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MEASUREMENTS OF ULTRASONIC CAVITATION IN LIQUIDS AND TISSUE MIMICKING MATERIALS

Adriano Troia, Pietro De Nicola

Metrology for Quality of Life, National Institute of Metrological Research, strada delle Cacce 91, 10135 Turin, Italy
email: a.troia@inrim.it

Today the acoustic cavitation is used in many fields, from industrial applications for the cleaning technology, to the research applications in fields of nanotecnologies and enviromental, up to therapeutic applications in the biomedical field. However it is not yet clear which of the different phenomena induced by acoustic cavitation plays a fundamental role respect to the several applications: from the mechanical effects resulting from the violent collapse of bubbles typically driven at low frequency (20-40 kHz), to the chemical effects mostly induced by high frequency ultrasound (500-800 KHz), until to the heating effects which dominate in therapeutic applications (1-3 MHz). The research is still affected by lack of measuring instruments appropriate to characterize the various techniques which generate ultrasonic cavitation. In this work we will be presented different measurement techniques to assess the acoustic cavitation induced in different liquid and semisolid media, by using different ultrasound sources.

Keywords: ultrasound, cavitation, tissue mimicking materials

1. Introduction

The use of high-power ultrasound has many applications. From acceleration of chemical reactions, to the mechanical erosion of solid surfaces or the activation of drug release, the involved mechanisms are induced by acoustic cavitation, that is the formation of gas/vapour bubbles in a liquid subject to local pressure variations phenomena, and their rapid and violent collapse [1,2]. A large amount of ultrasound devices are employed in sonochemistry or biomedical applications ranging from ultrasonic cleaning vessels, to purpose-built ultrasonic horns or focused ultrasonic transducers. All of these are likely to produce different “amounts” of cavitation activity, depending on factors such as the acoustic pressure levels generated from the source, the vessels and device characteristics, the nature of the medium and finally the working frequency of the transducer. Up today different indirect cavitation measuring techniques (calorimetric, reaction’s rate, optical method) have been proposed but they are affected by several factors and they have not provided a real measuring of cavitation activity. The development of cavitation sensor, cavitometer, have been proposed by different research groups [3,4] in these years. It is well know that in response to a forcing acoustic field, the bubbles act as secondary acoustic sources whose emission spectra contain a substantial amount of information related to the dynamics of the cavitation process. Basing on the analysis of the “broadband white noise” in MHz frequency region generated by the shock waves emitted by collapsing bubbles, of the sub harmonics produced by bubbles which undergoing to inertial collapse mechanism [3] or ultra harmonics generated by stable bubbles oscillations [4], is possible to obtain different analysis parameters whereby cavitation activity can be characterised. Following the work carried out during these years by Zequiri et al [3] we have developed a cavitation sensor, based on similar assumptions, in order to evaluate the cavitation activity performed by a custom ultrasonic vessel operating in the low frequency region (20-40kHz). After validation of the experimental set-up using a commercial ultrasonic bath we have investigated the cavitation activity as function of liquid media and a correlation between the physical properties of the solution with “cavitation noise” and sub-harmonics emission have been found. Successively this set-up of measurement has been employed for investigations of cavitation activity induced by high intensity focused ultrasound (HIFU) in tissue mimicking materials. Tissue mimicking materials (TMM) are commonly used to investigate the effect induced by diagnostic and therapeutic ultrasounds in vitro. In particular, studies on HIFU treatments are of great interest since cavitation phenomena and formation of lesions present some unclear aspects, which have caused different side effects in clinical trials, limiting HIFU therapeutic treatments. In this case measurements of the bubbles acoustic emissions was affected by the presence of tissue mimicking media and the operating frequency of HIFU transducers, which was in MHz spectral region analysed. A preliminary investigations on different spectral contributions (broad band, ultra harmonics and sub harmonics) will be reported as function of acoustic properties of the tissue mimicking materials.

2. Material and methods

2.1 Cavitation sensors

The monitoring of the broadband and harmonic acoustic emission produced by bubbles collapse and bubbles oscillations, respectively, have been performed by using three sensor types: a Bruel & Kjaer 8103 hydrophone for detection of low frequencies subharmonics emission; a piezoceramic needle hydrophone (Dapco NP 10-3) and a PVDF gold coated thin film with annular geometry as can be seen in Fig. 1, for the acoustic broadband emission. The blue rubber around the thin film have been used in order to insulate the sensor from outside and monitoring only inner cavitation events, in order to have a good spatial resolution.

2.2 Measurements set-up

In Fig. 2 the measurement set-up scheme is depicted. The acoustic emissions detected by sensor/cavitometer is amplified and then acquired by a spectrum analyser (Agilent N9320B) or oscilloscope (Agilent DSO-X-2022A). The signal analysis have been performed using a PCI/LabView custom software. All the measures reported here are the results of several acquisitions, and only the medium value of cavitation noise, or spectra, are shown. External parameters as temperature and concentration of dissolved gas have been monitored by using an optical oxygen sensor (LDO-Hach Langhe). In Fig. 3 the sonication vessel in which the measures of the cavitation activity, as a function of different solutions and for different driving voltage to the transducer, is shown. On the right of the same figure, the set-up for cavitation activity measurements in TMM exposed to an HIFU transducer, as function of different driving voltage and different types of TMM.

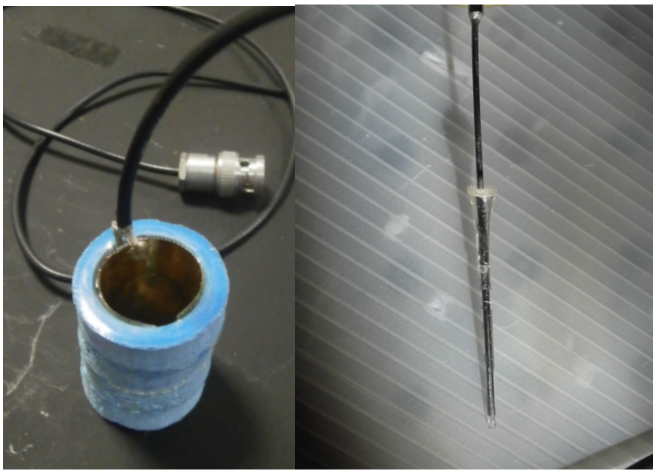

Figure 1: On the left the cavitometer realized at INRM; on the right the needle hydrophone Dapco NP 10-3 with a glass coating tube to prevent possible damage when inserted in tissue mimicking materials.

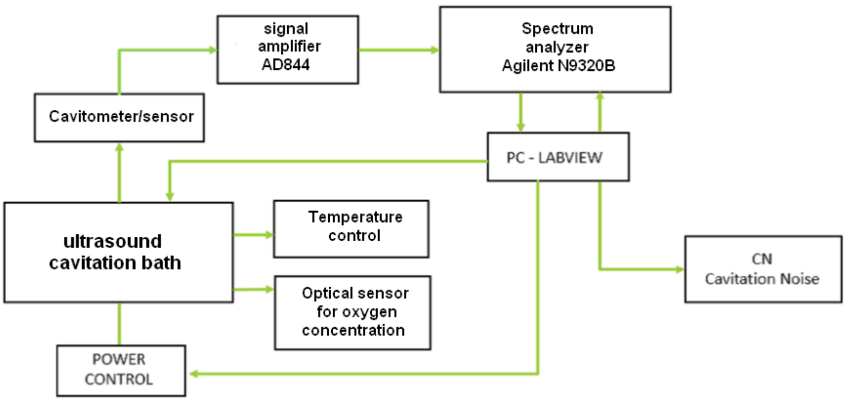

Figure 2: Scheme of experimental apparatus for cavitation activity measurements .

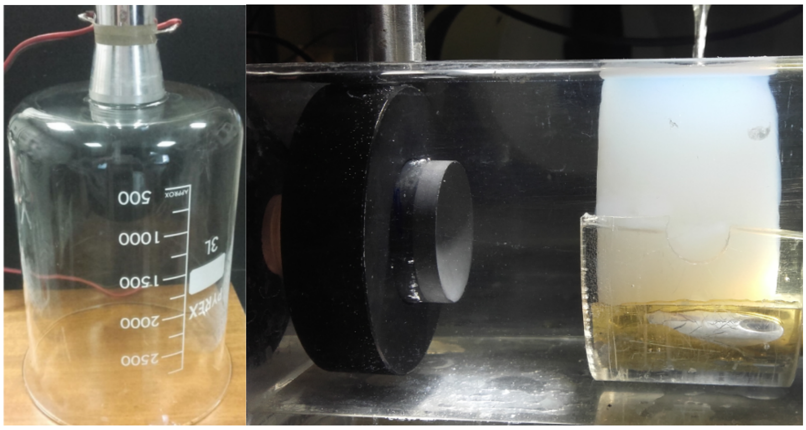

Figure 3: On the left, the sonication vessel realized at INRIM; on the right, the HIFU transducer and tissue mimicking materials with the thin film cavitation sensor and needle hydrophone.

2.3 Tissue mimicking materials and liquids tested

Tissue mimicking materials (TMM) are of great interest to investigate the effects induced by therapeutic ultrasounds in vitro. In this work Agar based TMM have been used, starting with our previous results here reported [5]. The modulation of TMM acoustic attenuation has been performed using concentrated adsorbing salt solution [6] while other parameters like density speed of sound, and Young's modulus have been maintained constant. More details on this point can be found in [6,7]. Cavitation activity measurement in ultrasonic vessel have been performed in three different liquids: water, a 25% aqueous solution of Ethanol and a 25% aqueous solution of Glycerol. Since from the theory is accepted that more volatile or more viscous solutions should have an effect on cavitation activity and cavitation threshold, our scope was to verify this point by means of our cavitometer, into these solutions.

2.4 Generation of high intensity acoustic fields

The high intensity ultrasound fields have been generated using a function generator (Standford DS345) connected to an high intensity amplifier (Amplifier&Research AR-800A3). The working frequency of the vessel was of 32 KHz while the working frequency of HIFU transducer (Blatek Industries) was of 1.5 MHz.

3. Experimental results

3.1 Acoustic cavitation measurement in sonication vessel

In Fig. 4 the cavitation noise, intended as the total area of the broad band signal within the frequency of 1-3.MHz, measured in cavitation vessel, as function of ultrasound intensity and for different solutions, is reported. It is possible to note that the cavitation activity rises, in general, as the driving voltage sent to the transducer, i.e. intensity of ultrasounds field, increases, but some features respect to different liquids tested can be extracted. At low ultrasound intensity the cavitation noise results more intense in ethanol solution, while at higher ultrasound intensity, a lower cavitation noise has been measured in this medium. On the contrary, the cavitation noise detected in glycerine solution is the lower at low intensity while is the highest when the driving voltage is increased to the maximum. This features can be explained considering that in a more volatile solution (ethanol) the cavitation threshold is lower; consequently, the nucleation of bubbles and cavitation activity can be obtained for low intensity ultrasounds. On the other side, in more viscous media (glycerol), which have higher cavitation threshold, a lower cavitation activity is expected at low intensity ultrasounds; nevertheless, when the intensity rises, a more violent bubbles collapse is expected, which results to a greater cavitation activity, as measured. The reduction of cavitation noise for ethanol solution at higher ultrasounds intensity, finally, is due to the formation of bigger bubbles which have a cushioning effect respect to the acoustic emission produced by cavitation and behave as energy absorbing zones released from cavitation, thus decreasing the effectiveness of both from an acoustic point of view that the chemical-physical. In general for all the liquids is possible to identify these higher thresholds, beyond which the cavitation noise decreases. In this case the more volatile is the liquid the less is the intensity of ultrasound necessary to reach it. A further increase of ultrasound field have been limited by motion instability, due the pressure radiation force, that influenced the cavitometer/hydrophone system stability. On Fig. 4 (right graph) is reported also the value of sub-harmonic frequency (around 16 kHz, depend on the liquid). Since the formation of this spectral component has been related to inertial cavitation phenomena or non- linear bubbles oscillations [8], we measured the intensity of this band using the Bruel & Kjaer 8103 hydrophone, near the inner region of cavitometer, in order to assess the cavitation threshold of the three different liquids media and, as expected, the lower threshold has been found in ethanol solution, while the glycerol solution has the higher.

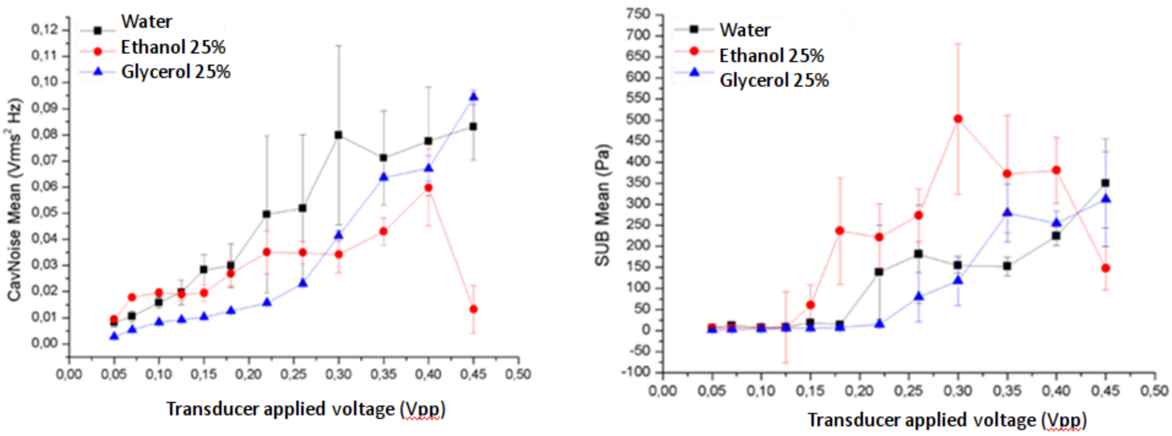

Figure 4: Cavitation noise measurements with relative uncertainty performed in different solutions. The Vpp refers to the applied voltage to signal generator connected to the amplifier. On the right graph the measurement of subharmonic at same conditions.

3.2 Acoustic cavitation measurements in tissue mimicking materials

The cavitation measurement in tissue mimicking materials have been performed using the experimental set-up showed in Fig.3. For this purpose the cavitation activity have been measured using the needle hydrophone (DAPCO NP 10-3). For each measurement the needle hydrophone was positioned with XYZ motorized slides, which have allowed a reproducibility of +/- 1 mm. The hydrophone was positioned laterally, with a distance of about 5 mm from the focus. The analysis of the broad band noise, in this case, is affected by the transducer operating frequency and from the presence of several frequency contributions, in terms of sub/ultra harmonics which can be ascribed to different bubbles dynamics (stable oscillation, collapse, sound absorption phenomena), as reported in [9,10]. Thus for this case, the results analysis on the single spectra detected in TMM will be presented. For cavitation threshold detection a commercial cavitometer high frequency (ICA-5D) have been used. The value reported by this device did not provide a unit measure, but has a good sensitivity on detecting the rise of cavitation activity and allowed to acquire the raw signal data using the spectrum analyser, so that have been correlated to the signals detected by needle hydrophone, under HIFU exposure, in water. As can be seen in Fig. 5, as the power increase, four different spectra of acoustic emission of bubbles can be identified and correlated to different cavitation activity, as it was reported in [9]. This kind of spectra have been also detected in TMM exposed to focused ultrasound as function of HIFU intensity. We performed several experiments using Agar based TMM. In our previous work [5] we found as using a concentrated solution of inorganic salt, like zinc acetate, is possible to vary the attenuation coefficient of a TMM without affecting its mechanical properties; in this case two Agar based TMM have been used: the first contained simply Agar, second contained also a solution of zinc acetate (0.4 M), further details can be found in [5,6]. The acoustic spectra detected in these two sample are shown in figure 6 and 7. It is possible to note that for the more attenuating TMM, the broad band characteristic of cavitation activity appears for lower HIFU intensity. This can be explained considered that a higher absorption would lead to formation of cavity even at lower intensity, which would lead also, as confirmed from the pictures in Fig. 8, to a larger lesion.

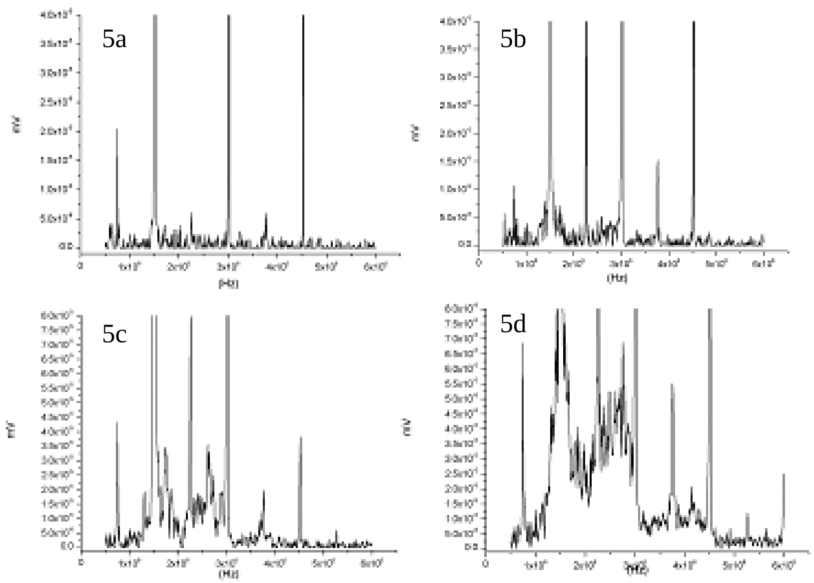

Figure 5: High frequency spectra (0.5 kHz – 6 MHz) recorded with needle hydrophone in water, as function of focused acoustic field intensity (from 5a to 5d). Spectrum of figure 5c refers to the condition in which the cavitometer (ICA-5D) detects a cavitation activity.

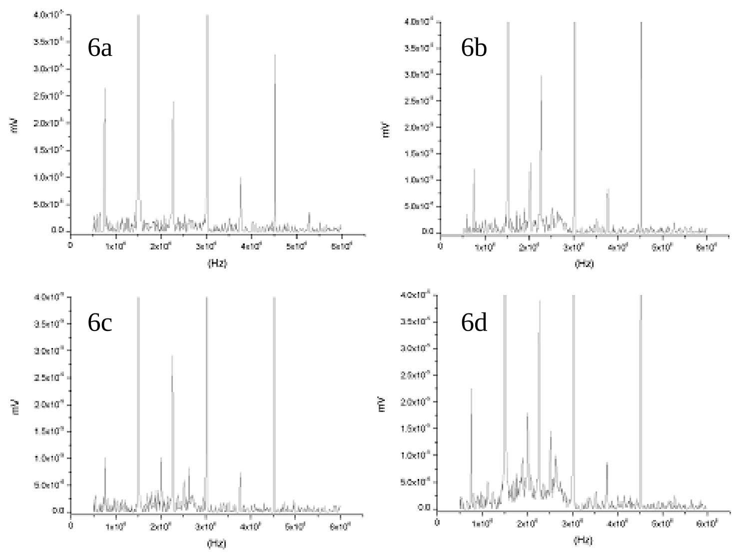

Figure 6: Spectra (0.5 kHz – 6 MHz) recorded with needle hydrophone in Agar (3% in wt.)based TMM, as function of focused acoustic field intensity (same conditions of Fig.5).Attenuation coefficient for this TMM was of about 0.05 ± 0.01 dB/(cm•MHz^n)

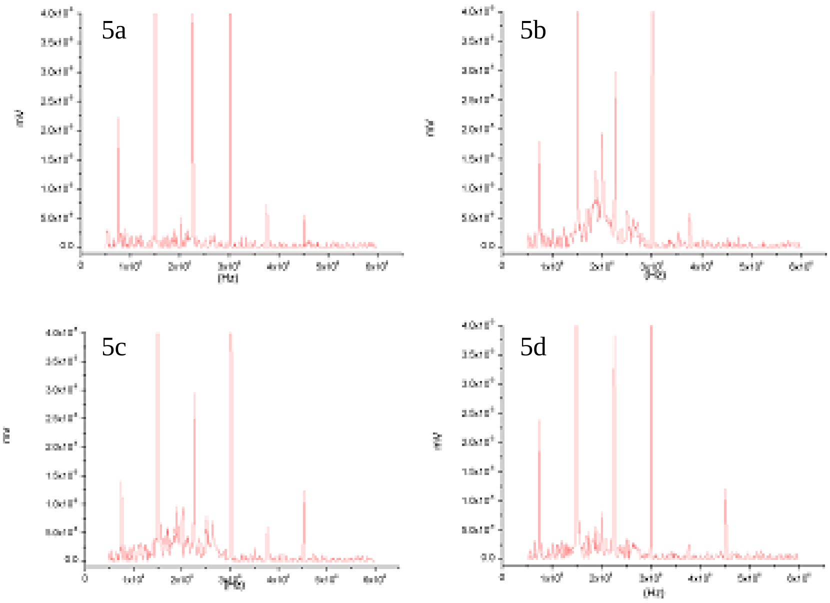

Figure 7: Spectra (0.5 kHz – 6 MHz) recorded with needle hydrophone in Agar (3% in wt.) based TMM prepared in a 0.4 M solution of zinc acetate, as function of focused acoustic field intensity as reported in figure5.Attenuation coefficient for this TMM was of about 0.53± 0.02 dB/(cm•MHz^n)

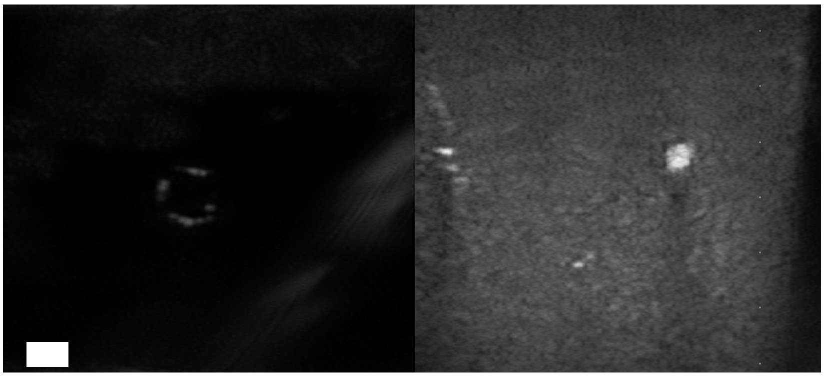

Figure 7: Images on the lesion induced by HIFU transducer in Agar TMM congaing zinc acetate, on the left, and without zinc acetate, on the right. Scale bar 5 mm. The images were acquired by means of a research ultrasound scanner (Ultrasonix, Sonictouch)

4. Conclusions

An experimental set up for cavitation activity measurement has been developed and, for the first time, cavitation activity measurements have been correlated to the physical parameters of liquids tested. Experimental investigations on cavitation activity induced by HIFU transducer in tissue mimicking materials have been performed and a correlation with the broadband noise relative to cavitation activity, respect to the attenuation properties of TMM, have been found. Since from the literature different stage of cavitation activity have been identified in high frequency ultrasonic cavitation, the detection of cavitation thresholds in these media still appears a challenge. Further trials in which a modulation of acoustic field (pulsed regime) and mechanical properties of TMM (different polymers, dispersion of solid particles), even using a multi component TMM, will be explored, in order to assess the different cavitation stages in these tissue simulating materials.

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