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Towards Comparison of Ultrasound Dose Measurements - Current Capabilities and Open Challenges -

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Abstract

The aim of this work is to evaluate measurement methods for dosimetry and exposimetry quantities that were developed in the EMRP project "Dosimetry for Ultrasound Therapy - DUTy" by comparing the measurement results for three common quantities from three national laboratories. It further aims to investigate the general feasibility of possible future (key) comparisons for dosimetry and exposimetry quantities and to identify possible open challenges towards this goal. The general format is similar to a metrological comparison, with which the National Metrological Institutes, NMIs, are already familiar. The first step involved the agreement of the protocol that was to specify the set of transducers to be circulated and the measurement conditions. Two transducers were circulated and different drive voltage levels and pulsing regimes were defined and tissue mimicking materials (TMMs) characteristics were specified. Each lab was asked to prepare the TMMs for their own measurements with the inclusion of formulations and preparation instructions specified in the protocol. Uncertainties of the input data were to be declared by the participating laboratories.

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Keywords: Ultrasound dose; High Intensity Focused Ultrasound, Tissue Mimicking Material

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1. Introduction

The word “dose” commonly takes one of two meanings: the amount of something administered, usually a medicine; or the energy deposited by the absorption of ionising radiation, such as X-rays or electrons. For therapeutic ultrasound, the term ‘dose’ however has never gained clear definition and usage in the context of the interaction of ultrasound with tissue (Shaw et al. 2015a). The lack of such a definition has led to confusion in the description of the conditions governing the treatment of the patient or, more generally, the interaction with tissue. For example, it is not uncommon for physiotherapists to use the word ‘dose’ to refer to the acoustic output, as indicated by the acoustic power in watts, or by the output intensity in watts per metre squared displayed on the ultrasound equipment. In this work, a part of HLT03 Dosimetry for Ultrasound Therapy “DUTy” project, three common proposals of ultrasound dose definition were investigated with respect to their suitability for interlaboratory comparisons based on measurements with different methods.

2. Ultrasound dose definitions used in comparison

In order to investigate the opinion of stakeholders and the therapeutic ultrasound community, a questionnaire had been circulated previously within the framework of this project among metrologists, researchers, clinicians, and other people working in the field of therapeutic ultrasound (Shaw et al. 2015b). From the results, three common definitions have been identified to be of high relevance and to be suitable for this work. Two are related to energy, namely the Applied Total Acoustic Energy (ATAE) and the Applied Total Electrical Energy (ATEE), , and the third , the Thermally Equivalent Time (TET) to temperature and time.

A Technical Protocol was prepared and approved by all participants in the comparison. In the Technical protocol in addition to the timetable, two travelling transducers were specified (Transducer 1: Piston like Transducer f_0 = 2.01 MHz, Transducer 2: Sonic Concepts focused bowl transducer f_0 =2.00 MHz and f_3 = 6.38 MHz). The nominal levels of ultrasonic power P, the corresponding electrical voltage U_s to apply to the transducers for the insonation phase, and the times for insonation, t_{ON}, and for zero signal applied, t_{OFF}. It was discovered before the definition of the comparison that the TMM was not able to withstand a despatch by courier. Therefore in the technical protocol the recipe and procedure for preparing a Gellan Gum (PHYTAGEL) based TMM was specified, in order to enable each laboratory to prepare the TMM for his own measurements.

The NMIs involved were: **INRIM** - Istituto Nazionale di Ricerca Metrologica - Italy (Pilot Institute), **NPL** - National Physical Laboratory - UK, **PTB** - Physikalisch-Technische Bundesanstalt - Germany, **TÜBİTAK-UME** - Ulusal Metroloji Enstitüsü - Turkey

2.1. ATAE and ATEE definitions

The ATAE, E_{TOT_AC}, is the applied total acoustic energy, which is emitted from an ultrasound transducer and ATEE, E_{TOT_EL}, is the applied total electrical energy, provided to an ultrasound transducer during an application:

$$E_{TOT\_AC} = P_{AC} \times t_{ON}$$
$$E_{TOT\_EL} = P_{EL} \times t_{ON} \quad (1)$$

The acoustical and electrical energy were calculated from measurements of acoustic and electric power, P_{AC}, and P_{EL}, using equation (1), where the time of transducer supply, is defined by $t_{ON} = N_{Cycles}\, t_{US\_ON}$.

During the t_{ON} time it was necessary to perform 10 shorter insonations of duration $t_{US\_ON,}$ each followed by a gap of duration t_{US_OFF} (equal to 70 ms). This gap was necessary in order to permit acoustic temperature measurements at PTB.

The intervals, $t_{US\_ON,}$, $t_{US\_OFF,}$ were specified in the technical protocol along with the overall times $t_{ON,}$, $t_{OFF,}$, and the total measurement time $t_{final.}$.

2.2. TET definitions

The Thermally Equivalent Time (TET) for a given time temperature profile $T(t)$ at any point x in heated medium is the time t_{REF} over which a constant temperature T_{REF} is supposed to yield the same biological effect in the same medium. Typically, a reference temperature of T_{REF} = 43 °C is used in most considerations. Since the medium employed in this work, a TMM, does not show any biological effect, the empirical formula for the calculation of TET from $T(t)$ was used here (Sapareto and Dewey, 1984). In this comparison, furthermore the baseline of the data was shifted from ambient temperature T_{amb} to 37 °C by adding an offset of 37 °C - T_{amb} to all measured temperature values, so that a physiologically relevant TET could be calculated with a reference temperature of 43 °C.

Note that shifting the baseline to 37 °C is equivalent to redefining the thermal dose to be based on a temperature rise, $dT(t)$, instead of an absolute temperature, so that:

$$t_{+6} = \int_{t=0}^{t=t_{final}} R^{\left(\frac{6-dT(t)}{°C}\right)} dt \qquad \begin{cases} R = 0.50 \text{ for } dT(t) > +6°C \\ R = 0.25 \text{ for } dT(t) < +6°C \end{cases} \tag{2}$$

For 'engineering' measurements and comparisons which are generally not carried out at 37 °C, this redefinition is probably clearer and may be more useful. The laboratories have measured two values of t_{+6}:

t_{+6_ON}: t_{+6} calculated with $t_{final} = t_{ON}$ (which includes only the TET delivered during the insonation period);

t_{+6_ON+OFF}: t_{+6} calculated with $t_{final} = t_{ON} + t_{OFF}$. (which also includes the TET delivered whilst cooling after the end of the insonation period).

In order to determine thermally equivalent time, it is necessary to know the time temperature profile $T(t)$ at any point x in heated tissue (or TMM in this case).

3. Methods for determination of ATAE and ATEE definitions

For determination of the ATAE, the applied total acoustic energy of the transducers for the given conditions, a radiation force balance with absorbing targets was used by NPL, PTB, UME laboratories. In addition, NPL measured ATAE values also with a buoyancy balance system using a castor oil filled target. The target had a thin F28 absorber layer in the base and an integral heating coil for calibration. The acoustic output power P_{AC} was measured for continuous sonications at the given input voltages with different ON-times. The measurements were performed at different distances and extrapolated to zero-distance. From the extrapolated output power values, the ATAE was calculated following equation (1). For determination of the ATEE, the electrical input power P_{EL} was measured for sonications at the given input voltages with different ON-times. The measurements were performed with a power reflection meter with a sensing head (PTB), or using an in-house system assembled from a oscilloscope and current transformer terminated in a 50 Ω shunt, coupled to a software to acquire date from the oscilloscope and calculate the electrical power (NPL, TÜBİTAK-UME). From measured electrical power values, the ATEE was calculated following equation (1).

4. Methods for determination of TET definition

PTB measured the temperature variation in TMM using a method based on the thermal dependence of the ultrasound echo that accounts for two different physical phenomena: local change in speed of sound due to changes in temperature and thermal expansion of the propagating medium. The former produces an apparent shift in scatterer location, and the latter leads to a physical shift. Along an A-line, however, the two effects lead to echo time-shifts that can be estimated and are shown to be related to local change in temperature in the propagating medium. These effects are typically small, so that a linearized approach can be used in the analysis. The measure system is based on imaging probe: linear phased array with a centre frequency of 7.14 MHz, sampling frequency of 50 MHz. The diagnostic probe was attached to a 3-axis positioning system for precise alignment with the ultrasound source and the sample. A diagnostic probe was mounted from the top side of the phantom, perpendicularly to the therapeutic transducer axis. From an Esaote imaging system, beam formed RF-data were collected in real-time and saved for later processing. To avoid interference between the therapeutic source and imaging system, the image data were acquired during an interruption of the therapeutic transducer, t_{US_OFF}. Before the measurements, a Type IT-23, Coated copper-constantan thermocouple sensor was placed at the centre of the TMM, which was then heated in a water bath to obtain reference temperature readings, which were then used to calculate the material dependent constant *k* that is needed for conversion of echo-shift measurements to temperatures (Fuhrmann et al. 2015).

In the NPL system configuration the transducers were mounted with their radiating surfaces pointing downwards into a tank of degassed, deionised water. The horizontal position of the transducers was adjusted using computer controlled motors. An NPL made thin film thermocouple (consisting of 200 nm thick electrodes on a 8 µm kapton substrate) was sandwiched between two sections of the TMM and held in a motorised stage with vertical movement controlled by computerised motors. The sensitivity of the thermocouple was determined by heating the thermocouple element with a small heater, the temperature during heating was measured by another thermocouple placed against the element then this was used to calculate the sensitivity of the thin film thermocouple. The acquired data was the temperature rise during the period of interest which consisted of t_{ON} during which the transducer was powered on and t_{ON+OFF} which included a period after this as set out in the intercomparison protocol. The temperature rise data was corrected for any cooling or drifts in temperature by fitting a straight line to the data before the heating period and subtracting this trend from the data. The rate of change of temperature prior to insonation was typically a few thousands of a degree per second which would introduce an uncertainty of less than 0.1°C in the peak temperature rise even over the longest t_{ON} period of 20 s.

The temperature measurement system developed by TÜBİTAK-UME was realized using TMM implanted with a Physitemp type IT-24P, polyurethane coated T-type thermocouple of wire diameter approximately 100 µm. The transducer was placed at the bottom of the water tank. The whole assembly was inside the water, in order to simulate the real human body conditions. The TMM was arranged so that the temperature sensor was placed at the focal point of the transducer. Plane and concave focused transducer was used in the same configuration. The drive voltage and current were monitored using a digitizing 1 GHz oscilloscope. Exposures were made in degassed water at room temperature. All wire thermocouples were inserted into the tissue phantom perpendicular to the beam axis.

5. Results and data analysis

Measurements results of ATAE and ATEE are shown in Fig. 1.

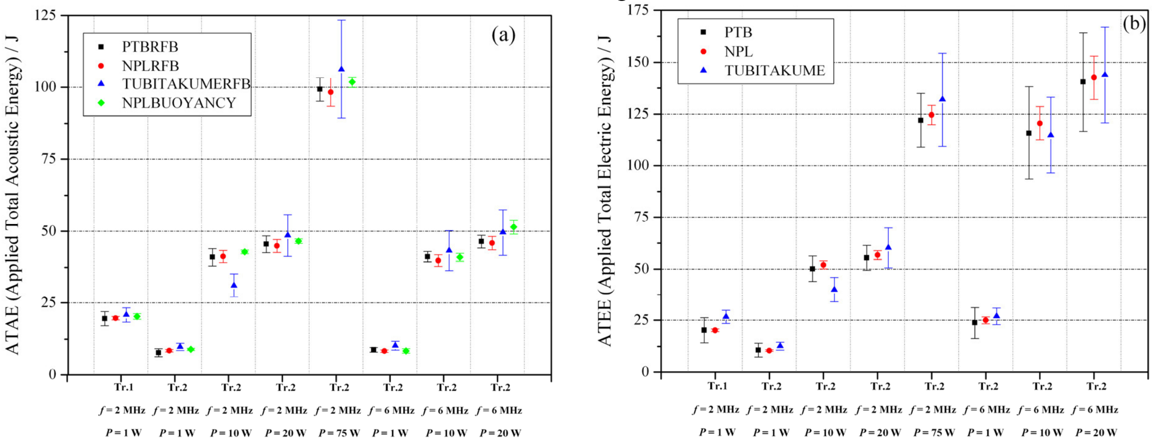

Fig. 1. (a) ATAE measurements, E_{TOT_AC}; (b) ATEE measurements, E_{TOT_EL}

Results of TET measurements are shown in Fig. 2.

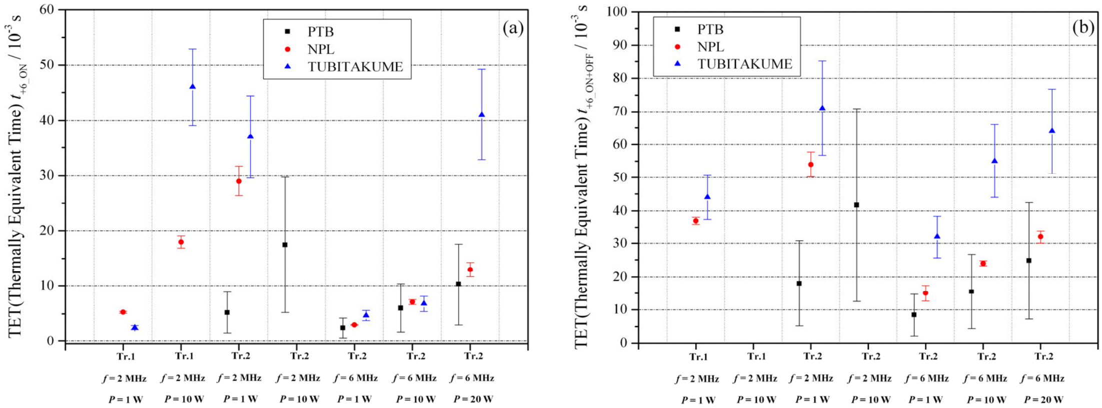

Fig. 2. (a) TET, t_{+6_ON}, measurements; (b) TET, t_{+6_ON+OFF}, measurements

In order to check the consistency of data and to calculate the reference values least-squares adjustment analysis was used (Cox, 2002). Reference values, x_{REF}, associated uncertainties, $U(x_{REF})$, of reference values and degree of equivalence of laboratories, (d, $U(d)$) from a set of measurements: $\{x_1,\cdots,x_N\}$, with associated uncertainties $\{u(x_1),\cdots,u(x_N)\}$, for ATAE, E_{TOT_AC}, ATEE, E_{TOT_EL}, TET, t_{+6_ON}, $t_{+6\_\mathrm{ON+OFF}}$, for every nominal power level were obtained.

6. Discussion and conclusion

Most of ATAE and ATEE measurements resulted to be consistent among the three labs involved, while TET measurements were not consistent, almost for every considered power level. This is probably due to the fact that the TMMs used for measurement were prepared on site at each laboratory following a shared protocol. It was not possible to prepare all the TMMs in the same laboratory, as the material could not withstand transportation without alteration of its properties. The calculation of TET it very sensitive to changes in the maximum measured temperature, and this is in turn dependent on the thermal and physical properties of the TMM and the thermal stability during the experiment. An imperfect execution of the procedure of TMM preparation might have lead to significant differences in the parameters that have an influence on ultrasound energy absorption. Not all the laboratories were equipped with a measurement system for the absorption coefficient measurement, therefore the compliance of the TMM with the requirements of the protocol could not be verified.

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