

# Use of Chemical Dosimetry for Comparison of Ultrasound and Ionizing Radiation Effects on Cavitation

B. KRATOCHVÍL<sup>1</sup>, V. MORNSTEIN<sup>2</sup>

<sup>1</sup>*Department of Biochemistry, Chemistry and Biophysics, University of Veterinary and Pharmaceutical Sciences, Brno,* <sup>2</sup>*Department of Biophysics, Medical Faculty, Masaryk University, Brno, Czech Republic*

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## Summary

A comparison of the effects of ultrasound produced by low- and high-frequency ultrasonic apparatuses upon biological systems is one of the basic problems when studying ultrasound cavitation effects. One possibility for how to compare these effects is the indirect method which uses well-known physical quantities characterizing the interaction of ionizing radiation with matter and which also converts these quantities to one common physical quantity. The comparison was performed with two methods applied to the chemical dosimetry of ionizing radiation. The first method employed a two-component dosimeter which is composed of 50 % chloroform and 50 % re-distilled water (i.e. Taplin dosimeter). The other method used a modified iodide dosimeter prepared from a 0.5 M potassium iodide solution. After irradiation or ultrasound exposure, measurable chemical changes occurred in both dosimeters. The longer the exposure, the greater the chemical changes. These effects are described by the relationship of these changes versus the exposure times in both dosimeters. The UZD 21 ultrasonic disintegrator (with a frequency of 20 kHz, 50 % power output) was used as a low-frequency ultrasound source, and the BTL-07 therapeutic instrument (with a frequency of 1 MHz and intensity of 2 W/cm<sup>2</sup>) was used as a high-frequency cavitation ultrasound source. For comparison, a <sup>60</sup>Co gamma source was applied (<sup>60</sup>Co, gamma energies of 1.17 and 1.33 MeV, activity of 14 PBq). Results of this study have demonstrated that the sonochemical products are generated during exposure in the exposed samples of both dosimeters for all apparatuses used. The amount of these products depends linearly upon the exposure time. The resulting cavitation effects were recalculated to a gray-equivalent dose (the proposed unit is cavitation gray [cavitGy]) based on the sonochemical effects compared to the effects of ionizing radiation from the <sup>60</sup>Co source.

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## Key words

Cavitation effects • Ultrasound • Ionizing radiation • Gray equivalent dose • Dosimetry

## Introduction

The objective of this study is to quantify the cavitation effects for different ultrasonic apparatuses and to compare the cavitation effects with the radiochemical

effects of high-energy ionizing radiation. In the past, the problem of comparing ultrasonic chemical effects with ionizing radiation effects was studied by many authors, for example, (Portenlänger and Heusinger 1992) and (Jana and Chatterjee 1995).

Ultrasonic cavitation is a physical phenomenon which manifests itself by chemical, mechanical and thermal effects (Mornstein *et al.* 1992). Sonochemical reactions may be used to monitor ultrasonic effects on biological systems, and moreover, a new chemical discipline (sonochemistry) has been developed on this principle which deals with the ultrasonically catalysed synthetic and other reactions (Kimura *et al.* 1996). In sonochemistry, low-frequency power ultrasound generated by ultrasonic disintegrators or cleaners is mainly used (Mornstein and Kaplan 1994). Ultrasonic sonochemical effects are based upon a similar mechanism as the indirect effect of ionizing radiation. They relate to ultrasonic cavitation, which are radial oscillations and/or the collapses of microscopic gas bubbles driven by the oscillating acoustic pressure. Adiabatic heating of cavitation bubbles produces temperatures sufficient to split water molecules to the free radicals which, after that, initiate a series of other chemical reactions (Suslick 1990).

Investigation of the effects of ultrasound cavitation is of great importance in medicine. In ultrasound diagnostics and physical therapy, cavitation is considered to be a risk factor and the intensities used must be kept below the cavitation threshold. IN ultrasonic surgery this threshold is exceeded and it is generally assumed to play a role in the destruction of the tissue. Moreover, free radicals formed during cavitation may damage biological structures at the molecular level. Cavitation phenomena accompanying sonication by means of disintegrators are often disregarded in spite of their possible effect on the biological samples prepared by sonication. Our efforts to quantify the chemical effects of cavitation are thus well substantiated (Mornstein *et al.* 1992). Several attempts were undertaken to quantify sonochemical effects using units of absorbed dose common in radiation physics. Birkin (Birkin *et al.* 2002) report on an electrochemical technique for the detection of oxidizing radical species, produced by ultrasound cavitation. A study of two example reactions is reported: the Weissler reaction and the Fricke reaction. In both cases, redox-active materials trap oxidative radicals. Electrochemical detection within a flow cell system is then used to sense redox-active products of the reactions between a chosen trapping agent and radicals produced within an ultrasonically irradiated aqueous solution. A demonstration of the sensitivity of electrochemical detection of radical products is presented. The physical quantity of "equivalent dose" with the unit of "gray [Gy]"

is employed to express the effects of cavitation ultrasound in sonochemistry. Rassokhin *et al.* (1995) measured with the argon-saturated Fricke dosimeter. The gamma-equivalent dose rate of ultrasound in the sonochemical cell was 2.6 kGy/h ( $1.6 \times 10^{22}$  eV dm<sup>-3</sup> h<sup>-1</sup>). In very dilute solutions the yields of formaldehyde and ethylene glycol were measured to be 1.5 and 0.64 molecules per 100 eV chemically active acoustic energy and did not depend upon the concentration of methanol unless that reached 0.02 M in case of formaldehyde and 0.1 M in case of ethylene glycol. The experimental data are discussed in terms of distinction and similarity between the sonolysis and the radiolysis of methanol in aqueous solutions.

However, we suppose that the unit "gray" used for ionizing radiation does not fully express the nature of the ultrasonic effects (e.g. the mechanism of free radicals production), and as seen from the above mentioned references, this has not been unified so far.

This study investigates mainly the chemical effects of cavitation ultrasound. Chemical dosimetry makes it possible to simulate and quantify the phenomena related to the indirect effects of ionizing radiation upon the biological systems through cavitation ultrasound (Heusinger 1990).

In the final step of comparing the cavitation effects of ultrasound and ionizing radiation in this study, the different physical quantities are converted to a proposed "gray equivalent dose" quantity with a unit of "cavitation gray [cavitGy]".

## Methods

### *Dosimeters used*

To monitor the sonochemical effects of cavitation, two chemical dosimeters were used enabling the determination of the equivalent "doses" for the different ultrasonic apparatuses which differ from each other by their intensities, frequencies and by the methods and the types of application.

Firstly, a two-component dosimeter (Taplin dosimeter) was used in this study as a chemical dosimetric system which consisted of 50 % chloroform and 50 % redistilled water (Pikaev 1975) while chloroform is collected in the lower part of the dosimeter volume. After irradiation or ultrasound exposure, chloroform dissociated to Cl<sup>-</sup> ions which reacted with water to hydrochloric acid, and reduced the pH value in the aqueous dosimeter phase. The pH-values in the

aqueous dosimeter phase were measured by means of the pH-meter PHYWE while the upper (aqueous) dosimeter phase was always separated from the lower one within 30 min after radiation or ultrasound exposure and measured immediately after separation. The pH values were converted to the concentration of  $\text{H}_3\text{O}^+$  hydroxonium ions by using the formula  $\text{pH} = -\log[\text{H}_3\text{O}^+]$ . The time needed for separation of the upper (aqueous) dosimeter phase after exposure was determined to be 30 min and was kept constant.

Secondly, a modified iodide dosimeter prepared from a 0.5 M potassium iodide solution was used (Walmsley *et al.* 1990). At the beginning, 0.5 % (V/V) carbon tetrachloride was added to the solution. Before exposure, this dosimeter solution was aerated for 10 minutes. Afterwards, carbon tetrachloride was filtered off the solution. The dosimeter prepared in such a way was a colorless solution. KI dissociated to  $\text{K}^+$  and  $\text{I}^-$  ions, and during irradiation and/or ultrasound exposure  $\text{I}^-$  oxidized to  $\text{I}_2$ . This reaction colored the dosimeter solution. The intensity of coloration was determined by means of the Spekol 11 spectrophotometer and the absorbance  $A$  at a wavelength of 350 nm was measured in the individual samples immediately after exposure.

The statistic parameters of all measured values were calculated using the Microsoft Excel 2000 and statistic program QE Expert.

#### Chemicals

Potassium iodide (p.a.), chloroform (p.a.) and carbon tetrachloride (p.a.) were from Fluka, Sigma-Aldrich family, Germany. The redistilled water was neither filtered nor degassed concerning the experimental design – the solutions were either shaken with chloroform or bubbled by air to achieve saturation of sample solutions with given substances as well as their identical chemical composition.

#### Apparatuses used

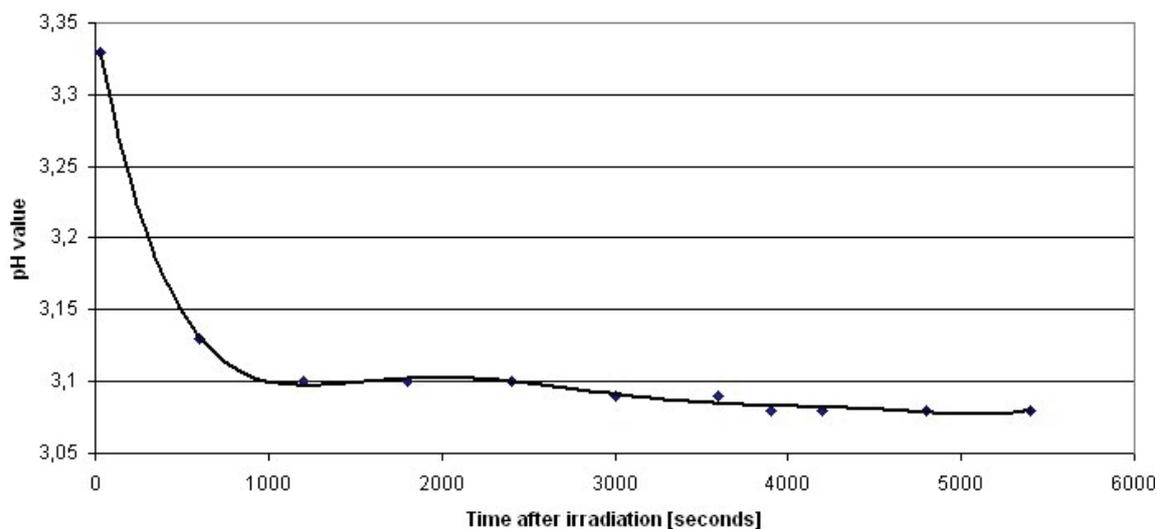
The BTL-07 therapeutic instrument (produced by the Beautyline Ltd., Prague, the Czech Republic) was used as a high-frequency cavitation ultrasonic system. The samples were exposed to continuous wave mode ultrasound with a frequency of 1 MHz emitted from an ultrasonic probe having an active transducer surface of 4  $\text{cm}^2$ . The probe (head) was fixed in the bottom of a Perspex vessel to form vertically oriented ultrasound field. The dosimeter sample was exposed to ultrasound in a plastic cylindrical vessel (10 × 3.5 cm) which bottom

was made of a very thin polyethylene membrane to achieve full transmission of acoustic energy. The cylindrical vessel was then placed directly on the surface of the transducer surrounded by cooling bath, avoiding air bubble capture in the gap between the transducer surface and the membrane. Power output of the instrument was set to a spatial average value of 2.0  $\text{W}/\text{cm}^2$ . Reliability of the instrument readings was checked by a calibrated hydrophone MH-28/6 made by Force Institutes (Denmark). The ultrasound exposure times were selected so that an uniform distribution of their values on the time axis was achieved, with the longest time interval not exceeding 600 s, which corresponded to the longest selectable time on the instrument display.

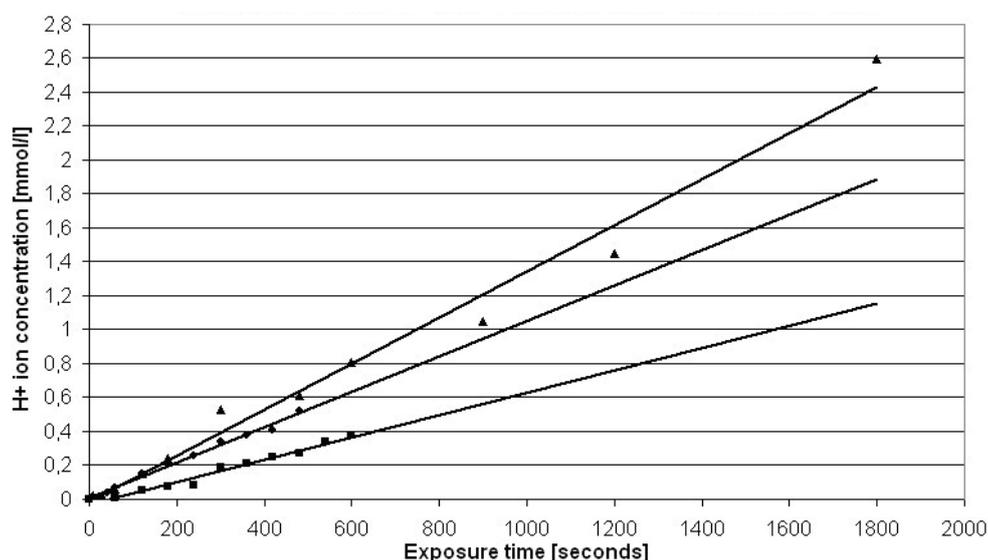
The UZD 21 ultrasonic disintegrator (Faculty of Electrical Engineering, Czech Technical University, Prague) was used as a low-frequency cavitation ultrasonic source. The samples were exposed to ultrasound with 50 % power output setting at a frequency of 20 kHz. During ultrasound exposure, the lower concentrator part (so-called horn, producer identification KV 40/5/182, with a tip diameter of 5 mm) was always immersed 1 cm below the level of the exposed samples of the chemical dosimeter and the concentrator vibrated at the amplitude of 55  $\mu\text{m}$ . The near acoustic field produced by such a disintegrator is disturbed by bubbles and very instable in a small sample volume so that intensity could not be determined.

The industrial cobalt-60 source (Atomic Energy Canada Limited, Canada) for radiation sterilization of medical products, was applied as an ionizing radiation source. The source is installed at the BIOSTER Company which resides at Veverská Bitýška, Czech Republic. The cobalt-60 is a gamma radiation source with two gamma energies of 1.17 MeV and 1.33 MeV. The source activity was at the time of measurement approximately 14 PBq. A distance between the source and the vessel glass wall was always set to 140 cm during exposure. Irradiation was carried out on the glass vessel side (the vessel dimensions – height of 10 cm, diameter of 4 cm). Based on the  $^{60}\text{Co}$  source data and ionizing radiation absorption in the matter, the median of absorbed dose in the exposed samples was calculated. The absorbed doses given in this study are always represented by the median.

We tried to provide the radiation and ultrasound exposure conditions as similar as possible in all the experiments to achieve the best conditions for mutual comparison. The samples were always prepared from the 50 ml of dosimeter solution and they were put into the



**Fig. 1.** Dependence of pH value on time after irradiation of 500 Gy (10 min);  $R^2 = 0.9989$  ( $R^2$  = determination coefficient)



**Fig. 2.** Dependence of  $\text{H}_3\text{O}^+$  ion concentration on exposure time;  $\blacktriangle$   $^{60}\text{Co}$ ,  $\bullet$  UZD21,  $\blacksquare$  BTL-07

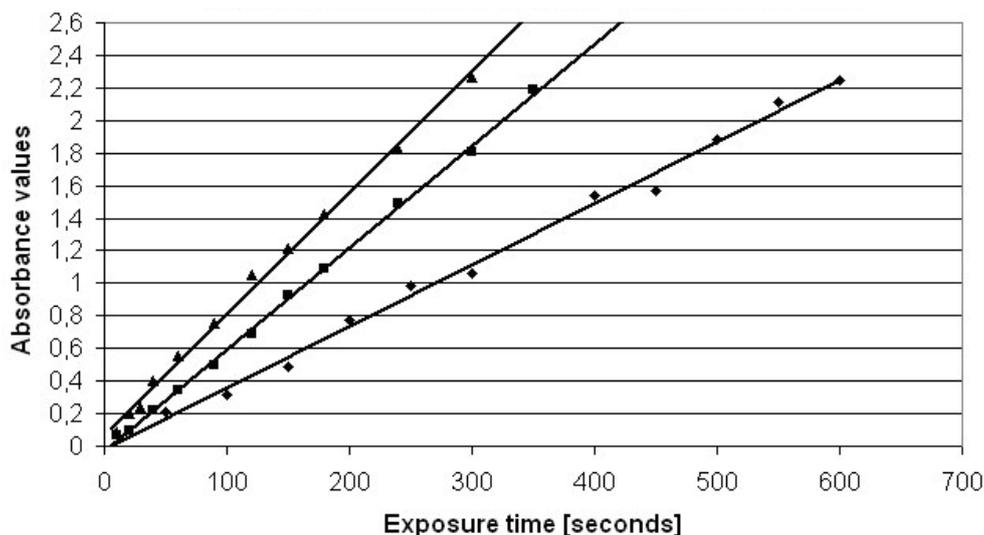
same cylindrical glass vessels during exposure, while the chemical dosimeter samples were cooled in an ice/water bath. This secured to maintain the temperature of insonated samples in a range from 20.0 °C to 21.0 °C. During gamma radiation exposure, the samples were stirred using a magnetic stirrer to be homogenized, and to simulate acoustic streaming present in ultrasound field. All measurements for each exposure time were repeated five times and the arithmetic means were plotted in the diagram.

## Results

In Fig. 1, a reduction of the pH value in the aqueous phase after a 10-min exposure for a dose of 500

Gy from the  $^{60}\text{Co}$  source is shown. An interval of 30 min after exposure seemed to be the most suitable because the pH value was already stabilized. Under above described conditions, three curves showing the relationship between the hydroxonium ion concentration and the exposure were obtained (Fig. 2). The pH values were measured for 11 different exposure times ranging from 10 to 1 800 seconds, which corresponds to the median of absorbed dose ranging from 6 to 1 080 Gy. For each exposure time, the measurement was five-times repeated, and the median values of absorbed doses plotted in the graph.

The curve for the BTL-07 high-frequency ultrasonic apparatus was obtained from the pH-value measurements for 11 different ultrasound exposure times ranging from 1 to 600 seconds. With the UZD 21 low-



**Fig. 3.** Dependence of absorbance on exposure time; ▲  $^{60}\text{Co}$ , ● BTL-07, ■ UZD21

frequency ultrasonic apparatus, we measured pH values for 11 different exposure times from 1 to 480 seconds. As a result, linear relationships of the hydroxonium ion concentration versus the radiation/ultrasound exposure times were obtained (Fig. 2).

We also obtained three straight lines as relationships of iodine absorbance versus radiation/ultrasound exposure times (Fig. 3). The relationship for  $^{60}\text{Co}$ -radiation source was measured again for 11 different exposure times ranging from 10 to 300 s, which is represented by the median of absorbed dose from 6 to 180 Gy. With the BTL-07 high-frequency ultrasonic apparatus, 11 ultrasound exposure times were measured in a range from 50 to 600 seconds. Eleven different times in a range from 5 to 350 s were also measured with the UZD 21 low-frequency ultrasonic apparatus. For each exposure time, the measurements were repeated five-times and only the average absorbance was plotted in the resulting diagram. After exposure, the median of absorbed dose for the individual samples of both dosimeters was calculated.

Moreover, we replaced the exposure time by the mean of the median of absorbed dose (we calculated medians of absorbed doses for each individual sample, five samples were obtained for any exposure time and averaged consequently) in the diagrams relating to the  $^{60}\text{Co}$  source. As a result, the relationship of the absorbance and the hydroxonium ion concentration versus mean of the median of absorbed dose was obtained.

Finally, we replaced the absorbance and the hydroxonium ion concentrations by the mean of median

of absorbed dose at both ultrasonic apparatuses, and we have named this quantity "gray equivalent dose", with the conversion ratio of 1:1. For the BTL-07 apparatus, we obtained a diagram in which two straight lines of the relationship of the "gray equivalent dose" versus the ultrasound exposure times are shown (one straight line is for the iodide dosimetry and the other represents the chloroform dosimetry) (Fig. 4).

The straight line for the iodide dosimetry is represented by the following equation:

$$Y = 0.2568x + 1.1858$$

$$R^2 \text{ (the determination coefficient)} = 0.9884$$

Standard deviation (SD) of gray equivalent dose for intercept: 48.81 cavGy, confidential intervals (CI) of gray equivalent dose for intercept: left = 43.81 cavGy, right = 41.73 cavGy.

The straight line for the chloroform dosimetry is as follows:

$$Y = 0.2550x - 1.6809$$

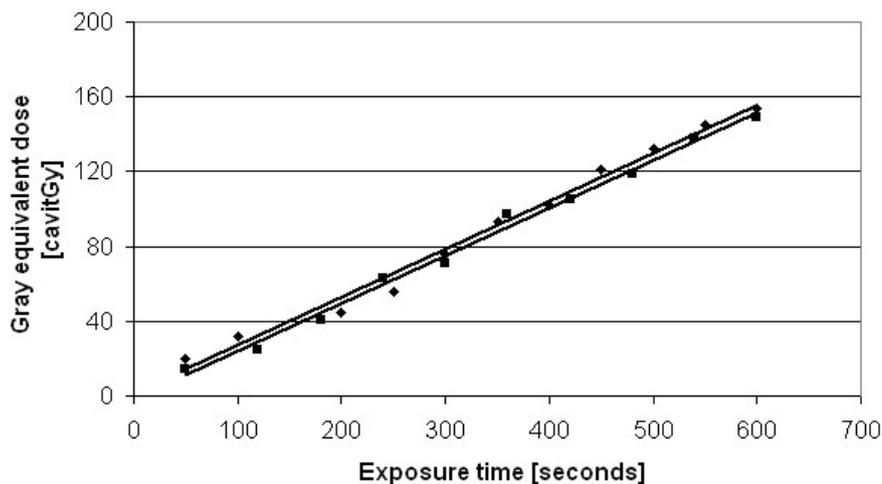
$$R^2 = 0.9939$$

SD of gray equivalent dose for intercept: 59.17 cavGy, CI of gray equivalent dose for intercept: left = 26.49 cavGy, right = 47.85 cavGy.

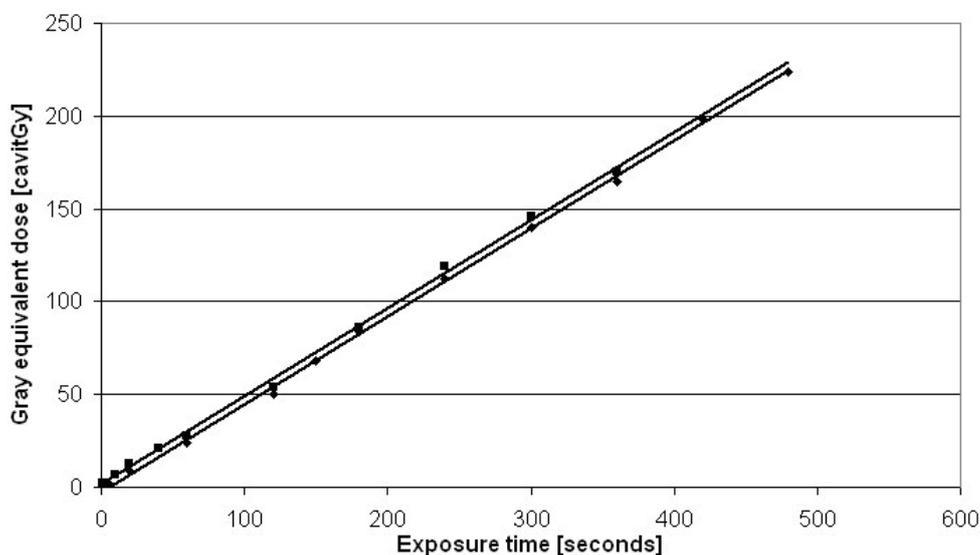
For the UZD 21 apparatus, we also obtained the diagram in which two straight lines with the relationship of the gray equivalent dose versus the ultrasound exposure times are plotted (see Fig. 5). The straight line for the iodide dosimetry is represented by the following equation:

$$Y = 0.4745x + 1.4381 \quad R^2 = 0.9985$$

SD of gray equivalent dose for intercept: 53.96 cavGy  
CI of gray equivalent dose for intercept: left = 48.41



**Fig. 4.** Dependence of gray equivalent dose on exposure time – BTL-07; ● KI dosimetry, ■ Chloroform



**Fig. 5.** Dependence of gray equivalent dose on exposure time – UZD-21; ● Chloroform, ■ KI dosimetry

cavGy, right = 52.75 cavGy.

The straight line for the chloroform dosimetry is as follows:

$$Y = 0.4720x - 2.3722 \quad R^2 = 0.9992$$

SD of gray equivalent dose for the intercept: 51.71 cavGy

CI of gray equivalent dose for the intercept: left = 40.36 cavGy, right = 51.48 cavGy.

## Discussion

The attempt to compare the cavitation effects between the low-frequency and high-frequency ultrasonic apparatuses using the effect of high-energy ionizing radiation was a difficult task. The dosimetric systems used must serve for both the ultrasonic effect quantification and the ionizing radiation quantification. Also, it was necessary to find the dosimetric systems

which were sensitive to low, middle and high exposure times. With respect to the results measured, it may be stated that the selected chemical dosimetric methods were suitable for the comparison of ultrasonic and ionizing radiation effects.

Since it is not possible to eliminate the ultrasonic thermal effects during ultrasound exposure, all samples were intensively cooled in an ice water bath while the bath was not necessary during  $^{60}\text{Co}$  irradiation.

For each of the three apparatuses, the diagram showing the relationship of the pH-value in the dosimeter aqueous phase versus the radiation/ultrasound exposure times was plotted, while the values of pH values were converted to the concentrations of hydroxonium ions. To compare their effects, it was necessary to select the exposure times for which the lowest measured pH value was approximately the same for all three apparatuses.

Based on the ratio of the exposure times, it is evident that the UZD 21 ultrasonic disintegrator has shown the higher chemical effects in comparison with the BTL-07 therapeutic ultrasonic apparatus under the specified exposure conditions.

Comparison of the results found by using the modified iodide dosimeter is also interesting. We selected the longest ultrasound and/or radiation exposure time so that the absorbance was lower than 2.5 (considering the accuracy and sensitivity of the spectrophotometer used). Similarly, in the Taplin dosimeter, the higher chemical effects were found with the iodide dosimeter for the UZD 21 ultrasonic disintegrator rather than the BTL-07 therapeutical ultrasonic apparatus.

Based on the minimum variance of the values of the determination coefficient  $R^2$ , it is evident that the dependence measured approaches a straight line. The slopes of a pair of the corresponding curves are nearly identical, and the minimum difference is probably caused by the measurement error. The data shift on the Y-axis is also minimal. This is evidently due to the different chemical background of both dosimetric methods because the same shift direction for both apparatuses is always observed (Fig. 3 and Fig. 4).

Hence, it may be concluded that both dosimetric methods provide the same relationship of the "gray equivalent dose" versus the time.

To summarize the results obtained for both cavitation ultrasonic apparatuses, we may state that in all cases the higher effect has been observed for the UZD 21 ultrasonic disintegrator. This is probably due to the substantially higher acoustic power output of the ultrasonic disintegrator, as well as by the different way of the ultrasound application because the concentrator used was directly immersed into liquid. The ultrasonic exposure with the BTL-07 apparatus approached better the conditions of gamma-irradiation because the ultrasonic head was not immersed in the chemical dosimeter solution and the streaming in the bulk of both chemical dosimeter phases was not so vigorous.

The conversion to the "gray equivalent dose" was made successively in the individual steps. Knowledge of ionizing radiation absorption in the matter was applied to calculate the median of absorbed dose for each exposure time in the individual samples of the chemical dosimeters. After that, the exposure time was replaced by the median of absorbed dose in the diagrams with  $^{60}\text{Co}$ . This resulted in two diagrams which show the relationship of the absorbance and the hydroxonium ion

concentrations versus the absorbed dose.

Our next consideration was based on the following idea. If the same absorbance is achieved for both ionizing radiation and cavitation ultrasound under similar exposure conditions and if the same detection methods are applied, we can express this same effect by the same physical quantity (gray equivalent dose).

Hence, the absorbance data and the hydroxonium ion concentrations for cavitation ultrasound were replaced with the corresponding medians of absorbed dose obtained in the diagrams with  $^{60}\text{Co}$ . The name of the physical quantity "absorbed dose" was replaced for the cavitation effects with the "gray equivalent dose", and its magnitude was converted in a ratio of 1:1. Then, the unit of gray for the equivalent dose was replaced by "cavitation gray [cavitGy]". It is obvious that this is not a new physical quantity but only a special tool for expressing the chemical effects of ultrasonic cavitation.

Many different types of the ultrasonic apparatuses with the different clinical effects have been used for decades. Efforts to compare the different particular effects and to unify the results of various studies have pointed the authors to the attempt to compare the cavitation effects of two different ultrasonic apparatuses through the radiochemical effect of ionizing radiation in two chemical dosimeters – a modified iodide dosimeter and a chloroform dosimeter.

Well measurable sonochemical effects of cavitation ultrasound were obtained in all investigated cases. Comparing the ultrasonic apparatuses, a considerably higher effect for the UZD 21 ultrasonic disintegrator (frequency of 20 kHz) was obtained relative to the effects of the BTL-07 therapeutic apparatus (frequency of 1 MHz).

The cavitation ultrasound effects were converted to "gray equivalent dose" with the unit of "cavitationGray" [cavitGy].

After this conversion, a linear relationship for both the iodide dosimetry and the chloroform dosimetry results for both cavitation ultrasonic apparatuses has been found. Based on this investigation, it is evident that the chemical effects of cavitation may be expressed through a single physical quantity – gray equivalent dose, with a unit of cavitation gray [cavitGray]. The introduction of this unit gives a chance to express the cavitation effects, particularly in low-frequency apparatuses where ultrasound field intensities are poorly defined.

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## Corresponding author

Bohdan Kratochvíl, Department of Biochemistry, Chemistry and Biophysics, University of Veterinary and Pharmaceutical Sciences, Banskobystrická 153, 621 00 Brno, Czech Republic. E-mail: kratochvilb@vfu.cz