, GEC-Marconi Research Center, Chelmsford, UK), respectively. The pressure amplitudes were measured and limited to 5 MPa (this seems to be peak negative pressure), so as not to damage the membrane hydrophone. These measurements were extrapolated, based on the acoustic power measurements, to cover the whole application range. They claim to make allowance for the nonlinearity of the amplifier at high input voltage by measuring the acoustic pressure in pulsed mode using the radiation force method, – although the method of making this correction is not clear.

Miller and Dou (2004) measured six transducers with resonance frequencies of 1,0, 2,25, 3,5, 5,0, 7,5 and 10 MHz. During exposure, a transducer was mounted in a 37 °C water bath and directed upwards at the exposure chamber located at the focus. A function generator (model 3314A, Hewlett-Packard, Palo Alto, CA) and power amplifier (model A-300, Electronic Navigation Industries, Rochester, NY) supplied two cycle pulses with a 1 % duty cycle to the transducer. The duration of the 60-s exposures was controlled by manually switching the signal on and off. These parameters were chosen to simulate some parameters of diagnostic US. The exposure fields were calibrated by scanning a hydrophone (model 805 pvdf bilaminar membrane hydrophone, Sonora Medical Systems) at the focus. Pulse duration was calculated from the pulse intensity integral, and the pulse repetition period was set to 100 times the pulse duration. The frequency band widths of the pulses were measured using a spectrum analyzer (model 89410A, Hewlett-Packard). The peak-rarefactional pressure amplitude of the largest negative cycle of each pulse was specified as the primary exposure parameter. The effective diameter of the hydrophone's sensitive spot was 0,44 mm. This was less than the expected diameter of the beam at the higher frequencies and corrections were made for the resulting spatial averaging of the spatial maxima (reference is made to Zeqiri and Bond, 1992, and Radulescu *et al*., 2001 for these corrections). The corrections were calculated assuming that they were small (*i.e.,* not including side lobes) and that the acoustic fields were linear (*i.e.,* not highly distorted).

Pernot (2004) was concerned with motion-tracking experiments performed using a 200-element ultrasonic sparse array. This high-power ultrasonic probe was initially designed and

optimised for HITU transcranial therapy and consisted of 200 high-power piezocomposite transducers of 8 mm in diameter and 900 kHz central frequency (Imasonic, Besançon, France). These were mounted in a sealed, spherically curved holder with a 120-mm radius of curvature. The focal zone dimensions of the HITU probe were measured at low acoustic intensity (5 W cm^{-2}) in a tank filled with degassed water using a 0,4 mm polyvinylidenefluoride (pvdf) bilaminar calibrated hydrophone (Golden Lipstick model, SEA, Soquel, CA) mounted on a stepper-motor-controlled 3-D positioning system (MM4006, Newport, Irvine, CA). The 6-dB focal zone was 1,2 mm × 1,2 mm × 7,5 mm.

Denbow *et al* (2000) carried out a study to investigate the ability of focused ultrasonic surgery to occlude blood flow *in vivo*. A 5-mm linear track exposure of 1,7 MHz focused ultrasound was applied across the femoral vessels for 5 s. Free field spatial peak intensities in the range of (1 000 to 4 660) W cm^{-2} were used. Vascular occlusion was confirmed after demonstration of an absent distal arterial pulse and an absent flow signal on magnetic resonance angiography. The minimum intensity for consistent vascular occlusion in this study was 1 690 W cm^{-2} at a focal depth of 5 mm when the transducer was moved at 1 mm s^{-1} orthogonal to the direction of blood flow. All intensities are claimed to be free field spatial peak values determined with radiation force balance measurements and hydrophone-measured beam profiles according to the method described by Hill and accurate to within ±10 %.

Miller and Song (2003) characterised an air backed 1,55 MHz spherically focused transducer with diameter and radius of curvature both equal to 2,54 cm. The peak rarefactional pressure amplitude (PRPA) was measured with a hydrophone (Model 805, Perceptron, Hatboro, PA). The temporal peak intensity was also estimated by assuming that the waveform was sinusoidal with intensity proportional to the square of the PRPA. Exposures were 2 MPa (133 W cm^{-2}), 4 MPa (533 W cm^{-2}), 6 MPa (1 200 W cm^{-2}) and 8 MPa (2 133 W cm^{-2}). It seems here that 'temporal-peak' is incorrect terminology since the true temporal-peak is an instantaneous value: the authors mean the temporal-average intensity during the time when the ultrasound output is active and stable. Providing the toneburst is long enough that the beginning and end of the burst can be ignored, this is more correctly termed the pulse-average intensity. In addition, the calculation of intensity assumes that the waveform is sinusoidal with an amplitude equal to the peak negative pressure. Due to nonlinear distortion of the waveform, the intensity would be expected to be higher than the calculated value.

Owen *et al* (2003) measured output power using a radiation force balance fitted with a right-angled conical reflecting target (Ohmic Instruments Co. model UPM-DT-10E). The transducer was facing down and positioned as close as possible to the metal cone reflector in distilled and degassed water without an anti-streaming foil. Transducer efficiency values were determined by the ratio of acoustical power to electrical power. The acoustic field near the face of the transducer was also measured with a membrane hydrophone (Reference Shockwave Hydrophone System, Sonora Medical Systems, Membrane SN: D-155). The hydrophone was positioned about 15 mm from the transducer, which was as close as the arrangement allowed.

Shaw (2004) describes a novel design of sensor based on the pyroelectric principle for monitoring the output power from HITU transducers. The sensor itself is a pvdf membrane which is intended to be minimally perturbing to the ultrasound field, so that it can remain in the ultrasound field throughout treatment and provide a constant monitor of ultrasound power. This also simplifies routine QA, since measurements can be made more simply and quickly than using a radiation force balance. Since the publication of this paper, further research has indicated that the sensor output is linear up to powers of at least 140 W.

Schafer *et al* (2006) describe a measurements made by scattering the main ultrasound field and measuring the scattered signal with a large area pvdf detector, similar to the approach by Kaczkowski *et al* (2003). The purpose is to avoid placing a fragile and expensive detector in the ultrasound field. The scattering element was a fused silica optical fiber with a polyamide protective coating. The receiver, made from 25 µm thick, biaxially stretched pvdf with a Pt-Au electrode on the front surface, was a segmented, truncated sphere of 10 cm radius; the scattering element was positioned at the centre of the sphere. Each segment of the receiver has its own pre-amplifier. Initial tests of the system have demonstrated a receiver array

sensitivity of -279 dB re 1 μVolt/Pa (before preamplification), with a scattering loss at the fibre of approximately 39 dB, producing an effective sensitivity of –318 dB re 1 μVolt/Pa. The preamplifier boosts the signal to a range which is sufficient for the measurement of HITU transducers. The effective bandwidth of the system is claimed to exceed 15 MHz. The major problem with this configuration is that the wave travels 10 cm after it is scattered: in this distance high frequency components which are present due to nonlinear propagation in the wave incident on the fibre will be attenuated more than the low frequency components. Any frequency dependence in the scattering function must also be accounted for.

Zanelli and Howard (2005) have taken a different approach and developed a hydrophone which is protected from the risk of cavitation damage. The design consists of a miniature piezoceramic sensing element encased in a metallic coating twenty to seventy microns thick. They claim that the coating provides a smooth outer surface to minimize nucleation sites for cavitation, and its thickness is chosen to preserve the hydrophone's acoustic response while providing a level of "blast protection". From the data presented for the prototype design, the probe has a maximum sensitivity around 5 MHz and the response decrease by about 3dB/MHz between 0,5 MHz and 2 MHz, which is likely to introduce substantial uncertainties in determining absolute pressure values at HITU frequencies.

Maruvada *et al.* (2007) compared measurements of total power made with different radiation force balance targets. Total power output was restricted to less than 16 W by pulsing the transducers at a duty factor of approximately 10 %. Three absorbing targets of two designs (two ‘brush’ targets and one made from a high quality absorbing rubber (NPL, UK)) were used, and powers agreed for all targets to within the measurement uncertainty at all drive levels indicating that all three are suitable as absorbing targets. No evidence of cavitation (e.g., balance instability) was observed at the 500 Hz and 1 000 Hz pulse repetition frequencies used and a duty factor of about 10 %. The surface temperature of the targets was also measured: brush target temperature rises were less than a few degrees; the rubber absorber temperature rises were greater, with thermal damage occurring if it was placed near the focus. For the brush targets, no significant variation in measured power was seen for the transducer-to-target distances used.

Shaw (2006 and 2008) described the development of a reference device for measuring output powers up to at least 150 W. The use of castor oil in a container sealed with a thin, low reflection plastic membrane was found to make a satisfactory target with claimed uncertainty of less than ±10 %. He also presented a new method of determining incident ultrasound which is based on measuring the change in buoyancy of the castor oil volume when it is heated by the absorption of ultrasound. The method is claimed to offer potential advantages over the radiation force method because it is not sensitive to streaming or to the direction of the ultrasound. This method should be particularly useful for very strongly focused transducers (F-number less than 1,5) where measurement errors due to focusing in the radiation force technique become significant even for absorbing targets, or for systems with phased array or multiple transducers oriented at different angles to the vertical. The paper also analyses measurement errors in strongly focused fields and concludes that the use of conical reflecting radiation force balance targets is not recommended: absorbing targets are preferable provided that they are not damaged by exposure. Approximations based on ray acoustics were found to be useful for determining both corrections and additional uncertainty contributions for focused fields.

Jenderka et al. (2009) measured output powers up to 420 W using a radiation force balance equipped with an absorbing target placed close to the transducer. The stated uncertainty is 4.3 % (k=2). The ratio between acoustic output power and electrical net input power was found to be constant over the examined power range (100 W to 420 W). The dependency of the radiation conductance (ratio between output power and squared rms input voltage) on the transducer-target distance, investigated at low power levels (< 250 mW), showed no focal anomalies, except for an increased variation of the radiation force during sub-wavelength distance changes.

Optical methods can also be used to measure ultrasound fields. Such methods may involve the use of a fibre-optic hydrophone (Eisenmenger and Staudenraus, 1988; Wang *et al*, 1999;

Zhai *et al*, 2004) or the modulation of a laser beam *via* the acousto-optic effect in a water bath. In a fibre-optic hydrophone, a laser is directed along an optical fibre and the end of the fibre is placed in the ultrasound field. The reflection from the end is modulated by the acoustic pressure which changes the refractive index of the water adjacent to the exposed end. The internal reflection off the end of the fibre is monitored and can be quantitatively related to the pressure around the end. Devices of this sort were developed initially for use in lithotripter fields but have also been used recently in HITU fields (Parsons *et al*, 2006; Khokhlova, 2005). The reported advantages relate to the small diameter of the fibres, uniform directional response, broad bandwidth, and the low cost of the optical fibre (which can be damaged by cavitation but is easily repaired by re-cleaving). Disadvantages relate to poor signal-to-noise ratio, non-uniform magnitude and phase response in the frequency domain, and the effects of outgassing near the fibre tip. Alternative approaches also using optical fibres (Wilkens and Koch, 1999; Beard *et al*, 2000; Zhou *et al*, 2006; Lewin *et al*, 2005; Morris *et al*, 2009) have also been suggested and these may offer advantages over the Eisenmenger technique; however, they have not yet been tested in HITU fields.

Local density variations induced by the passage of an ultrasonic wave in water give rise to local perturbations in the refractive index. This acousto-optic effect can be utilised in a number of ways to perform optical measurements of the acoustic field. If the optical beam is allowed to enter a water tank, traverse the acoustic field and reflect back through the acoustic field from a mirror external to the tank, the interferometer will respond to the change in path length or the rate of change in path length. This acousto-optic effect is the basis of schlieren imaging but can also be used more quantitatively to perform non-invasive measurement of acoustic pressure using interferometric measurement techniques (Harland *et al*, 2002; Theobold *et al, 2004*). It is, however, a 'line-of-sight' technique so does not directly measure the pressure at a point: the pressure field must be reconstructed tomographically.

6 Discussion

6.1 General

This report concentrates on the requirements and potential future requirements for International Standards related to HITU. Only standards related to manufacture, market-access, Quality Assurance and safety are considered since these are generally the aspects considered by the standards bodies. Other important aspects such as standards for clinical practice are not addressed: these are more properly the preserve of professional clinical bodies. Many of the areas discussed in this clause will require substantial further research – either metrological or biological – before useful standards can be written. Clearly this research is essential and it should generally take place in the academic and commercial arenas and not within standards bodies. However, there can be benefit in producing 'pre-standard' publications such as Technical Reports or Technical Specifications, since these can focus attention on specific questions where a clear consensus is needed before advancing to a validated and widely-accepted standard.

6.2 Measurement of power

In ultrasound fields at megahertz frequencies, output power is typically determined by measuring the force on a target using a radiation force balance. However, the relationship between the radiation force and the output power is affected by the focusing or other geometrical aspects of the field, by the type and shape of the target, by the distance of the target from the transducer, by absorption (including 'shock-loss) in the water path, and by acoustic streaming currents. Highly focused fields created by large physical apertures and short focal distances typical in HITU applications require a more thorough accounting of angular contributions than those described in existing standards. Whilst many of these effects are small for typical diagnostic or physiotherapy ultrasound fields, they cannot generally be ignored for HITU fields. Furthermore, in HITU, the quantity of interest is the power incident on the patient rather than the output power at the transducer face. Since it is common for there to be a water stand-off between the transducer and the patient, attenuation and shock-loss in the water path may be significant and will vary depending upon the chosen distance.

Consequently, there is a need for a measurement method, including alternatives to the radiation force balance method which can determine the true acoustic power at any appropriate distance from the transducer and which can be used in strongly focused fields with acceptable accuracy. New approaches are also needed to cover a variety of cases such as those including moving sources, unusual configurations, intersecting beams or special combinations of electronically or mechanically scanned beams.

6.3 Specification of field parameters related pressure and intensity distribution

Definitions of field parameters in existing standards are generally related primarily to either a simple physical description of the ultrasound field or to safety. Some of these parameters which simply describe the field will still be relevant to HITU fields for 'engineering' purposes but they may not be the parameters which are most closely related to effectiveness or clinical performance.

For example, beamwidths are normally determined from the points where the temporal-average intensity falls to 6dB below the peak value in the plane. However, for short insonation times in which thermal conduction has only a minor effect on the temperature distribution, the temperature rise on the -6dB intensity contour is a quarter of the temperature rise on the beam-axis and the thermal dose is negligible (since, according to the Sapareto-Dewey model, it is exponentially related to the temperature). Hence it may be appropriate to determine a –1dB intensity beamwidth, for instance, instead of or in addition to the –6dB beamwidth. Alternatively, beamwidths below -6dB may need to be measured to account for sidelobes.

To take another example, the spectral distribution of intensity is not considered in any existing IEC definitions for diagnostic or physiotherapy fields. However, it has an important influence on the heating produced because the absorption coefficient of tissue is frequency dependent. There may therefore be value in defining an acoustic quantity related to the frequency-weighted intensity. Nonlinear effects need to be examined. Other new quantities could arise from the process of characterising a field at low output settings and then extrapolating to equivalent values at higher, clinical settings: for instance, Hill's proposed quantity I_{SAL}; or to the maximum sidelobe level along specified axes.

Those quantities which are appropriate to thermal effects and those appropriate to cavitation or some other mechanical effect in tissue should be considered.

6.4 Robust methodology for measuring pressure at a point

A validated measuring device and measurement procedure for determining the time variation of the acoustic pressure at a well-defined location is needed. The method needs to be robust with respect to damage from cavitation or thermal effects; it must also provide adequate spatial resolution and frequency response – the question of what is 'adequate' should also be specified within the standard. Any limitations due to, for instance, directional response, finite spatial dimensions, or imperfect phase and amplitude frequency response of the measurement system should be addressed also.

Membrane hydrophones with sufficiently small active elements may fulfil some of the requirements but are generally expensive and considered vulnerable to damage by cavitation.

Whilst it is often beneficial to drive the transducer in toneburst mode rather than continuous-wave to avoid acoustic interference and the risk of thermal damage to the measuring device or the transducer, it should be noted that the acoustic output may be sensitive to the temperature of the transducer and may therefore be different in toneburst conditions than in continuous operation.

The measurement capabilities needed to deal with the high harmonic content of these extremely nonlinear fields are also important. Severe distortion of waveforms in water as they relate to those in tissue need to be considered. Unlike diagnostic ultrasound field

measurements which are primarily axial, more complete field characterization away from the acoustic axis will be necessary.

6.5 Direct measurement of intensity

The relationship between pressure and particle velocity in wide aperture or multi-source fields needs to be studied since it is critical in predicting heating patterns from hydrophone measurements. A validated measuring device and measurement procedure for determining the acoustic intensity (rather than simply the square of the acoustic pressure) at a well-defined location would therefore be beneficial. The method needs to be robust with respect to damage from cavitation or thermal effects; it must also provide adequate spatial resolution and frequency response – the question of what is 'adequate' should also be specified within the standard. Any limitations due to, for instance, directional response, finite spatial dimensions, or other systematic effects within the measurement system should be addressed also.

In some fields of acoustics, it is possible to determine time-varying intensity using two closely spaced receivers to measure the pressure and particle velocity. This has not been successfully implemented at megahertz frequencies. In a monofrequency field, it is possible to determine time-averaged intensity from a measurement of temperature rise in materials of known acoustic and physical properties. Complications can arise due to enhanced heating near the thermal sensor, thermal drift and temperature-dependent physical properties amongst other influences.

As before, whilst it is often beneficial to drive the transducer in toneburst mode rather than continuous-wave to avoid acoustic interference and the risk of thermal damage to the measuring device or the transducer, it should be noted that the acoustic output may be sensitive to the temperature of the transducer and may therefore be different in toneburst conditions than in continuous operation.

There is also a different point of view in the literature supporting the measurement of pressure only (Nyborg, 1981; Cavicchi and O'Brien, 1984). In this perspective, the heat production rate, q_v, is proportional to pressure squared and not intensity as in the general case, if effects of shear viscosity are negligible. When the wave is plane, then intensity can be used, but otherwise pressure squared is to be used. To reconcile these different viewpoints, the measurement conditions most appropriate for the extreme conditions of HITU ought to be reconsidered.

6.6 Measurement of temperature rise and temperature distribution

A validated measuring device and measurement procedure for determining the temperature rise at a well-defined location or over a specified region is needed. Existing standards generally cover only steady state temperature effects. The method needs to be robust with respect to damage from cavitation or thermal effects; it must also provide adequate accuracy and spatial resolution – the question of what is 'adequate' should also be specified within the standard. Any limitations due to interaction between the ultrasound field (especially viscous heating, see for example Morris *et al*, 2008) and the measuring device, finite spatial dimensions, directional response, or other systematic effects within the measurement system should be addressed also. Since the temperature rise depends on the properties of the medium around the measurement point and between the transducer and the measurement point, consideration should be given to the specification of the medium (see separate item later). An additional complication that will need to be addressed is the effect of moving the beam through a pattern at a certain speed to obtain thermal coverage over a tissue region.

6.7 Thermal dose

Thermal dose relates tissue effects not to temperature, but to temperature history. The association between tissue time-at-temperature and thermally induced lesion formation (cell death; necrosis) is the most thoroughly studied dose relationship in therapeutic heating, and has been found applicable to predicting lesions in human and animal tissues across several

heating modalities (Dewhirst *et al*., 2003). In HITU, an advantage of using thermal history over "acoustic dose" approaches (e.g., base on intensity), is that the limitations on interpreting data attached to specific detailed acoustic parameters (frequency, peak intensity, beam dimensions, etc.) and experimental conditions (with or without blood flow, etc.) can be avoided because temperature captures an energy balance incorporating these parameters, and because of the well established link in the literature between time-at-temperature and tissue effects. The central difficulty of the thermal dose approach is that it depends on a knowledge of tissue temperatures (as discussed in 6.5) over the treatment time (e.g., through thermometric monitoring) or on prediction of them (e.g., computational thermal models).

The most widely accepted thermal dose relationship (from Sapareto and Dewey, 1984) is:

$$CEM_{T\mathrm{ref}} = \sum_{t=0}^{t=final} R^{(Tref-T)}\,\Delta t$$

where $CEM_{T\mathrm{ref}}$ refers to "cumulative equivalent minutes" at the reference temperature, T_{ref}, and R is a constant with different values for different temperature ranges. Based on a considerable body of biological heating studies, a reference temperature of 43 °C is most often used, i.e., the isoeffect dose CEM_{43}, or equivalent minutes at 43 °C, is found using the constant R= 0,25 for T < 43 °C and R = 0,5 for T > 43 °C (Dewey, 1994).

The data underpinning Sapareto-Dewey (S-D) dose relationships have been validated primarily with regard to "moderate temperature" heating regimes (42°C – 45°C) lasting from a very few minutes to over an hour. This has caused some to speculate about the validity of S-D dosimetry for the high intensity short duration acoustic doses typical of HITU. Significantly, S-D dose relationships have been successfully used, based on both thermal model prediction of temperatures, and on temperature monitoring, to predict HITU lesioning (creation, geometry and size) in various tissues. In in vivo animal studies using short (≈ 1 s to 10 s) HITU doses, Damianou and Hynynen (1994) and Damianou et al., (1995) predicted lesion dimensions rather well with thermal models using S-D dosimetry, especially where cavitation and non-linear acoustic absorption coefficients could be neglected. Using temperature monitoring with MR thermometry, spatially mapped accumulated thermal dose profiles have been shown to be predictive of the size and shape of coagulated tissue in humans (uterine fibroid ablation) using an isothermal dose value of CEM_{43} ≈ 240 min (Hynynen and McDannold, 2004). In fact, in a variety of tissues thermal dosimetry based on MR thermometry has been shown to be both predictive of the threshold for ultrasound tissue lesioning (Vykhodtseva *et al*., 2000; McDannold et al., 2000) and predictive of the size and shape of acoustically ablated tissue (Chung *et al*., 1999; Hazle *et al*., 2002; Kangasniemi et al., 2002; Hynynen and McDannold, 2004).

Thermal dose addresses both tissue safety and efficacy and, typically, these are competing objectives. The clinical goal of thermal ablation is to cause tissue necrosis inside the target, so efficacy requires delivering a thermal dose exceeding the lesion threshold (e.g., CEM_{43} > 240 min) in the target region, while keeping tissues well below this dose in non-target normal tissues. Other therapeutic focused ultrasound applications (where ablation is not the objective), will have different thermal dose requirements for efficacy. Thermal tissue modification (e.g., collagen shrinkage processes), increase in cell permeability (e.g., for drug and gene delivery) or cessation of bleeding (acoustic haemostasis) and such applications do not have ablation as the clinical objective, and may therefore have doses above or below those for ablation. Acoustic haemostasis, for example, involves localized acute thermal tissue injury (focal coagulation necrosis), as for other forms of cauterization, because it requires temperature ranges above 65°C. Thus, although necrosis is not the clinical objective here, it is an unavoidable by-product of efficacy. HITU safety objectives can also be more complicated than efficacy in that, in addition to avoiding excessive thermal dose in non-target tissue, it may also require limiting temperatures there to mitigate patient pain, not just non-target burns. Interestingly, Arora *et al* (2005) have demonstrated the feasibility of monitoring and controlling a HITU ablative treatment using S-D dosimetry to guide efficacy (i.e., the minimum CEM_{43} at the target) while maintaining upper limits on non-target tissue temperatures, not thermal dose, to assure safety.

Based on the significant data that supports S-D thermal dosimetry, and on the well defined methods used to calculate it, the standards development effort will likely involve refining some form of the Sapareto-Dewey dose formulation for specific HITU applications, but could also be supplemented by new thermal dose units based on new data. Under standards being developed in this effort, HITU thermal dose metrics should preferentially be validated for safety guidance (noting that thermal ablation thresholds apply also to efficacy). HITU treatment applications outside of ablation must be the subject of clinical trials and not of standards. In addition, practicality may limit the subject of dosimetry standards to a very finite number of specific tissues under specific treatment conditions and dose time ranges.

Following on from a defined term for thermal dose, a method would be needed for determining the dose at a specified location or mapping the distribution in a specified region including the effects of scanning.

6.8 Cavitation activity

Cavitation in tissue can assist thermal HITU treatment by enhancing tissue destruction, or it can hinder treatment by shielding the area of interest. Different treatment regimes may either aim to encourage cavitation or to avoid it altogether. Cavitation can be detected acoustically by the existence of subharmonics, harmonics, superharmonics or broadband signals: so far, there is no clear consensus on which feature or combination of features is preferable. Cavitation may also be seen on the imaging device which is associated with the HITU treatment system. However, there is no validated method for quantifying cavitation activity at megahertz frequencies or any definition of cavitation dose: both of these would be beneficial. Activity could perhaps be quantified in terms of number of cavitation events, or amount of released energy. Since the occurrence of cavitation depends on the properties of the medium around the measurement point and between the transducer and the measurement point, consideration should be given to the specification of the medium (see also 6.9 and 6.13).

6.9 Registration of the HITU field with the targeting system

In order to treat small lesions or to treat peripheral regions of larger lesions, it is essential that the ultrasound is delivered to the intended point accurately. A validated method to test this alignment would clearly be useful. Most likely, the method would involve some form of imaging phantom with a means for detecting temperature rise or acoustic pressure included within it.

6.10 Tissue-mimicking material for QA/engineering evaluation

There is a need for a widely accepted tissue-mimicking material for quantitative measurements of temperature rise or thermal dose, or cavitation activity for instance. It should be emphasised that the concern in this report is related to QA and engineering evaluation, not with finding a perfect substitute for bioeffects research. Consequently, reproducibility and lifetime are amongst the most important requirements. That said, to ensure that the engineering evaluation holds some relevance to either clinical performance or safety, the physical properties should not be too different to those found in the range of tissue.

Polyacrylamide gel has been quite extensively used as a method for visualising the focal region of a HITU field. With certain proteins added during the preparation, the gel changes from clear to white irreversibly when it reaches its transition temperature. However, its thermal properties are not well-matched to tissue and each piece can only be used once. In principle, a reversible colour change may be possible but has not so far been reported in the literature. There are two tissue-mimicking materials in existing IEC documents (IEC 60601-2-37 Ed1.1 and IEC 62306); both of these TMMs were designed to have thermal and acoustic properties typical of soft tissues and preparation methods are given in the referenced documents.

6.11 Electrical properties of the transducer

Electrical impedance and efficiency are important parameters for the transducer, as is the sensitivity to reflections or the acoustic environment in general. Measurement is not straightforward since the driving signal is often not continuous, the transducer is a complex reactive load and, in the case of phased arrays, is not even a single component. Methods for determining these and other relevant electrical properties should be specified or appropriate methods from electrical standards should be referenced. Because of the heating from large input electrical powers, changes in the properties of the transducer over time may need to be characterized. Because transducers are part of a system, system requirements and operation may need to be addressed.

6.12 Treatment monitoring

The ability to monitor transducer function and power delivery during clinical treatment would be valuable, as would the ability to compare these with the planned parameters. This would act as a warning in the event of excessive power delivery and potentially increased risk to the patient; it would also save time, money and discomfort by allowing the surgeon to immediately stop treatment in the event of a system malfunction. Most HITU systems have the ability to monitor changes in the treated tissue using either ultrasound or MRI, but individual patients vary greatly and an observed change which is either much faster or much slower than expected does not tell the surgeon whether the discrepancy is due to an unusual patient response or to a malfunctioning HITU system. Valuable additional information could come from appropriate monitoring of the transducer electrical characteristics and from an 'in-line' acoustic output monitor.

6.13 Equipment safety and essential performance

The IEC 60601 series of standards "General requirements for safety and essential performance" deal with electrical medical equipment. The parent standard is supported by collateral standards and particular standards; there are existing particular standards for physiotherapy equipment (IEC 60601-2-5), lithotripters (IEC 60601-2-36) and diagnostic and monitoring equipment (IEC 60601-2-37). If there are requirements related to safety (of the patient or the operator) or essential performance which are not adequately covered by the parent or collateral standards, these should be addressed by a new particular standard.

The particular standard should not only address issues directly related to ultrasound. For instance, it may be appropriate to address electrical safety issues caused by the use of RF amplifiers in close proximity to water baths for extracorporeal HITU systems, or of excessive electrical interference between the treatment and targeting parts of the system. Some aspects of the targeting systems associated with HITU may be adequately covered by IEC 60601-2-37 or by the particular standard for magnetic resonance equipment (IEC 60601-2-33). These should be referenced where possible. Under discussion are ways of conducting risk analysis for the system and major parts of the system.

6.14 Tissue properties

For modelling and treatment planning, it is important to have accurate values for the properties of different tissue types. Amongst the important properties are: speed of sound, attenuation, absorption, nonlinearity parameter, thermal conductivity and heat capacity; all of these are in principle dependent on temperature and some are dependent on frequency also. Whilst there are quite well established methods for measuring these quantities in, for instance, plastics, values reported in the literature for tissues show a wide variation. It is not clear how much of this variation is due to real variation within a single piece of tissue, or between different tissue samples of the same type and how much is due to the problems of acquiring, storing and preparing tissue samples. More information is needed and this would be greatly assisted by establishing validated methods where the source of uncertainty and error are well understood.

7 Recommendations

7.1 Items for immediate development

7.1.1 General

There are some topics where existing knowledge appears sufficient to produce a Committee Draft within approximately two years. Consequently, following recommendations made in draft versions of this Technical Report, three New Work Item proposals have been prepared and submitted as enumerated in 7.1.2 to 7.1.4. More detailed discussion of all the technical topics can be found in Clause 6.

7.1.2 Measurement of total output power as an International Standard or as an amendment to IEC 61161 Ed.2 in TC 87

This will include both radiation force and other measurement methods and should provide guidance on procedures for measuring phased arrays and the wide range of transducer geometries (E.g. radial outward firing, or cylindrical inward firing). The New Work Item proposal was submitted and approved in October 2007 as future IEC 62555 (Ultrasonics − Power measurement − Output power measurement for High Intensity Therapeutic Ultrasound (HITU) transducers and systems). The current intention is that this will become a separate International Standard.

7.1.3 Specification and measurement of field parameters as a Technical Specification (TS) in TC 87

Use of a TS was preferred as there is insufficient knowledge at present to write a full standard and the TS can be replaced once we have more experience. We anticipate that this TS will describe the measurement of fields at relatively low output levels and will include consideration of sidelobes/forelobes, moving transducers, and a definition of 'Thermal dose'. The New Work Item proposal was submitted and approved in October 2007 as future IEC 62556 (Ultrasonics – Surgical systems – Specification and measurement of field parameters for High Intensity Therapeutic Ultrasound (HITU) transducers and systems).

7.1.4 Equipment safety and essential performance as a Particular Standard in the 60601 series in TC 62.

This would benefit from input from SC 62D members. It should include specific issues where the general IEC 60601-1 standard is not appropriate or not sufficient: such as targeting accuracy, monitoring method for delivery, display of output or anticipated effect in some way, accuracy of temperature display, interaction of imaging with therapy beam; and it should provide guidance on management of risk specific to HITU. The New Work Item proposal was submitted and approved in September 2008 as IEC 60601-2-62 (Medical electrical equipment – Part 2-62: Particular requirements for basic safety and essential performance of high intensity therapeutic ultrasound (HITU) equipment).

7.2 Items for development within 5 years

7.2.1 General

Other topics require further development validation but appear to be sufficiently advanced to produce a Committee Draft within approximately five years.

7.2.2 Robust method of measuring pressure

If the method is a simple variation on common hydrophone measurements, this may be included as an amendment to one of the existing hydrophone standards. However, it may be more convenient to produce a separate document or to include the method description within the document which specifies the field parameters (see 7.1.3).

7.2.3 Measurement of temperature.

The measurement of temperature could be combined with measurements for items 7.2.4 and 7.2.5 below.

7.2.4 Electrical properties of therapeutic transducers

This broad topic includes a consistent description of transducer electrical and electro-acoustic properties and how these characteristics can change under typical drive (and temperature) conditions. Typically transducer requirements and descriptions are related to system requirements; therefore, universal means of measurement under specified load conditions may need to be devised. At the present time there is not a suitable standard for piezoelectric transducers, even for diagnostic applications; therefore generating a standard may take longer than two years.

7.2.5 Registration of the HITU field with the targeting system

See 7.2.3 above.

7.2.6 Tissue-mimicking material for QA/engineering evaluation

See 7.2.3 above.

7.3 Items requiring extensive further research

A number of other important topics appear to need extensive research before any standards would be desirable. These include:

a) measurement of intensity (rather than simply pressure squared);

b) measurement and mapping of cavitation activity;

c) monitoring equipment output during clinical treatment;

d) determination of tissue properties.

Annex A
(informative)

Detailed responses to questionnaire

The following tables contain the answers returned in response to a questionnaire sent initially to attendees of the 2003 International Society of Therapeutic Ultrasound (ISTU) meeting, which was held in Lyon, France. Further to this circulation, the questionnaire was handed out at the September 2004 ISTU meeting in Kyoto, Japan, and at the October 2004 meeting of Technical Committee 87 (Ultrasonics) of the International Electrotechnical Commission (IEC) held in Hangzhou, China.

Answers are compiled here for each question as they were received, except that obvious typographical errors have been corrected where necessary and modifications have been made to the presentation to provide some uniformity of presentation. Many replies were received in text email form, which preclude complex formatting of symbols etc In general, the formatting of symbols and individual terms has not been changed. Abbreviations and acronyms have not been expanded. Some acronyms used in the replies are: TAP = total acoustic power; ISTU = International Society for Therapeutic Ultrasound; ESWL = extra-corporeal shockwave lithotripsy; MRgFUS = magnetic resonance-guided focused ultrasound surgery; FL = focal length; ISPTA = spatial-peak temporal-average intensity; pvdf = polyvinylidene fluoride; cw or CW = continuous-wave.

Questions are divided into three sections:

- your application;
- your existing measurements;
- your perceived needs.

Names of companies and individuals have been removed to ensure anonymity.

A.1 Section A. Your application

A.1.1 What is your current involvement in therapeutic ultrasound?

C R&D on HIFU for hemostasis and tumor treatment

D New applications of HIFU

E Local therapy of prostate cancer

F Fundamental research of the relevant acoustics (nonlinearity, heating, cavitation, etc.)

G Research

H Research in thermal ablation with interstitial applicator

I Both for therapy and diagnostic applications. Have designed system for ESWL (Lithocut). Currently also interested in very high frequency ultrasound.

J Project Director, *[name removed]* – currently for hemostasis to prevent short-term exsanguination of victims of trauma

K Developing therapeutic ultrasound equipment

L *[name removed]* is developing a system to ablate cardiac tissue for the treatment of atrial fibrillation.

M High intensity focused ultrasound for the treatment of localised prostate cancer using the *[name removed]*

N Basic research on ultrasound-tissue interaction;
Patient treatment: HIFU therapy of breast cancer, MRgFUS

O Our group is developing interstitial ultrasound heating applicators for MRI-guided thermal therapies.

P Manufacturer

Q Design and development of medical products to treat cancer that use high intensity focused ultrasound
Research and development of systems, applicators, software, electronics, signal processing, etc. for the medical applications of high intensity focused ultrasound

R Theoretical field modelling, thermal conduction

S HIFU hemostasis of solid organ incisions and occlusion of blood vessels (rabbit and pig model), HIFU hemostasis in the presence of ultrasound contrast agents

T Tumor treatment, drug delivery

U Specific research topics: active research in passive acoustic monitoring of lithotripsy + research into acoustic activation of contrast agents.
General interest in topic esp. HIFU + bioeffects of ultrasound resulting from cavitation.

V The use of extracorporeal shockwave lithotripsy to treat kidney stones. We do use both a clinical and bench-top lithotripter. The aim of our project is the monitoring of the treatments, we do not treat patients ourselves.

W Development of HIFU apparatus and clinical trial

X *[name removed]* is a specialist company in researching, developing, designing and manufacturing ultrasound therapeutic systems. The commercialized products of the company are now used to treat some solid malignancies and gynecological diseases in humans.

Y Development; manufacturing and sales of HIFU equipment (*[name removed]*)

Z Member ISTU committee
Honorary Professor at *[name removed]*
HIFU
Sonodynamic therapy
Transdermal drug delivery

AA clinical research projects @ UW

BB Design and manufacturing transducers

A.1.2 What is the therapeutic mechanism (eg cavitation, thermal…)?

C Both thermal and mechanical mechanisms
D Thermal
E Cavitation + thermal ablation/coagulation
F My studies currently involve cavitation, propagation modelling, linear heating mechanisms, and bubble-enhanced heating mechanisms
G Thermal and cavitation, possibly radiation force in vascular occlusion
H Thermal ablation
I In ESWL both cavitational erosion and “elastic blast”. We have been investigating both thermal effects and impulse forming in cavitation.
J Whatever works – different for different tissues and tissue motion.
K Thermal
L The mechanism is thermal.
M Thermal and cavitation
N Patient treatment: thermal
Research: thermal, cavitation and other mechanical effects
O Thermal (primarily)
P Mechanical Disruption and Cavitation
Q Thermal, cavitation
R Thermal
S Both thermal and cavitational
T Nonthermal-cavitation
U Cavitation in my specific research topics, but my general interest covers thermal. Also formation of stable bubbles (outgassing) – see below (B4)
V The therapeutic effect are the fragmentation due to direct stress of the shock and the indirect erosion by cavitation.
W Thermal ablation
X Heat produced by focused ultrasound in biological tissues.
Y Thermal and cavitation
Z Cavitation
AA Primarily thermal/hemostasis
BB All types of mechanism

A.1.3 What ultrasonic power level range are you interested in?

C 50 W and greater
D 10 W -100 W
E 20 W -70 W
F Anything below 1 kW/cm^2
G Low fu ((1 500 to 2 500) Wcm^{-2} *in situ*)
H Less than 50 W/cm^2
I We work from mW to MW per sq cm.
J As much as we can get
K 500 W – 5 000 W cm^{-2}
L 50 watts
M Details from *[name removed]*
N Patient treatment: in MRgFUS approx. 20 Wac - 70 Wac
Experimentally from 0,1 W up to 300 Wac
O We are delivering between 7 W – 10 W of acoustic power per element (typically 3-5 elements)
P 80 W input

Q 0W to 100+W total acoustic power.
R Power = x*100 W, intensity 500 W/cm^2 – 2 000 W/cm^2
S 80 W - 100 W of acoustic power, *in situ* intensities of (1 000 to10 000) W cm-2
T Diagnostic to HIFU
U I am not that happy working in powers, because of time-averaging issues – I keep to pressures, pulse lengths & prfs
V Power levels up to 100 MPa per 10 µs
W 300 W cm^{-2} and less
X 0 W ~ 500 W
Y 30 W to 60 W (acoustical power)
Z (2 to 4) Wcm^{-2}
higher for HIFU
AA 000 W/cm^2 – 5 000 W/cm^2
BB Up to 1 000 W

A.1.4 What frequency range are you interested in?

C 2 MHz – 7 MHz
D 1 MHz – 4 MHz
E 2,25 MHz – 3,5 MHz
F Anything below about 10 MHz
G 0,8 MHz to 3 MHz
H 1 MHz – 20 MHz
I Approx. 0,5 MHz to 5 MHz and the 1 GHz range
J 0,5 MHz to 5 MHz
K 1 MHz –12 MHz
L 5 MHz –10 MHz
M 3 MHz – firing transducer
N 0,5 MHz –3 MHz
O 4 MHz –10 MHz
P 20 kHz – 36 kHz
Q 500 kHz to 10 MHz
R 500 kHz to 5 MHz
S 1 MHz – 6 MHz
T 0,2 MHz – 2,0 MHz
U 0,5 kHz to 5 MHz
V The pulses have a repetition frequency of 1-2 per seconds and a main frequency component of 0,15 MHz
W 1,0 to 2,0
X 0,2 MHz ~10 MHz
Y 3 MHz
Z 20 kHz – 40 kHz
1 MHz – 3 MHz
AA 1 MHz – 5 MHz
BB From 150 kHz up to 20 MHz

A.1.5 What acoustic pressure range are you interested in?

C 1 MPa and greater
D
E ?
F Anything below about 60 MPa peak pressure
G No idea
H Less than about 1 MPa
I
J See A3
K --
L
M Details from EDAP – Technomed
N 0 MPa -15 MPa
O
P Na
Q See A3
R See above
S I usually work in terms of *in situ* intensity not pressure
T 0,5 - 5 MPa
U 40 Pa (e.g. Faraday waves on bubbles walls enhance mass transfer of bubble contents to exterior) up to 100 MPa (lithotripsy)
V 10 MPa -100 MPa
W
X To tell the truth, I don't have any idea about it, because I have not tested it directly before.
Y 10 bar to 300 bar
Z Do not know
AA
BB Up to 10k bar

A.1.6 What exposure mode are you interested in? E.g. pulse length, tone burst, cw.

C CW, tone bursts, and pulses
D 1s - 30 s bursts separated by blanks intervals
E Pulse length: 4 s; 4,5 s or 5 s.
Pulse delay 5 s, 7 s or 12 s
F All of them: CW, long pulse, short pulse, low duty cycle
G CW (possibly pulsed if interleaving imaging with therapy)
Is the image guidance an issue since this could be Doppler?
H CW
I CW and pulse mode down to ns.
J Any or all
K CW, tone burst
L Intermittent CW
M 4 s to 5 s
N Patient treatment: cw , (1 to 9) s.
Research: any form and length
O CW (primarily)
P Continuous and pulse

Q Short pulses (~1 ms) to CW exposures extending to several minutes
R Pulsed mode, 1 s – 5 s
S CW, and pulse mode (duty cycles of 25 % - 90 %), pulse length of about 100 ms
T Pulsed
U From cw to micro-second duration pulses
V Tone burst
W 5 s to 15 s
X PW and CW
Y 1 s to 10 s burst
Z Do not know
AA Short pulses <1 s >1s, cw
BB All types of exposure modes

A.1.6.1 What transducer size and f-number or focal length are you interested in?

C 1 cm < aperture < 10 cm
0,8 < f-number < 1,8 (f-number is focal length/aperture width)
D 3 cm -10 cm diameter and FL
E F = 40 mm Focal length 19 mm – 25 mm
F Order 2 cm - 6 cm diameter, order f-1
G Diameter: 8,4 cm, 11,5 cm, 3,5 cm
Frequency: 1,7 MHz, 1,7 MHz, 2,4 MHz
H Flat transducer, ~1 cm^2
I Approx. 30 cm for ESWL.
J See A6
K Size: 5 mm to 125 mm.
F#: 0,75 to 2
L Proprietary
M Focal length: 40 mm of firing transducer
N Clinically typical: Ø60 mm, focal length 68 mm
research: a lot of different transducers
O Our transducers are small (4 mm × 10 mm) and are planar (unfocused)
P NA
Q Size: application specific; from a few [mm] aperture to many [cm]. Typically, around f/1
R 4 cm – 10 cm dia, 3 cm – 20 cm focal length (radius of curvature)
S Transducer diameters of 2 cm – 7 cm, focal lengths of 3 cm – 7 cm, f numbers of 0,9 – 1,4
T Normally 2 cm - 5 cm size and 1-2 f number
U 2 cm diameter up to 10 cm diameter, but mostly 2 cm diameter for projector (and as small as I can get for the receiver)
V The bench-top lithotripter transducer has a focal length of 10 cm and a diameter of circa 20 cm. While our diagnostic sensor is broadband (up to 100 MHz) and has a diameter of 2 cm.
W 1) 10 cm or less for intra-operative use
2) 15 cm or more for extracorporeal use
X Emission aperture ≤250 mm
Focal length ≤250 mm
Y Diameters: 30 mm to 60 mm
Focal length: 30 mm to 60 mm
Z Do not know
AA Varies, 3 cm -15 cm

BB All sizes and F number, in practice up to 300 mm in diameter, down to F number 0,5

A.1.7 Is there a particular exposure geometry that makes calibration difficult in your application?

C Perhaps transvaginal applications for uterine fibroid treatment

D Focused fields are difficult to measure

E ?

F No

G Extra corporeal – horizontal or vertical
Transrectal device could be difficult

H No

I

J Yes, but we don't know what it is yet. Multiple independent beams will present a problem.

K NA

L No

M Prostate glands > 50 mls; Rectal wall thicker than 6 mm

N We have built up a special phantom for quality assurance. This thermocouple-based system is dedicated for the special geometry of our setup..

O The small transducers are difficult to measure output power from. At lower frequencies the beam becomes divergent and it is difficult achieve repeatable measurements.

P NA

Q No

R NA

S Not currently

T Any standing waves

U *In vivo*! Procedures for derating broadband/impulsive and nonlinear fields seem to be inadequate

V Not in the bench-top lithotripter

W No

X Yes

Y Long and high power burst that make cavitation on the measurement equipment (hydrophones)

Z Cavitation presents a problem for calibration

AA

BB Small F number transducers, with array pattern are the most difficult to calibrate

A.2 Section B. Existing measurements

A.2.1 How do you routinely test that your equipment is working properly?

C Tissue mimicking phantoms

D Power calibration in water tank. Accuracy checking by targeting and exposing a slab of acrylic (see B4)

E Automatic self-control included in *[name removed]* by *[name removed]*

F We test when something doesn't "look" right.

G Force balance (~weekly), might use pyrosensor in future.

H Force balance, pressure field measurements

I ESWL pvdf and model stone fragmentation

J Beam maps via hydrophone & and force balance. Water fountain gives a quick check.

K Use engineering test and measurement equipment – oscilloscopes, impedance meters, hydrophones, function generators, power amplifiers, TAP meters etc.

L Burn test materials under known exposure conditions

M Six monthly recalibration of the firing transducer

N Patient treatment unit: In general, test of components. After a defined time span we measure the pressure field and electrical and acoustic power. See B5
To test the function of the setup routinely before treatment: We use a special phantom adapted to the setup. It is based on thermo couples at different positions. Herewith we can test the positioning of the transducer and the output of the transducer. Sometimes we use thermo sensitive foils to visualize the focus position.
During operation of the therapy setup:
In our treatment setup we have integrated a permanent SWR (standing wave ration) measurement, to control transducer matching and to detect short cuts or a broken RF-cable. In addition the applied electrical energy is measured and compared with the pre-selected values (pulse duration and electrical power). We use an additional timer to control pulse length. In addition we get the MRI temperature information
Experimental: At regular intervals we test the transducer and the equipment, see above. During operation we control the SWR and sometimes induced temperature by MRI or small thermo couples.

O Radiation force balance measurements, impedance spectrum measurements, MR thermometry during heating

P Reserve power = Full load -Quiescent is the best indicator

Q Total acoustic power measurements, HIFU phantoms

R NA

S *In vitro* testing in tissue mimicking phantom, electrical power measurements, radiation force balance, beam plots, schlieren imaging

T Aim at surface of water bath

U Secondary standard hydrophone measurements every 6 months for work at *[name removed]*. Note that at *[name removed]* I do not do ANY clinical or clinical-related work. I do theory and some lab work. The clinical and *in vivo* work is done at *[name removed]*, I will forward this questionnaire onto *[name removed]* to ask her how she looks into the equipment at *[name removed]*.

V Direct measure of the shockwave on a scope with the electromagnetic source at a set energy level

W Thermal degeneration of plastic cup in water vasen

X A full-scale absorption method is used to measure the output value of acoustic power, and a cymometer is used to measure the working frequency.

Y Calibration procedures included in the manufacturing process: US beam geometry, acoustical power measurements, burning test, electrical controls (impedance matching)

Z Calorimetry

AA

BB Using force balance and absorbent targets + low intensity beam pattern measurement in water tank.
Yes, however our measurements are not Fully traceable which makes sometimes difficult to compare results with measurement mode in other labs.

A.2.2 How do you currently determine the effectiveness of the therapy in your application?

C Biological effects (i.e. gross and histological examination, physiology, function)

D Pathology and tumour reduction using ultrasound imaging and bettering of clinical signs / biology

E PSA percourse, biopsies of prostate and cystoscopy

F All our work is done in phantoms.

G Gels – temperature measurements
Ex-vivo expts – visual inspection
Clinically – histology or MR scans

H Image guidance (US, MRI), temperature measurements with thermocouples and macroscopic examination of treated sample when possible

I

J Visual result on phantom, and histology

K Still at engineering development stage

L Animal experiments, canine model

M PSA testing, and post treatment biopsy

N Patient treatment and animal trials:
MRI Monitoring: T1 weight and T2 weight morphology to monitor the changes in the tissue. In addition after US-therapy contrast enhanced T1w images to image the perfusion stop.
MRgFUS breast study (interrupted at the moment): open surgery ca. 5 days after HIFU. Histology of resected tissue

O MR imaging

P Tissue aspiration is visually verified. Sample cores establish margin

Q PSA, biopsy.

R Calculated temperature rise, or NA

S Measuring time needed to achieve hemostasis, Observation of vessel occlusion/ hyperechoic region using Doppler mode/B-mode imaging during therapy, gross and histological analysis

T Tumor progression, sonoporation

U I do not do any therapy work at *[name removed]* – I will forward a copy to *[name removed]* (see above) and ask her to send you details of how she does it for us.

V It is the aim of our project to develop a diagnostic method

W Histological examination of target area

X The grey scale changes of ultrasonographic images of the treatment region before and after treatment are used to evaluate the therapeutic effect. In follow-up process, imaging methods such as MR and CT images are used to assess treatment effect, comparing with images before treatment.

Y Control of the electrical power supplied to the transducer (direct & reflected).
Patient follow up (biopsies, PSA level)

Z N/A

AA Observation, pathology

BB We do not work on this aspect

A.2.3 Which parameters do you generally quote to describe your fields?

C Acoustic intensity and duration of exposure

D Electrical & acoustical power; transducer size, focal length

E Number of lesions

F Peak positive and peak negative pressure, pulse duration, duty cycle, frequency

G Ispta (*in situ* or free field), exposure duration

H Frequency, ultrasound intensity (W/cm^2), transducer dimensions

I

J Intensity contours & total power, frequency, duty cycle

K Frequency, intensity, beam shape, focal spot size, depth of field

L Intensity, focal spot size

M Prostate dimensions

N If we use a fixed-focus transducer with a regular formed focus geometry (elliptical) we give the parameters values of the transducer (numerical aperture, focal length) and the (-3dB or -6dB) focus dimensions (length and diameter). In addition we quote the maximum intensity ISPTA of the focus and/or the applied acoustic power.
If we have irregular focus geometry, e.g. use of phase shift lenses or from a phased array, we quote the acoustic power and the transducer parameters, but not the ISPTA value.

O Total acoustic power (W)

P Max and Reserve Powers. Standards indicate that we should quote acoustic power but empirical results indicate that the acoustic power has little to do with efficacy.

Q Total acoustic power, -6 dB beam width/length, location/magnitude of sidelobes, low-power field plot, simulation results

R Intensity, pressure amplitude

S *In situ* intensity, exposure time, duty cycle, cross-sectional area of the focus

T Frequency, focal diameter, peak rarefactional pressure amplitude, pulse parameters

U I give a graph of the pulse profile (pressure/time history) with an indication of pulse repetition frequency. Note however that I can afford to give this amount of detail as I seldom have to quote these outside journal papers and conference presentations. If forced to make a quotation verbally, I give peak positive/negative pressures, pulse length and fundamental frequency, and pri because I very seldom talk to non-experts, so they know, for example, what a lithotripter pulse should look like.

V Amplitude, duration time of occurrence

W Histological classification of the ablated area

X They are –6 dB focal region, focal length, acoustic power and first side lobe.

Y Beam geometry, transducer efficiency (ratio between acoustical power and electrical power)

Z W cm^{-2} or W cm^{-3}

AA

BB Acoustic pressure. Acoustic intensity

A.2.4 Do you currently use a phantom? If so, what type of phantom and for what purpose?

C Yes, Bovine Serum Albumin embedded in Polyacrylamide

D Target for accuracy checking

E Water bath for calibration test, no phantom clinically available

F We use agar & graphite phantoms (for heating experiments) and transparent acrylamide gel phantoms (for visualization)

G Ex-vivo liver – phantom of clinical tissue
Gel – perfusion phantom
Perfused liver – clinical phantom
In vivo expts – human phantom

H No

I In our research from time to time

J Liver from a butcher; to confirm thermal dose.

K No

L Yes. Phantom is used for imaging and HIFU testing

M No

N We use phantoms to mimic tissue. To observe lesion formation or to measure temperature.
Agar-, gel- or polyacrylamide based phantoms

O Yes. Comprised of polyacrylamide gel with dissolved BSA to mark region of thermal coagulation

P No

Q Yes
Rubber phantom (for R&D investigations), acrylic phantom (for evaluation of device parameters)

R NA

S We use BSA-polyacrilamide phantom as a tissue mimicking phantom. Purpose: to determine position, size and shape of the lesion at different ultrasound parameters. To test the equipment (determine focus at the ultrasound imager screen) before *in vivo* experiment.

T No

U No, as I have no such projects, but I am pressing for 2 phantoms to be developed, and am actively seeking research funds for (in confidence): *[details removed]*

V Yes, we do use kidney stones phantoms and soft tissues phantoms.

W Use but not routinely

X No

Y No, but still looking for an appropriate phantom.

Z N/A

AA Use gel phantom, targeting & lesion size

BB We currently do not use phantoms, but would like to use them if reproducible and quantitatively relevant.

A.2.5 Briefly describe the equipment and method you use to measure pressure, intensity or power

C Standard needles hydrophones, and radiation force balance

D Ultrasonic force balance for total power + hydrophone for acoustic field plotting

E ...ask *[name removed]*, clinically not available, we have to trust that the internal security circuits work properly

F We use a pvdf membrane hydrophone and short pulses (low duty cycle) in a water bath. We do not exceed a peak positive pressure of 3 MPa during calibration. We assume electromechanical linearity thereafter and use a propagation code to account for nonlinearity

G Reflective target force balance (in house) and membrane hydrophone (0,5 mm diameter, Marconi)

H Calibrated “golden lipstick” hydrophone for pressure measurements and force balance with an absorbing material for intensity. Electrical power measured with a 2-channel wattmeter

I Tektronix DSA, needle shaped pvdf hydrophones etc.

J Liquid crystal sheet.

K Ultrasonic test tank, calibrated hydrophone and TAP meter

L Power in measured using an absorbing balance. Intensity is measured using a calibrated hydrophone but with the excitation amplitude reduced by a known amount. This avoids destroying the hydrophone.

M Built into the *[name removed]*

N We measure the ultrasound field with calibrated hydrophones, positioned by a computerized scanning mechanism. These measurements are performed at low power levels to avoid heating of the hydrophones. Thus we get the field geometry of the transducer source and by integration of the whole ultrasound field the acoustic output at low levels.
In addition the total acoustic outputs of the transducers are measured with a radiation force balance.
Thus we have the pressure field, the acoustic power. We calculate the intensity (Ispta)

O Pressure measured in hydrophone tank with bilaminar membrane hydrophone.
Power measured with radiation force balance using conical reflector

P Mechanical amplitude
Quiescent power and power under full load

Q Calibrated hydrophone, TAP meter

R NA

S Electrical power: Electrical power meter (forward and reverse powers)
Acoustic power: Reflective radiation force balance
Acoustic power: Absorptive radiation force balance
Focal area (-3 dB, – 6 dB): Ultrasound field mapping (pressure field)
Intensity: Acoustic power/ focal area (-3dB)
Pressures are usually not measured.

T Calibrated membrane hydrophone

U Currently hydrophone (membrane or needle) in degassed water (as my method is to quote a pressure time history (see above, B3)). I have issues regarding derating though (see above, A8).

V The pressure is measured using a membrane hydrophone placed at the focus of the benchtop lithotripter.

W

X The acoustic pressure cannot be measured directly by hydrophone under high power output. So we use a hydrophone to measure the acoustic pressure under the low power output to get the distribution of the acoustic field.

A full-scale absorption method is used to measure the ultrasonic radiation force of the running transducer, and the acoustic power and intensity are drawn by theoretical deduction.

Y Pressure: hydrophones (ONDA corp or others)
Intensity: Field mapping (Marconi hydrophones)
Power: Balance with absorbing or reflecting targets

Z Difficult with high power

AA

BB B5: Acoustic power is measured with force balance. Pressure and intensity are measured with hydrophones.

A.2.6 Briefly describe the equipment and method you use to measure heating, cavitation or other relevant effect

C Thermocouples, passive and active cavitation detectors

D ***confidential***

E See above

F Heating: 125 micron thermocouples with temperature artefact correction.
Cavitation: a focused active cavitation detector operating at greater than 15 MHz or a focused passive cavitation detector whose output is high pass filtered above 2*Fo. We use a microscope and camera to visualize cavitation fields in transparent phantoms (measure Rmax and the bubble field geometry).

G Fine wire thermocouples
PCDs
Force balance – radn force

H For heating: thermocouples
Gel – perfusion phantom

I Microscope, stroboscope etc.

J Intensity contours calculated from hydrophone measurements. Power via force balance.
Visual results. Doppler blood flow to measure coagulation in rabbit ear vessels.
Liquid crystals films. Headed for passive and active cavitation detection, streaming/tissue displacement, harmonic generation, thermocouple temp. measurement..

K Heating: Thermocouples

L

M We do not, other than ultrasound imaging

N Heating by MRI or with small thermocouples.
To monitor cavitation we have the ability to detect sub-harmonic signals with hydrophones and a frequency analyzer.

O Heating measured with MRI (thermal imaging)

P Mass of tissue aspirated per minute

Q Thermocouple arrays

1D and 2D RF data acquisition

R NA

S Heating: Thermocouples connected to a scopemeter
Cavitation: Passive cavitation detection

T Cavitation by nonlinear emissions.

U I have not studied heating experimentally. For cavitation I employ a range of sensors, depending on the environment: sonochemical, luminescence, acoustic emission, occasionally erosion (although quantification using erosion is misleading).

V Cavitation is measured indirectly through the recording of the bubble acoustic emissions at the shock-bubble interaction

W

X A thermocouple is used to measure the temperature rising in biological tissues after being irradiated by an ultrasonic beam, and to study the relationship between the temperature changes and shape and size of coagulative necrosis.

Y Heating: Thermocouple (not used in current clinical use of the *[name removed]*).
Cavitation: ????

Z Simple calorimetry using thermocouples/thermistors

AA

BB We do not measure these parameters at the moment.

A.3 Section C. Perceived needs

A.3.1 What characteristics of the u/s field do you think are important for effective therapy in your application?

C 3-dimensional beam plots

D Power concentration

E Correct overlapping of the single lesions and treatment blocks. Low cooling by blood flow

F Good cavitation noise diagnostics. A non-invasive way to measure temperature in real time.

G *In situ* intensity or temperature

H Frequency, ultrasound intensity (W/cm²), exposure duration, transducer dimensions

I Frequency spectrum is essential

J Intensity contours & frequency.

K Frequency, intensity, beam shape, -6 dB focal spot size, -6 dB depth of field.

L Intensity and duration at a given frequency

M Small gland close to rectal wall

N HIFU, FUS: Frequency and pressure field distribution in the focal area and maximum pressure or maximum intensity or total acoustical power. Pulse length and pause time.

O Reliable output power, stable efficiency

P Mechanical size

Q TAP, HIFU duty cycle, placement of focal spot, focal spot size

R Time and temperature

S Thermal, cavitation, radiation force (for blood vessel occlusion applications)

T Penetration and uniform coverage

U Usually cavitation (given my specific research applications of lithotripsy and contrast agent activation). Hence peak positive/negative pressure, fundamental frequency, prf and spatial distribution of the sound field (e.g. focusing, local maxima caused by reflections etc.) are important. However the formation of bubbles through outgassing is becoming more prominent (see e.g. B4, and possibly HIFU).

V Amplitude

W Liver surgery and other organ tumors

X We think the key parameters influencing the therapeutic ultrasound are size of a -6 dB focus, the level of the first side lobe, working frequency, acoustic intensity/power, and the focal length.

Y Beam geometry

Acoustical power

Z Uniformity at point of application

AA Accurate targeting & intensity

BB This is defined by our clients. It seems that intensity and pressure are the most important.

A.3.2 Do you feel you are able to characterise your equipment or the u/s field satisfactorily? If not, what do you perceive to be the shortcomings of your existing measurement methods?

C Our current characterization is based on 2D beam plots. 3D plots are certainly desirable.

D Shortcomings:
a) directional sensitivity of hydrophones. One cannot reliably calculate the total power from the acoustic fields.
b) Because of non linear effects, the fields are measured at lower powers than emitted during the treatments.

E I am working clinically and not in technical development.

Physical characterisation of the acoustic field is not necessary for me.

F Yes – at least in the phantom experiments

G Characterisation in terms of repeatability is good, but in terms of absolute values is probably only within 20 %.

H Power measurements are difficult to perform. The results we get with the force balance are sometimes questionable.

I Difficult task, non-linear effects etc.

J Yes, but not from manufacturer's data.

The most basic shortcoming is non-linearity in water. A measurement fluid in which non-linearity doesn't occur, or is repeatable and predictable up to very high intensities, would help.

K Not enough data yet.

L Yes we can characterize the fields adequately.

M Yes in the majority of cases

N I think we have enough information to characterise our equipment.
Problem: hydrophones and their calibration are expensive.

O Generally happy. The biggest shortcoming is with respect to our uncertainty in output power measurements (currently about 5 % - 10 %)

P Yes – The mechanical systems are analyzed by fundamental equations and finite element. Stoke, power, and resonant frequencies are easily measured.

Q Yes

R NA

S So, so. Shortcomings in determining the peak intensities, and actual pressures.

T Mostly yes, but transfer of water measurements to tissue needs work. Knowledge of expected temperature, finite amplitude effects and cavitation initiation would be valuable.

U OK at present, given that I can almost set my own tolerances as I am able to define the problem on which I work – which is not the case in clinical work to such an extent. However if I were using 80 MHz I would be very concerned at ability to find a suitable hydrophone.

V Enough

W Monitoring the tissue temperature during exposure

X There are no standard methods and measures to test the acoustic field under high power. Normal hydrophone is unable to be used to directly measure the acoustic pressure under high power. We use normal hydrophone to test the acoustic field under low power, and calculate the theoretic focal intensity under high power, supposing the acoustic distribution keeps stable. Since we ignore the nonlinear influencing factors, we cannot evaluate the errors.

Y In the manufacturing site: OK

On the field (clinical practice): Needs for transportable measurement equipment and methods, phantoms…. to measure acoustical transducers performance.

Z There is no good method for power ultrasound.

AA

BB The precision of our force balance is not defined in a traceable way and the uncertainty of power measurement at high power level is not known.

A.3.3 Do you have an opinion on how therapy fields/treatments should be measured or characterised?

C 3D

D
- Total acoustic power emitted by the transducer.
- Total power in the focus region, the latter would be defined by the manufacturer.
- For transients: peak acoustic power.
- Geometry of the transducer active area.
- Eventually : Uniformity of emission field over that geometry BUT how do you measure that uniformity ?

E On effective tissue coagulation in targeted area

F Yes, measure pressure as well as intensity. Measure both peak positive and peak negative pressure.

G The way we do it! But more accurately, and in a standard way so that everyone can compare systems.

H I have not much experience with HIFU transducers, which seem to be the most difficult to characterize.

I Possibly

J Intensity contours, time, & frequency

K Make measurements first *in vitro* followed by animal models. Correlate equipment settings to the measured parameters.

L Intensity in water appears adequate.

M N/A

N See C1

O Acoustic efficiency is an important parameter, and acoustic power should be quoted more often instead of electrical power delivered to transducer.

P NA

Q Hydrophone at low power levels, schlieren at low power levels, TAP, comparison with simulations, gel phantoms, in-vitro tissue exposure, in-vivo tissue exposure, thermometry arrays (if applicable), thermal dose.

R NA

S I know that the current measurements (described above) are not sufficiently precise. A calibrated hydrophone would improve the measurements in the case of my experiments.

T Research fields should give as much information as possible.
Medical instruments should provide users with real time feedback on quantities like thermal and mechanical indices, and cavitation emissions.

U I need to know more to be able to speak with confidence, but certainly I do worry about derating nonlinear fields.

V The characterisation should depend on the basic physical phenomenon exploited (in our case cavitation).

W Clinical standard evaluation, such as phase 1 clinical trial, phase 1/2 clinical trial. It must have research protocol and IRB approval.

X We would prefer to find a way of using a hydrophone to directly measure relevant acoustic parameters.

Y 1: Transducer calibration at the end of the manufacturing process (US beam measurement, transducer efficiency)
2: Transducer control during treatment (electrical power measurement, electrical matching control)
3: Any methods to measure and control the effectiveness of tissue destruction (????)
4: Periodic control of the transducer's performance (before each treatment, every week or month …)

Z Do not know

AA W/cm^2

BB I think methods like the one demonstrated by Peter Kaczkowski at the APL Washington or the use of Optison from ONDA using a special device to take into account non-linear modes could be very useful to measure high intensity fields.

A.3.4 Do you feel aspects of your work would benefit from the widespread use of more standardised measurement or evaluation methods? If so, which aspects?

C Indeed. Examples include reporting to the scientific community, FDA submissions, and device development.

D Absorber / reflector used together with force balance.

E We treated 1 055 patients in 8 years and have documented it.

All pre-operative, therapy-relevant and post-operative data about machine, patient and his disease, as well as about influence of technical changes.

F No, not at this point, for we are doing fundamental investigations rather than clinical therapy.

G All clinical and lab work would benefit from standardised measurements.

H No

I

J Regarding lesions, short term necrosis is commonly reported, but there is also long term necrosis at temperatures between hyperthermia (44 °C) and an immediate thermal lesion. More attention needs to be paid to this latter effect.

Power transducer temperature, PROBE temperature rise in °C per watt of input (not reflected) power, per second and probe cooling time-constant.

K It would be useful to have a table relating acoustic power levels measured in a water tank to intensities delivered to tissue as function of frequency, organ type, depth, exposure time etc.

L Yes. Not sure what these should be.

M Use of a urethral temperature probe would be of interest.

N For publication it would be helpful to have a set of standard parameters. This is a prerequisite to understand articles and to compare different publications.
For patient therapy, we need a standard for quality assurance and to compare the performed studies at different times and places. In addition a standardized instruction "how to measure" these parameters would be helpful.

O Yes. It would be easier to compare other work in the field against ours.

P No

Q Yes

Mainly, reports using transducer/field intensity are extremely misleading. Any reporting of intensity must also include: tissue depth, attenuation, cross-sectional area, spatial average? or time average?, and TAP values.

R If there were some standard physical characteristics or parameters to aim for, it would be relatively easy to make estimates.

S I think that a standardized reporting of therapeutic ultrasound parameters would be beneficial.

T The research is presently uncertain in this regard. Better measurement methods are a research goal.

U Yes, because although I define my own problems in my *[name removed]* work (*[name removed]* will reply on the *[name removed]* half of our collaborative lithotripsy study), I would like to be able to relate these fields and measurements to standard methods.

V Yes.

W Endpoint of our studies is histological examination. This is one of the standards in his field.

X It is hopeful that methods and standards for measurement of acoustic field could be established, and an international language in such a field could be formed.

Y Acoustical power measurement for highly focused transducers.

Z Yes.

Do not know

AA

BB Yes:

- measurement method for absolute acoustic output at high power level (up to 500 W , preferably 1 000 W with CW operation);
- measurement method for relative of preferably absolute beam intensity at the focus in water or other reproducible material.

A.3.5 Would you be willing to participate in development of standards by providing written comments, drafting documents or attending committee meetings?

C I'll be happy to participate in this effort.

D See C6

E It would be more feasible if somebody (*[name removed]*) from *[name removed]* who is "*[name removed]*" would be included in such a "technical development" influencing committee.

F Yes, depending on the time requirements. I would be happy to serve as an expert on cavitation-related physical effects. I could also assist in developing standards for the detection of thermally relevant cavitation activity.

G Written comments.

H Eventually.

I

J Yes.

K Not at this time.

L Yes.

M Yes, if applicable to this application.

N

O Yes, I would be willing to participate in such a process.

P No.

Q Possibly.

R Not likely to be of much help.

Written comments, yes.

Drafting documents, not likely.

Committee meetings, not likely, travel?

S If a postdoctoral fellow is good enough for such work.
T In an informal way, but not in one of those big, endless committees.
U Yes, given juggling the workload – depends on the commitment.
V Yes.
W Yes.
X We would be very glad to participate.
Y Yes, I would greatly appreciate participating.
Z Yes.
AA
BB Yes

A.3.6 Please add any other comments or observations you would like to make.

C I think it would be important to coordinate this effort for standardization with overall guidelines of clinical regulatory bodies in the EC and US.

D As a company, I feel uneasy about disclosing all the acoustic parameters that make a particular treatment successful. At present there is a considerable amount of trial and error to reach a point where HIFU is effective in a given pathology, those trials being backed by much knowhow.
I fear that by setting standards, or rather by publishing the data, life will be made much easier to new coming competitors for whom the development would be spared.

E ISTU 2004 in Kyoto will show more.

F The need for non-invasive temperature measurement is acute. In addition, we need to develop techniques for sensing the onset of lesion formation and (preferably) imaging the lesion based on irreversible changes in tissue properties. It would be very helpful if we had a database of measured cavitation thresholds for various organs. This issue of registering images generated by a guidance device (MRI) and the therapy beam is a difficult problem. (Image registration has been extensively studied by other communities – maybe we could transfer some of their knowledge and expertise?) Finally, there is much work to be done vis-a-vis cavitation bubble dynamics in non-Newtonian media, as well as developing techniques for nucleating cavitation activity at safe pressure levels.

G
H
I

J Universal standards are needed for equipment performance – e.g. probe temperature rise per above; probe thermal and acoustic energy tolerance; and system parameters such as frequency, probe temperature, forward and reflected power, probe information keyed to equipment, and more.
With respect to patient safety, standards are needed, but it's hard to imagine what they will be, beyond the obvious. One needs to look outside the ultrasound discipline, e.g. electrosurgery, radiation therapy, etc.
Since we're in an equipment development stage, rather than a clinical applications stage, standards should address equipment/probe issues. Patient efficacy and safety will come later.

K

L

M

N

O I feel that there is a wide variation in the methods used for characterisation among groups as well as the preferred measurement/characterisation parameters quoted.

P As we manufacture an *[name removed],* which is a mechanical system, I am not sure it is information that is particularly useful, though it is an interesting comparison to high frequency ultrasound devices you work with. I forwarded your questionnaire to our sister company *[name removed]* as they are now the engineering group responsible for the *[name removed]* system. We still manufacture the *[name removed]* at *[name removed]*. If you have received reply from their side, this may be redundant. I hope it is helpful.
As I follow the progress of the development of HIFU systems, I hope that someday we may contribute directly to that application. *[name removed]* has a significant investment in related clinical applications. Many people at *[name removed]* recognize that one day we will be competing directly with HIFU systems. *[name removed]* is a leader in preoperative planning and markets the *[name removed]*, *[name removed]* as well as *[name removed]*. *[name removed]* produces the *[name removed]* above and the *[name removed]* system and is the leader in electrosurgery and vessel sealing.

Q

R

S

T Standardization is most important for clinical HIFU instruments now becoming available. Standardization could borrow from experience with diagnostic machines, but with much improved exposimetry and dosimetry available in real-time.
My answers were mostly concerning the field measurement and dosimetry. However, a complete standard would also include various typical instrument standards (e. g. electrical insulation, non-allergenic, etc.).

U (i) I understand that my answers are given from a usual perspective. I have forwarded a copy of the questionnaire to *[name removed]* (see B1) to answer on our clinical research project. But for myself and the answers given above, much of my work is theoretical or *in vitro*, and hence does not raise the complex issues surrounding *in vivo* and clinical work.

(ii) I think the idea behind this questionnaire is an excellent one – this is very timely.

V

W

X It is important to create standards and criteria for clinical treatment using focused ultrasound.

Y

Z It is difficult to characterise ultrasound at a level high enough to cause cavitation. A recent trial of the “new” NPL device proved inconclusive.

AA

BB I believe a specialised seminar would be useful to define objectives in the development of new measurement methods taking into account the experience and HIFU System developers and HIFU transducers manufacturers.

Annex B
(informative)

Definitions in selected ultrasound standards

B.1 General

The following definitions are duplicated from IEC standards which are technically identical to their British counterparts (i.e. IEC 61157 is equivalent to BS EN 61157).

The IEC hydrophone standards referenced here are now obsolete and replaced by IEC 62127 Parts 1 to 3. However, the definitions were current at the time of first drafting this Technical Report and have in general been carried across to the recent IEC 62127 standards with only minor changes. The current definitions can be found in the online IEC Glossary.

The standards referred to are:

- IEC 61101:1991, *The absolute calibration of hydrophones using the planar scanning technique in the frequency range 0,5 MHz to 15 MHz*
  (equivalent to BS EN 61101:1994)
- IEC 61102:1991 (and its Amendment 1:1993), *Measurement and characterisation of ultrasonic fields using hydrophones in the frequency range 0,5 MHz to 15 MHz* (equivalent to BS EN 61102:1994)

B.2 Terms taken from BS EN 61101

1	**beam centre**: Point in a plane in the **far field**, usually perpendicular to the beam alignment axis, at which the spatial-peak temporal-peak acoustic pressure occurs. See IEC 61102 for the definition of spatial-peak temporal-peak acoustic pressure	From 61101
2	**diametrical beam scan**: Set of measurements of the hydrophone output voltage made in a straight line passing through the **beam centre** and normal to the beam alignment axis. The **diametrical beam scan** may extend to different distances on either side of the **beam centre**	From 61101
3	**effective radius of an ultrasonic transducer**: Radius of a perfect disc piston-like ultrasonic transducer which has a predicted axial acoustic pressure distribution approximately equivalent to the observed axial acoustic pressure distribution over a limited axial distance. Symbol: *a* Unit: metre, m	From 61101
4	**effective radius of a hydrophone active element**	From 61101 – See definition 3.13
5	**end-of-cable loaded sensitivity of a hydrophone**	From 61101 – See definition 3.14
6	**far field**	From 61101 – See definition 3.16
7	**hydrophone reference point** Point to which electroacoustic characteristics of a hydrophone are referred. See IEC 60050	From 61101
8	**instantaneous acoustic pressure**	From 61101 – See definition 3.20
9	**instantaneous intensity**	From 61101 – See definition 3.21
10	**transducer reference point** Point to which electroacoustic characteristics of the ultrasonic transducer are referred. See IEC 60050	From 61101

B.3 Terms taken from BS EN 61102

1	**acoustic pulse crest factor** Ratio of the **spatial-peak temporal-peak acoustic pressure** to the **r.m.s. acoustic pressure** calculated over the **pulse-peak cycle.** Both pressures are measured at the position in the acoustic field corresponding to the **spatial-peak temporal-peak acoustic pressure.** Symbol: ***not given***	From 61102
2	**acoustic pulse waveform** Temporal waveform of the **instantaneous acoustic pressure** at a specified position in an acoustic field and displayed over a period sufficiently long to include all significant acoustic information in a single pulse or tone-burst, or one or more cycles in a continuous wave. See 2.3.1 of IEC 60469-1.	From 61102
3	**acoustic repetition period** **Pulse repetition period** for non-automatic scanning systems and the **scan repetition period** for automatic scanning systems. Equal to the time interval between consecutive cycles for continuous-wave systems. Symbol: ***not given*** Unit: second, s	From 61102

4	**acoustic-working frequency (awf)** Frequency of an acoustic signal based on the observation of the output of a **hydrophone** placed in an acoustic field at the position corresponding to the **spatial-peak temporal-peak acoustic pressure.** The signal is analysed either using the zero-crossing frequency technique or using a spectrum analysis method. The following acoustic-working frequencies are defined:	From 61102
	Zero-crossing acoustic-working frequency This is determined according to the procedure described in IEC 60854	From 61102
	Arithmetic-mean acoustic-working frequency The arithmetic mean of the frequencies f_1 and f_2 at which the amplitude of the acoustic pressure spectrum is 3 dB below the peak amplitude NOTE Arithmetic-mean acoustic-working frequency is equivalent to center frequency in [1].| Symbol: f_{awf} Unit: hertz, Hz	From 61102
	Geometric-mean acoustic-working frequency The geometrical mean of the frequencies f_1 and f_2.	From 61102
	Modal acoustic-working frequency The frequency corresponding to the maximum amplitude in the acoustic pressure spectrum	From 61102
5	**beam-alignment axis** Used for alignment purposes only, beam-alignment axis is a straight line joining two points of **spatial-peak temporal-peak acoustic pressure** on two hemispherical surfaces whose centres are at the approximate geometrical centre of an **ultrasonic transducer** or **ultrasonic transducer element group.** One hemisphere has a radius of curvature of approximately $A_g/\pi\lambda$, where A_g is the **geometrical area of the ultrasonic transducer** or **ultrasonic transducer element group** and λ is the wavelength of the ultrasound corresponding to the **nominal frequency.** The second hemisphere has a radius of curvature either $2A_g/\pi\lambda$, or $A_g/3\pi\lambda$, whichever is the more appropriate. For the purposes of alignment, this line may be projected to the face of the **ultrasonic transducer** or **ultrasonic transducer element group.** For most practical applications, two plane surfaces perpendicular to the direction of propagation of the ultrasound are used. In cases where a unique peak is not located on a hemispherical surface, another hemispherical surface is chosen with a different radius of curvature yielding a unique peak. (See Figure 2.)	From 61102
6	**beam-area** Area on a specified surface consisting of all points at which the **pulse-pressure-squared integral** is greater than a specified fraction of the maximum value of the **pulse-pressure-squared integral** in that surface. The specified surface is cylindrical for **ultrasonic transducers** with cylindrical active elements and spherical for **ultrasonic transducers** with spherical active elements, and at a specified radius. The specified levels are 0,25 and 0,01 for the -6 dB and -20 dB **beam-areas**, respectively. Symbol: A_b Unit: metre squared, m^2	From 61102 Amendment 1
7	**beam-average pulse acoustic pressure** **Pulse acoustic pressure** from one **ultrasonic transducer** or **ultrasonic transducer element group** averaged over the **–6 dB beam-area** in a specified surface or in a surface containing the **spatial-peak temporal-peak acoustic pressure** for that particular **ultrasonic transducer** or **ultrasonic transducer** element group. NOTE **–6 dB beam-area** is commonly used. However, other **beam-areas** may be used (see 3.6). Symbol: p_{bap} Unit: pascal, Pa.	From 61102 & Amendment 1

8	**beam-average pulse-average intensity** **Pulse-average intensity** from one **ultrasonic transducer** or **ultrasonic transducer element group** averaged over the **–6 dB beam-area** in a specified surface or in a surface containing the **spatial-peak temporal-peak acoustic pressure** for that particular **ultrasonic transducer** or **ultrasonic transducer element group.** NOTE –**6 dB beam-area** is commonly used. However, other beam-areas may be used (see 3.6). Symbol: I_{bapa} Unit: watt per metre squared, W/m^2	From 61102 & Amendment 1
9	**beam-average r.m.s. acoustic pressure** **R.M.S. acoustic pressure** from one **ultrasonic transducer** or **ultrasonic transducer element group** averaged over the **–6 dB beam-area** in a specified surface or in a surface containing the **spatial-peak temporal-peak acoustic pressure** for that particular **ultrasonic transducer** or **ultrasonic transducer element group.** NOTE –**6 dB beam-area** is commonly used. However, other beam-areas may be used (see 3.6). Symbol: p_{bar} Unit: pascal, Pa	From 61102 & Amendment 1
10	**beam-average temporal-average intensity** **Temporal-average intensity** from one **ultrasonic transducer** or **ultrasonic transducer element group** averaged over the **–6 dB beam-area** in a specified surface or in a surface containing the **spatial-peak temporal-peak acoustic pressure** for that particular **ultrasonic transducer** or **ultrasonic transducer element group.** NOTE –**6 dB beam-area** is commonly used. However, other **beam-areas** may be used (see 3.6). Symbol: I_{bata} Unit: watt per metre squared, W/m^2.	From 61102 & Amendment 1
11	**central scan line** For automatic scanning systems, the **ultrasonic scan line** closest to the **symmetry axis of the scan plane**	From 61102
12	**effective area of an ultrasonic transducer** Area of a perfect piston-like **ultrasonic transducer** which has a predicted axial acoustic pressure distribution approximately equivalent to the observed axial acoustic pressure distribution over a limited axial distance, see IEC 60866. Symbol: A_1 Unit: metre squared, m^2	From 61102
13	**effective radius of a hydrophone active element** Radius of a stiff disc receiver **hydrophone** which has a predicted directional response function with an angular width equal to the observed angular width. The angular width is determined at a specified level below the peak of the directional response function. For the specified levels of 3 dB and 6 dB, the radii are denoted by a_3 and a_6 respectively. Symbols: a, a_3, a_6 Unit: metre, m.	From 61102
14	**end-of-cable loaded sensitivity of a hydrophone** Ratio of the voltage at the end of any integral cable or connector of a **hydrophone,** when connected to a specified electrical input impedance, to the **instantaneous acoustic pressure** in the undisturbed free field of a plane wave *of a specified frequency* in the position of the acoustic centre of the **hydrophone** if the **hydrophone** were removed. Symbol: M_L Unit: volt per pascal, V/Pa	From 61102

15	**end-of-cable open-circuit sensitivity of a hydrophone** Ratio of the open-circuit voltage at the end of any integral cable or connector of a **hydrophone** to the **instantaneous acoustic pressure** in the undisturbed free field of a plane wave *of a specified frequency* in the position of the acoustic centre of the **hydrophone** if the **hydrophone** were removed, see IEC 60866 NOTE This definition differs from that given in 3.8 of IEC 60866 as the latter refers to a **hydrophone** excluding any integral cable. Symbol: M_c Unit: volt per pascal, V/Pa	From 61102
16	**far field** Acoustic (sound) field at distances from an **ultrasonic transducer** where the values of the **instantaneous acoustic pressure** and particle velocity are substantially in phase, see also 801-03-30 of IEC 60050-801. For the purposes of this International Standard, although strictly for planar ultrasonic transducers, the **far field** is at a distance greater than $A_1/\pi\lambda$, where A_1 is the **effective area of the ultrasonic transducer** or **ultrasonic transducer element group** *output beam area* and λ is the wavelength of the ultrasound corresponding to the **acoustic-working frequency.**	From 61102
17	**geometrical area of an ultrasonic transducer** Area defined by the **ultrasonic transducer** dimensions or **ultrasonic transducer element group** dimensions. Symbol: A_g Unit: metre squared, m^2.	From 61102
18	**geometrical radius of a hydrophone active element** Radius defined by the dimensions of the active element of a **hydrophone** Symbol: a_g Unit: metre, m	From 61102
19	**hydrophone** Transducer that produces electrical signals in response to waterborne acoustic signals, see also 801-12-26 of IEC 60050-801 and also IEC 60866	
20	**instantaneous acoustic pressure** Pressure amplitude minus the ambient pressure at a particular instant in time and at a particular point in an acoustic field, see also 801-01-19 of IEC 60050-801. Symbol: p Unit: pascal, Pa	From 61102
21	**instantaneous intensity** Acoustic energy transmitted per unit time in the direction of acoustic wave propagation per unit area normal to this direction at a particular instant in time and at a particular point in an acoustic field. It is not possible to measure the true instantaneous intensity. However, for historical reasons, it is preferable in this International Standard to derive certain intensity parameters from hydrophone measurements. Therefore, for the measurement purposes referred to in this International Standard, and if it is reasonable to assume **far field** conditions, the **instantaneous intensity,** I is expressed as $$I = \frac{p^2}{\rho c}$$ where: p is the **instantaneous acoustic pressure;** ρ is the density of the medium; c is the velocity of sound in the medium. Symbol: I Unit: watt per metre squared, W/m^2	From 61102
22	**mean-peak-cycle acoustic pressure** Arithmetic mean of the maximum positive and modulus of the maximum negative **instantaneous acoustic pressure** during a **pulse-peak cycle.** Symbol: p_m Unit: pascal, Pa	From 61102

23	**near field** For the purposes of this International Standard, the region of the acoustic (sound) near field an **ultrasonic transducer** where the relative phase of the **instantaneous acoustic pressure** and the particle velocity is continually changing with position in the acoustic (sound) field For planar transducers, this is at a distance less than $A_1/\pi\lambda$, where A_1 is the **effective area of the ultrasonic transducer** or **ultrasonic transducer element** *output beam area* group and λ is the wavelength of the ultrasound corresponding to the **acoustic-working frequency**	From 61102
24	**nominal frequency** Ultrasonic frequency of operation of an **ultrasonic transducer** or **ultrasonic transducer element group** quoted by the designer or manufacturer, see IEC 60854	From 61102
25	**nonlinear propagation parameter** Index which permits the prediction of nonlinear distortion of ultrasound for a specific **ultrasonic transducer,** and is given by σ_m from: $$\sigma_m = \frac{\beta\omega I_1}{\rho c^3} \; p_m \; \frac{1}{(F_g - 1)^{1/2}} \; \ln\left((F_g - 1)^{1/2} + F_g^{1/2}\right)$$ where: β is the nonlinearity parameter ($\beta = 1 + B/2A = 3{,}5$ for pure water at 20 °C [2]); ω is the angular frequency ($\omega = 2\pi f_{awf}$ where f_{awf} is the **acoustic-working frequency**); I_1 is the distance from the face of the **ultrasonic transducer** to the plane containing the point of **spatial-peak temporal-peak acoustic pressure**; F_g is 0,69 times the ratio of the **geometrical area of the ultrasonic transducer** to the **-6 dB beam-area**; p_m is the **mean-peak-cycle acoustic pressure** at the point in the acoustic field corresponding to the **spatial-peak temporal-peak acoustic pressure.** Symbol: σ_m NOTE The equation given above is applicable to ultrasonic fields in which $F_g > 2{,}1$. The specification of an index to cover $F_g < 2{,}1$ is under consideration	From 61102
26	**peak-negative acoustic pressure;** **peak-rarefactional acoustic pressure** Maximum of the modulus of the negative **instantaneous acoustic pressure** in an acoustic field or in a specified surface during an **acoustic repetition period. Peak-negative acoustic pressure** is expressed as a positive number Symbol: p_- (or p_r) Unit: pascal, Pa	From 61102 & Amend1
27	**peak-positive acoustic pressure;** **peak-compressional acoustic pressure** Maximum positive **instantaneous acoustic pressure** in an acoustic field or in a specified surface during an **acoustic repetition period** Symbol: p_+ (or p_c) Unit: pascal, Pa	From 61102 & Amend1
28	**pulse acoustic pressure** Square root of the ratio of the **pulse-pressure-squared integral** to the **pulse duration** at a particular point in an acoustic field. Symbol: p_p Unit: pascal, Pa.	From 61102
29	**pulse-average intensity** Ratio of the **pulse-intensity integral** to the **pulse duration** at a particular point in an acoustic field Unit: watt per metre squared, W/m^2.	From 61102

30	**pulse duration** 1,25 times the interval between the time when the time integral of the square of the **instantaneous acoustic pressure** reaches 10 % and 90 % of its final value. The final value of the time integral of the square of the **instantaneous acoustic pressure** is the **pulse-pressure-squared integral** Symbol: t_d Unit: second, s	From 61102
31	**pulse-intensity integral** Time integral of the **instantaneous intensity** at a particular point in an acoustic field integrated over the **acoustic pulse waveform** NOTE For many measurement purposes referred to in this International Standard, **pulse-intensity integral** is proportional to **pulse-pressure-squared integral.** Symbol: I_{pi} Unit: joule per metre squared, J/m^2	From 61102
32	**pulse-peak cycle** Single cycle of an **acoustic pulse waveform** between two points of zero **instantaneous acoustic pressure.** This single cycle is composed of the half cycle containing the **temporal-peak acoustic pressure** and whichever of the two adjacent half cycles contains the larger peak **instantaneous acoustic pressure.**	From 61102
33	**pulse-pressure-squared integral** Time integral of the square of the **instantaneous acoustic pressure** at a particular point in an acoustic field integrated over the **acoustic pulse waveform.** Symbol: p_i Unit: pascal squared second, Pa^{2}s	From 61102
34	**pulse repetition period** Time interval between two successive pulses or tone-bursts. This applies to single element non-automatic scanning systems and automatic scanning systems. See also 5.3.2.1 of IEC 60469-1. Unit: second, s	From 61102
35	**pulse repetition rate (p.r.r.)** Inverse of the **pulse repetition period.** See also 5.3.2.2 of IEC 60469-1. Symbol: *prr* Unit: hertz, Hz.	From 61102
36	**R.M.S acoustic pressure** Root mean square (r.m.s.) of the **instantaneous acoustic pressure** at a particular point in an acoustic field. The mean should be taken over an integral number of **acoustic repetition periods** unless otherwise specified. Symbol: p_{rms} Unit: pascal, Pa	From 61102
37	**scan-area** For automatic scanning systems, the area on the surface considered consisting of all points within the **beam-area** of any beam passing through the surface during the **scan repetition period.** For automatic scanning systems, the area on a specified surface consisting of all points at which the **temporal-average intensity** is greater than a specified fraction of the maximum value of the **temporal-average intensity** in that surface. The specified surface is cylindrical for **ultrasonic transducers** with cylindrical active elements and spherical for **ultrasonic transducers** with spherical active elements, and at a specified radius. The specified levels are 0,25 and 0,01 for the -6 dB and -20 dB **scan-areas**, respectively. Symbol: A_s Unit: metre squared, m^2.	From 61102
38	**scan plane** For automatic scanning systems, a plane containing all the **ultrasonic scan lines.**	From 61102

39	**scan repetition period** Time interval between identical points on two successive frames, sectors or scans. This applies to automatic scanning systems only. Unit: second, s.	From 61102 .
40	**scan repetition rate (s.r.r.)** Inverse of the **scan repetition period.** Unit: hertz, Hz.	From 61102 See 39
41	**spatial-average pulse acoustic pressure** For non-automatic scanning systems, the **beam-average pulse acoustic pressure.** NOTE **Spatial-average pulse acoustic pressure** does not apply to automatic scanning systems, **beam-average pulse acoustic pressure** applies only. Symbol: p_{s}ap Unit: pascal, Pa	From 61102
42	**spatial-average pulse-average intensity** For non-automatic scanning systems, the **beam-average pulse-average intensity.** NOTE **Spatial-average pulse-average intensity** does not apply to automatic scanning systems, **beam-average pulse-average intensity** applies only. Symbol: I_{sapa} Unit: watt per metre squared, W/m^2	From 61102
43	**spatial-average r.m.s. acoustic pressure** For non-automatic scanning systems, the **beam-average pulse acoustic pressure.** NOTE **Spatial-average pulse acoustic pressure** does not apply to automatic scanning systems, **beam-average pulse acoustic pressure** applies only. Symbol: p_{sap} Unit: pascal, Pa.	From 61102
44	**spatial-average temporal-average intensity** For non-automatic scanning systems, the **beam-average temporal-average intensity.** For automatic scanning systems, equal to the **temporal-average intensity** averaged over the **scan-area** where the **temporal-average intensity** is taken over the **scan repetition period.** Equal to the **temporal-average intensity** averaged over the **scan-area** or **beam-area** as appropriate. Symbol: I_{sata} Unit: watt per metre squared, W/m^2	From 61102
45	**spatial-peak pulse-average intensity** Maximum value of the **pulse-average intensity** in an acoustic field or in a specified surface. Symbol: I_{sppa} Unit: watt per metre squared, W/m^2	From 61102 & Amendment1
46	**spatial-peak pulse-intensity integral** Maximum value of the **pulse-intensity integral** in an acoustic field or in a specified surface. Symbol: I_{sppi} Unit: joule per metre squared, J/m^2	From 61102 & Amend1
47	**spatial-peak pulse acoustic pressure** Maximum value of the **pulse acoustic pressure** in an acoustic field or in a specified plane. Symbol: p_{spp} Unit: pascal, Pa.	From 61102

48	**spatial-peak r.m.s. acoustic pressure** Maximum value of the **r.m.s. acoustic pressure** in an acoustic field or in a specified surface. Symbol: p_{spr} Unit: pascal, Pa.	From 61102 & Amend1
49	**spatial-peak temporal-average intensity** Maximum value of the **temporal-average intensity** in an acoustic field or in a specified surface. Symbol: I_{spta} Unit: watt per metre squared, W/m^2	From 61102 & Amend1
50	**spatial-peak temporal-peak acoustic pressure; peak sound pressure** Larger of the **peak-positive acoustic pressure** or the **peak-negative acoustic pressure.** Symbol: p_{sptp} Unit: pascal, Pa	From 61102
51	**spatial-peak temporal-peak intensity** Maximum value of the **temporal-peak intensity** in an acoustic field or in a specified surface. Symbol: I_{sptp} Unit: watt per metre squared, W/m^2	From 61102 & Amend1
52	**symmetry axis of the scan plane** Imaginary line in the **scan plane** on each side of which an equal number of **ultrasonic scan lines** occur.	From 61102
53	**temporal-average intensity** Time-average of the **instantaneous intensity** at a particular point in an acoustic field. The time-average is taken over an integral number of **acoustic repetition periods,** unless otherwise specified. Symbol: ***not given*** Unit: watt per metre squared, W/m^2	From 61102
54	**temporal-peak acoustic pressure** Maximum value of the modulus of the **instantaneous acoustic pressure** at a particuar point in an acoustic field. Symbol: p_o Unit: pascal, Pa	From 61102
55	**temporal-peak intensity** Maximum value of the **instantaneous intensity** at a particular point in an acoustic field. Unit: watt per metre squared, W/m^2	From 61102
56	**ultrasonic scan line** For **automatic scanning systems,** the **beam alignment axis** for a particular **ultrasonic transducer element group,** or for a particular excitation of an **ultrasonic transducer** or **ultrasonic transducer element group.** NOTE Here, an **ultrasonic scan line** refers to the path of acoustic pulses and not to a line on an image on the display screen of a **system.**	From 61102
57	**ultrasonic scan line separation** For automatic scanning systems, the distance between the points of intersection of two consecutive **ultrasonic scan lines** of the same type and a specified surface. Symbol: s_s Unit: metre, m	From 61102 & Amendment1
58	**ultrasonic transducer** Device capable of converting electrical energy to mechanical energy within the ultrasonic frequency range and/or reciprocally of converting mechanical energy to electrical energy.	From 61102
59	**ultrasonic transducer dimensions** Dimensions of the surface of the element or elements of an **ultrasonic transducer.** Unit: metre, m	From 61102
60	**ultrasonic transducer element group** Group of elements of an **ultrasonic transducer** which are excited together in order to produce a single acoustic pulse.	From 61102

61	**ultrasonic transducer element group dimensions** Dimensions of the surface of the group of elements of an **ultrasonic transducer** element group which includes the distance between the elements, hence representing the overall dimensions. Unit: metre, m	From 61102
62	**bandwidth** Difference in the frequencies f_1 and f_2 at which the amplitude of the acoustic pressure spectrum first becomes 3 dB below the peak amplitude, *at a specified point in the acoustic field*.	From 61102, Amendment 1
63	**pulse beam-width** Distance between two points, on a specified surface and in a specified direction passing through the point of the maximum **pulse-pressure-squared integral** in that surface, at which the **pulse-pressure-squared integral** is a specified fraction of the maximum value of the **pulse-pressure-squared integral** in the surface. The two points are farthest from and on opposite sides of the point of maximum **pulse-pressure-squared integral.** If the position of the surface is not specified, then the surface passes through the point of **spatial-peak temporal-peak acoustic pressure** in the whole acoustic field. The specified levels are 0,25 and 0,01 for the -6 dB and -20 dB **pulse beam-widths,** respectively. The distance is measured on the specified surface. NOTE 1 The specified surface is usually a plane perpendicular to the **beam alignment axis** but can be cylindrical for **ultrasonic transducers** with cylindrical active elements or can be spherical for **ultrasonic transducers** with spherical active elements. Symbols: wpb_6, wpb_{20} Unit: metre, m	From 61102, Amendment 1
64	**pulse beam-radii** Two distances between the specified points defining the **pulse beam-width** and the point of maximum **pulse-pressure-squared integral.** The distances are measured on the specified surface. The specified level for **pulse beam-radii** is the same as that used for the **pulse beam-width.** Symbols: wpr_6, wpr_{20} Unit: metre, m	From 61102, Amend1

B.4 Terms taken from BS EN 61157

1	**accompanying literature** Operating and instruction manual provided by the **manufacturer** with each piece of **medical diagnostic ultrasonic equipment**	From 61157
2	**acoustic initialisation fraction** Ratio of the **peak-negative acoustic pressure** when a **system** is in **initialization mode** to the maximum value of the **peak-negative acoustic pressure** for any **system** settings of a specified mode of operation. This ratio is determined from measurements made at the position which yields the maximum **pulse-pressure-squared integral** (or maximum mean square acoustic pressure for continuous wave [cw] **systems**). The ratio is usually expressed as a percentage. NOTE The mode of operation of a **system** in **initialization mode** may be different from the specified mode of operation.	From 61157
3	**acoustic output freeze** A condition of a **system** for which the acoustic output is disabled when there is no active updating of ultrasonic echo information	From 61157
4	**acoustic power-up fraction** Ratio of the **peak-negative acoustic pressure** when the **system** is in **power-up mode** to the maximum value of the **peak-negative acoustic pressure** for any **system** settings of a specified mode of operation. This ratio is determined from measurements made at the position which yields the maximum **pulse-pressure-squared integral** (or maximum mean square acoustic pressure for continuous wave [cw] **systems).** The ratio is usually expressed as a percentage. NOTE The mode of operation of a **system** in **power-up mode** may be different from the specified mode of operation.	From 61157
6	**combined-operating mode** Mode of operation of a **system** which combines more than one **discrete-operating mode.** NOTE Examples of **combined-operating modes** are real-time B-mode combined with M-mode (B+M), real-time B-mode combined with pulsed Doppler (B+D), colour M-mode (cM), real-time B-mode combined with M-mode and pulsed Doppler (B+M+D), real-time B-mode combined with real-time flow-mapping Doppler (B+rD), i.e. flow-mapping in which different types of acoustic pulses are used to generate the Doppler information and the imaging information	From 61157
7	**discrete-operating mode** Mode of operation of **medical diagnostic ultrasonic equipment** in which the purpose of the excitation of the ultrasonic transducer or ultrasonic transducer element group is to utilize only one diagnostic methodology NOTE Examples of **discrete-operating modes** are A-mode (A), M-mode (M), static B-mode (sB), real-time B-mode (B), acoustic wave Doppler (cwD), pulsed Doppler (D), static flow-mapping (sD) and real-time flow-mapping Doppler (rD) using only one type of acoustic pulse.	From 61157
8	**inclusive mode** **Combined-operating mode** having acoustic output levels (p_- and I_{spta}) less than those corresponding to a specified **discrete-operating mode**	From 61157
9	**initialisation mode** A defined state of a **system** corresponding to the mode of operation and **system** settings when a new patient procedure is initiated	From 61157
10	**manufacturer** A company that makes, markets or distributes **medical diagnostic ultrasonic equipment**	From 61157
11	**medical diagnostic ultrasonic equipment (or system)** Combination of the **ultrasound instrument console** and the **transducer assembly** making up a complete diagnostic **system**	From 61157
12	**non-scanning mode** A mode of operation of a **system** that involves a sequence of ultrasonic pulses which give rise to **ultrasonic scan lines** that follow the same acoustic path	From 61157
13	**output beam area** Area of the ultrasonic beam derived from the **output beam dimensions** Unit: centimetre squared, cm^2.	From 61157

14	**output beam dimensions** Dimensions of the ultrasonic beam **(–6 dB pulse beam-width)** in a specified direction normal to the **beam alignment axis** and at the **transducer output face** Unit: millimetre, mm	From 61157
15	**output beam intensity** Temporal-average power output divided by the **output beam area** Symbol: I_{ob} Unit: milliwatt per centimetre squared, mW cm^{-2}	From 61157
16	**patient entry plane** Plane perpendicular to the **beam alignment axis,** or the axis of symmetry of the **scan plane** for an automatic scanner, which passes through the point on said axis at which the ultrasound enters the patient	From 61157
17	**power-up mode** A defined state of a **system** corresponding to the mode of operation and **system** settings automatically established when power to the **system** is first turned on. If the defined state is user dependent, **power-up mode** is referred to as "not applicable" (abbreviated n/a)	From 61157
18	**pulse beam-width**	From 61157, see definition 3.63
19	**reference direction** For **systems** with scanning modes, the direction normal to the **beam-alignment** axis for an **ultrasonic scan line** and in the **scan plane**. For **systems** with only non-scanning modes, the direction normal to the **beam-alignment axis** and parallel to the direction of maximum **–6 dB pulse beam-width**	From 61157
20	**scan direction** For **systems** with scanning modes, the direction in the **scan plane** and perpendicular to a specified **ultrasonic scan line**	From 61157
21	**scanning mode** A mode of operation of a **system** that involves a sequence of ultrasonic pulses which give rise to **ultrasonic scan lines** that do not follow the same acoustic path NOTE The sequence of pulses is not necessarily made up of identical pulses, such as in multiple focal-zone **systems**	From 61157
22	**transducer assembly** Those parts of **medical diagnostic ultrasonic equipment** comprising the ultrasonic transducer and/or ultrasonic transducer element group together with any integral components, such as an acoustic lens, integral stand-off etc. The **transducer assembly** is usually separable from the **ultrasound instrument console**	From 61157
23	**transducer output face** External surface of a **transducer assembly** which is either directly in contact with the patient or is in contact with a water or liquid path to the patient See Figures 1 and 2.	From 61157
24	**transducer stand-off distance** Shortest distance between the **transducer output face** and the **patient entry plane** The term "contact" is used to connote direct contact between the **transducer output face** and the patient, with the **transducer stand-off distance** equal to zero. Symbol: l_{ts} Unit: millimetre, mm. See Figure 1.	From 61157
25	**transducer to transducer-output-face distance** The distance along the **beam-alignment axis** between the surface containing the active face of the ultrasonic transducer or ultrasonic transducer element group and the **transducer output face.** Symbol: l_{tt} Unit: millimetre, mm See Figures 1 and 2.	From 61157

26	**type testing values** For acoustical output parameters, the maximum probable acoustical output levels for a specified **system**	From 61157
27	**ultrasonic scan line** For automatic scanning systems, the beam-alignment axis either for a particular ultrasonic transducer element group, or for a single or multiple excitation of an ultrasonic transducer or of an ultrasonic transducer element group See Figure 3 NOTE Here, an ultrasonic scan line refers to the path of acoustic pulses and not to a line on an image on the display screen of a system.	From 61157 – See clause 3.56
28	**ultrasound instrument console** Electronic unit to which the **transducer assembly** is attached	From 61157

Annex C
(informative)

Chinese national standard

The following annex is a translation by Prof. Shou Wende (Shanghai Jiaotong University, Shanghai) of a HITU measurement standard from the People's Republic of China. It is reproduced with his permission. Font changes and minor formatting alterations have been necessary to include it in this report.

The content of this translation has not been updated for new publications or any other aspects. It has not been reviewed for international consensus and it is not presented as an IEC document. It is a National Standard which may be of interest to HITU experts and is expected to provide useful source material for the development of IEC documents. The methods and requirements of any future IEC documents may be substantively different from those contained herein.

National Standard of the People's Republic of China

GB/T 19890—2005

Acoustics – High intensity focused ultrasound (HIFU)- Measurement of acoustic power and field characteristics

(This English draft translated from Chinese is only for information)

Issue date : September 9, 2005 Implementation date : April 1, 2006

Issued by The General Administration of Quality Supervision, Inspection and Quarantine of the People's Republic of China

FOREWORD

This national standard was proposed by the Chinese Academy of Sciences.

This national standard is under the jurisdiction of the national technical committee of standardization (SAC/TC17) for acoustics.

This national standard was drafted by Shanghai Jiao Tong University, the Institute of Acoustics of the Chinese Academy of Sciences, the Institute of Acoustics of Tongji University, the Hangzhou Applied Acoustics Research Institute, the National Wuhan Centre of Quality supervision and Test of medical Ultrasonic Apparatus, the Institute of Wuxi Haiying Electronic medical system Ltd., the Institute of Medical Ultrasonic Engineering of Chongqin University of Medical Sciences, Beijing Yuande Biomedical Engineering Ltd.

The draftmen of the national standard are Wende Shou, Rongmin Xia, Xiaowei Huang, Houqing Zhu, Fengqi Niu, Menlu Qian, Yuebin Wang, Anshi Mang, Xiaomin Geng, Faqi Li, Jinsheng Yu.

INTRODUCTION

The therapeutic technique of the high intensity focused ultrasound (HIFU) has advanced obviously in the world during the last ten years. The medical applications and the product manufacture of HIFU develop very fast in our country. The corresponding products of many companies have been granted to put on market and applied in clinics. The fast development in the preclinical medicine, the clinic medicine, and the product manufacture are urgent to need the standardization on measurements of the basic acoustic parameters and the field characteristics of HIFU. In order to promote the further development of technique of HIFU and to specify the drafting of the professional standard of products of HIFU, the national standard was worked out and laid down under the basis of the researches of draftsmen over the years.

Acoustics – High intensity focused ultrasound (HIFU) – Measurements of Acoustic Power and Field Characteristics

1 Scope

This national standard specifies the conditions and methods of measurement of the acoustic power and field characteristic parameters of high intensity focused ultrasound (HIFU) in water in the frequency range 0,5 MHz to 5 MHz.

This national standard is applicable to the system of high intensity focused ultrasound.

NOTE 1 This standard is in SI units. In some expresses, such as the parameters of beam area and intensity, it is more convenient to use other units. For example, the beam area is in cm^2, sound intensity unit is W/cm^2 or kW/cm^2.

NOTE 2 The measurement range specified in this standard is the acoustic power less than 500 W and the acoustic intensity less than 5000 W/cm^2.

2 Normative documents

The following normative documents contain provision which, through reference in this text, constitute provisions of this national standard. For dated reference, subsequent amendments to, or revisions of, any of these publications do not apply. However parties to agreements based on this standard are encouraged to investigate the possibility of applying the most recent editions of the standards indicated bellow. For undated reference, the latest edition of normative document referred to applies.

GB/T 3947-1996, *Terminology of acoustics*

GB/T 7966-1987, *Acoustics – Ultrasonic power measurement in the frequency range 0.5 MHz to 10 MHz*

GB/T 16540-1996, *Acoustics – Measurement and characteristics of ultrasonic field using hydrophone in the frequency range 0.5 MHz to 15 MHz (eqv. IEC 61102:1991)*

IEC 61828:2001, *Ultrasonics – Focusing transducers – Definitions and measurement methods for the transmitted fields*

3 Terminology and definitions

3.1
high intensity focused ultrasound (HIFU)
ultrasound with intensity high enough to cause violent physical effects, chemical reactions, bioeffects，etc. by using the methods of acoustics and electronics and gathering the ultrasonic beam into the narrow volume of the medium

3.2
sound intensity, acoustic intensity
acoustic energy transmitted per unit time in the direction of acoustic wave propagation per unit area normal to this direction at a particular instant in time and at a particular point in an acoustic field. In the steady field, the acoustic intensity is a time-average value of instantaneous intensity during a specified time, which is taken over an integral number of acoustic repetition periods

Symbol: I

Unit: W/cm^2

3.3
pressure focus
position of maximum pulse-pressure-squared-integral throughout the field. For continuous wave, it is the position of maximum root mean square of pressure throughout the field.

3.4
pressure focal plane
plane perpendicular to the beam axis that contains the pressure focus

3.5
temporal average intensity
time-average of the instantaneous intensity at a particular point in an acoustic field. The time-average is taken over an integral number of acoustic repetition periods, unless otherwise specified.

Symbol: I_{TA}

Unit: W/cm^2

3.6
focal region
spatial region in the focused field consisting of all points at which the temporal average intensity (or square of r.m.s pressure) is greater than a specified fraction of the maximum value of the temporal average intensity or the square of r.m.s. pressure in the field. The specified fraction are 0,5 and 0,25 for the –3 dB and –6 dB focal regions respectively.

3.7
temporal average intensity spatially averaged over the –6 dB beam area
spatial-average value of the **temporal average intensity** over the –6 dB beam area

Symbol: I_{sal}

Unit: W/cm^2

3.8
pulse-average intensity
ratio of the pulse-intensity integral to the pulse duration at a particular point in an acoustic field

Symbol: I_{pa}

Unit: W/cm^2

3.9
spatial peak(temporal-average) intensity
maximum value of the temporal-average intensity in an acoustic field or in a specified plane

Symbol: I_{sp} , I_{spta}

Unit: W/cm^2

3.10
peak-negative acoustic pressure; peak-rarefactional acoustic pressure
maximum of the modulus of the negative instantaneous acoustic pressure in an acoustic field or in a specified plane during an acoustic repetition period. Peak-negative acoustic pressure is expressed as a positive number.

Symbol: p_- , p_r

Unit: pascal, Pa

3.11
full width at half (pressure) maximum
maximum dimensions of –6dB focal region in the directions which are perpendicular to the beam axis and parallel to the beam axis

Symbol: *FWHM*

Unit: mm

3.12
maximum side lobe level
ratio of the secondary pressure maximum to the main (the first) pressure maximum in the pressure focal plane in dB

Symbol: L_{sm}

Unit: dB

3.13
axial secondary maximum level
ratio of the secondary pressure maximum to the main (the first) pressure maximum on the beam axis

Symbol: L_{asm}

Unit: dB

3.14
pressure focal length
distance from the effective radiation surface of focusing transducer to the pressure focus along the beam axis. Generally it can be expressed as the effective acoustic path in the medium during the time interval from the transmitting signal of the focusing transducer to the received signal of the hydrophone at focus.

Symbol: F_{pres}

Unit: mm

3.15
effective area of an ultrasonic focusing transducer
predicted radiation surface area of a ideal spherical focusing ultrasonic transducer which has an acoustic pressure distribution in the focal plane approximately equivalent to the observed acoustic pressure distribution in the same focal plane of the real spherical focusing ultrasonic transducer

Symbol: A_e

Unit: cm^2

3.16
pressure focal gain
square root of the pulse-pressure-squared-integral at the pressure focus, divided by the square root of pulse-pressure-squared-integral spatially averaged over the **effective area of an ultrasonic focusing transducer**

Symbol: G_{pfocal}

Unit: dimensionless

3.17
arithmetic-mean acoustic-working frequency
arithmetic mean of the frequencies f_1 and f_2 at which the amplitude of acoustic pressure spectrum is 3 dB below the peak amplitude

Symbol: f_{awf}

Unit: Hz

3.18
harmonic distortion coefficient
ratio of the root mean square value of all harmonic pressures except the fundamental frequency pressure to that of all harmonic pressures including the fundamental frequency pressure, the harmonic distortion coefficient is expressed as

$$D(\%) = \sqrt{\frac{\sum_{i=2}^{n} p_i^2}{\sum_{i=1}^{n} p_i^2}} = \sqrt{\frac{\sum_{i=2}^{n} H_i^2}{1+\sum_{i=2}^{n} H_i^2}} \times 100\% \quad (1)$$

where

p_i is the amplitude of the *i*th harmonic pressure;

H_i is the ratio of the *i*th harmonic pressure to the fundamental pressure, $H_i = \frac{p_i}{p_1}$;

n is the highest order number of the harmonic pressure.

Symbol: *D*

Unit: dimensionless

4 General

This national standard specifies the measurement of the acoustic power of the HIFU source using the radiation force balance. Several relationships between the acoustic power of several typical sources and the normal radiation force acted on the absorbing target are given in this standard to estimate the measurement uncertainty.

This national standard specifies the measurement of the field characteristic parameter of HIFU using the hydrophone. First detect the pressure waveforms and their spatial distribution then calculate the derived intensities and corresponding parameters and determine the geometry parameters of the focused acoustic field.

5 Requirements for the measurement system

5.1 Requirements for the radiation force balance system

5.1.1 Requirements for the target

This national standard recommends using the absorbing target whose pressure reflection coefficient should be equal to or less than 5 %, pressure transmission coefficient should be less than 10 %. The diameter or the minimum dimension of the target should be greater than the 1,5 times of –26 dB beam width on the beam cross-section plane where the target is placed.

5.1.1 Requirement for the supporting or suspending system of the target

The supporting member (or suspending wire) should have sufficient stability to minimize the transverse displacement of the target and to minimize its influence for the measurement result. The beam axis should remain to be perpendicular to the surface of the target.

5.1.2 Force measurement system

The electronic balance or the force sensor should be used as the force measurement device and their accuracy should be better than 10^{-3} N.

5.2 Requirements for measurement system using hydrophones

5.2.1 Requirement for hydrophones

5.2.1.1 Requirements for the sensitivity

The free field end-of-cable voltage sensitivity should not be less than 10 nV/Pa.

5.2.1.2 Requirement for frequency bandwidth

In the frequency range of one octave band, the sensitivity response shall not vary by more than ±6 dB.

5.2.1.3 Requirement for directivity

The –6dB beam width angle should be equal to or greater than 70°in the direction of the main beam axis at the arithmetic-mean acoustic working frequency.

5.2.1.4 Determination of the effective radius of the hydrophone

Measure $\theta_{\text{-3dB}}$ and $\theta_{\text{-6dB}}$, calculate $a_{\text{-3dB}}$ and $a_{\text{-6dB}}$ using equation (2), and equation (3); calculate the arithmetic mean value of $a_{\text{-3dB}}$ and $a_{\text{-6dB}}$ using equation(4):

$$a_3 = \frac{1.62}{k \sin \theta_{-3dB}} \tag{2}$$

$$a_6 = \frac{2.22}{k \sin \theta_{-6dB}} \tag{3}$$

$$a = \frac{1}{2}(a_3 + a_6) \tag{4}$$

where

k is the wave number, mm $^{-1}$.

θ_{-3dB} and θ_{-3dB} are halves of –3dB and –6 dB beam width angle in the directivity pattern of the hydrophone respectively.

5.2.1.5 Requirement for dimension of active element

Theoretically, the effective radius of active element of the hydrophone should be equal to or less than a quarter of wavelength. Maximum effective radius is:

$$a_{\max} = \frac{\lambda_{awf}}{8a_1}(l^2 + a_1^{\,2})^{1/2} \qquad (5)$$

where

λ_{awf} is the wave length corresponding the arithmetic-mean acoustic working frequency, mm;

a_1 is the effective radius of ultrasonic transducer or transducer array, or the half of maximum dimension, mm;

l is the distance between the surface of ultrasonic transducer and the hydrophone.

5.2.1.6 Linearity of hydrophone

The dynamic range should be the instantaneous pressure of at least 10 MPa within the nonlinear distortion (harmonic distortion coefficient) less than 10 %.

5.2.2 Requirement of hydrophone positioning system for the fixture and orientation

The hydrophone positioning system should securely fixed the hydrophone with its jig and can make the hydrophone rotate round two orthogonal axes for aligning. Both rotation axes should be normal to the direction of maximum sensitivity of the hydrophone and preferably pass through the center of the active element.

5.2.3 Requirement of hydrophone positioning system for scanning and anechoic covering

The system should be able to position the hydrophone in the vicinity of the pressure focus of HIFU system being measured and to scan the hydrophone step by step along two orthogonal axes on the plane normal to the beam axis of the focusing transducer or transducer array in the range of ±15 mm with reproducibility of the step not greater less than 0,1 λ_{awf} and along the beam axis in the range of ±25 mm with the step not greater than 0,2 λ_{awf} , where λ_{awf} is the wavelength at the arithmetic mean acoustic working frequency. All component structure parts or water level close to the active element of the hydrophone should been covered by acoustic absorbers sufficiently to ensure no echo signal influencing the measured results.

5.3 Requirement for water bath

5.3.1 Water bath of radiation force balance

For the transducer systems with the focused beam upward, the transducer or transducer array should be fixed on the bottom of the water bath, and the focused beam should be upward vertically by adjusting its directions. The suspended absorbing target with fibre wire is recommended. The wire should be as thin as possible and be caught on the hook in a hole of the base of the electronic balance to detect the normal radiation force acting upward on the absorbing target, as shown in Figure 1.