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An Experimental investigation on the temperature dependence of ultrasonic signal characterization in a phantom tissue

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Abstract: Thermal ablation techniques, which use various methods such as high-intensity ultrasonic heating, ohmic heating, microwave heating, and radiofrequency, are promising in effectively destroying tumor tissues. On the other hand, instantaneous temperature measurement in and around the target area during thermal therapy will facilitate the application of such treatments. A method for instantly determining temperature changes in tissues based on the change in ultrasound signals sent to the target. In this method, the temperature change in the tissue is calculated inversely based on the change in the speed of sound and the duration of flight. However, impurities and noise in the tissue make it difficult to monitor the change in the signal returning from the target area. In this study, silica gel- and silicon dioxide-added agar phantoms were prepared as tissue-like materials. The prepared phantoms were immersed in a water bath and heated, and the temperature changes in the phantom were measured using immersion sensors. On the other hand, ultrasonic signals were sent to the phantom structure throughout the process, and the changes in the return signals were observed. The results obtained by processing the changes in the signals show that the change in flight time can be used to determine the temperature change inside the phantom.

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Fantom dokuda ultrasonik sinyal karakterizasyonunun sıcaklık bağımlılığı üzerine deneysel bir araştırma

Anahtar Kelimeler
Termal terapi,
Tümör ablasyonu
Doku sıcaklığı izleme
Darbe-yankı ultrason
Doku benzeri malzeme

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Öz: Yüksek yoğunluklu ultrasonik ısıtma, omik ısıtma, mikrodalga ısıtma, radyofrekans gibi çeşitli yöntemler kullanılan termal ablasyon teknikleri, tümör dokularını etkili bir şekilde yok etmede umut vaat etmektedir. Öte yandan, termal terapi sırasında hedef bölgenin içinde ve çevresinde anlık sıcaklık ölçümü yapılması, bu tür tedavilerin uygulanmasını kolaylaştıracaktır. Dokularda sıcaklık değişiminin anlık olarak belirlenmesi için kullanılabilecek bir yöntem, sıcaklık değişiminin hedefe gönderilen ultrason sinyallerinin değişiminden hareketle hesaplanmasıdır. Bu yöntemde, ses hızının ve uçuş süresinin değişiminden hareketle tersine olarak doku içerisindeki sıcaklık değişimi hesaplanır. Ancak doku içersindeki safsızlıklar ve gürültü, hedef bölgeden dönen sinyaldeki değişimin izlenmesini zorlaştırmaktadır. Bu çalışmada, doku benzeri malzeme olarak silikajel ve silisyum dioksit katkılı agar fantomlar hazırlanmıştır. Hazırlanan fantomlar su banyosu içine daldırılarak ısıtma yapılmış ve fantom içindeki sıcaklık değişimleri daldırmalı sensörler kullanılarak ölçülmüştür. Diğer yandan, işlem süresi boyunca fantom yapıya ultrasonik sinyaller gönderilerek dönüş sinyallerindeki değişim gözlenmiştir. Sinyallerdeki değişimlerin işlenmesi ile elde edilen sonuçlar, uçuş süresindeki değişimin fantom içerisindeki sıcaklık değişimini belirlemek için kullanılabileceğini göstermektedir.

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1. Introduction

Medical ultrasound is a technique that uses sound waves beyond the range of human hearing to create images of the body. It is divided into two main types: diagnostic and therapeutic. Diagnostic ultrasound uses specialized probes that emit sound waves and capture their echoes to create real-time images of internal organs. It can be anatomical, providing detailed images of structures, or functional, providing data on tissue or blood movement to assist in diagnosis. Functional ultrasound allows practitioners to visualize changes in organs, increasing diagnostic possibilities.

On the other hand, therapeutic ultrasound uses sound waves to treat conditions such as pain or inflammation. It can promote healing or eliminate abnormal cells by delivering heat, mechanical energy, or drugs to target tissues. This dual role of ultrasound in both diagnosis and treatment underlines its versatility in the medical field [1].

Thermal therapy, such as high-intensity focused ultrasound (HIFU), can be used to ablate tumor tissues by heating. Monitoring temperature changes during therapy is crucial to ensure targeted treatment while minimizing damage to surrounding tissues. The temperature increase in the tissue can be monitored by inserting thin thermometer probes into the tumor [2]. Non-invasive thermal monitoring would be more convenient to avoid complications. CT, MR, and ultrasound-based thermal measurements have been developed for 3D thermal monitoring. Among them, ultrasound-guided thermal tracking provides significant advantages in terms of simplicity, portability, and ease of access. However, there are still many important questions and technical difficulties in ultrasound guidance thermal monitoring [4]. The inherent speed of sound is a function of temperature and is tissue-specific. Several studies have reported on the temperature dependence of the velocity of sound in biological tissue[5].

Due to temperature changes, thermal expansion occurs in the tissue, so the returning time of sound waves also changes. The literature contains various models that utilize ultrasound to determine tissue temperature by measuring changes in flight time and return energies. The flight time method leverages the variations in the return time of the signals. In the studies, temperature changes of approximately 1°C in local tissues could be measured with solution methods such as autocorrelation.

Simon, VanBarren, and Ebbini (1997) applied high-intensity ultrasound (HIU) heating to a rubber phantom with scatterers added. They estimated the temperature by evaluating the signals obtained from the ultrasound imaging system with the time shift method. They tested the method by comparing the temperature estimates with those obtained from thermocouples placed inside the phantom, yielding a result with a maximum error of 0.44°C [6].

Ultrasound-based temperature measurement techniques are generally classified as active and passive ultrasound thermometry methods; among these, echo shift and time-of-flight–based approaches are the most widely used active techniques (Amiri & Makkiabadi, 2020).

Amiri and Makkiabadi (2020) reviewed phantom-based studies reported in the literature and indicated that echo shift–based ultrasound thermometry methods are capable of tracking temperature changes with sub-degree accuracy; however, measurement deviations may arise due to medium inhomogeneity and temperature gradients [7].

Similarly, Zeng et al. (2018) reported that the accuracy of UTSI-based temperature estimation is mainly limited by factors such as tissue motion, temperature gradients, and calibration uncertainties; however, the method has been shown to perform well under controlled phantom conditions. Georg and Wilkens (2017) evaluated echo–shift–based ultrasonic thermometry in an agar-based tissue-mimicking phantom during HIFU exposure and demonstrated good agreement with thermocouple measurements during heating, with average and maximum deviations of approximately 0.8 °C and 1.1 °C, respectively. However, larger deviations occurred during the cooling phase due to material-related effects [8].

Park et al. (2019) performed laser ablation in cardiac tissue. In the study, temperature imaging was performed with the time shift method. Signals were converted to analytic signals, and phase shifts between them were calculated by cross-correlation. Time shift estimates were performed over phase shifts. Cardiac tissue moves during treatment, which causes noise in the image and affects temperature estimation. In the study, the movement that occurs in the heart tissue was modeled, and its effects on the time shift estimation were evaluated and corrected. The thermal strain "k" parameter, which determines the tissue temperature change characteristics, was initially accepted as a value. A feedback model was then created using thermal pairs placed in the tissue, and it was updated adaptively through this model [9].

In another study, Lee et al. (2019) created an acoustic gel phantom and performed temperature measurement estimation using a commercial ultrasound device. The drug release triggered by the temperature in the phantom was investigated using HIFU. The nanoparticles used in the study begin to release the drug quickly at 42°C. Thus, the control of drug release is performed by monitoring the temperature values in the tissue region. It is stated that temperature estimation with the phantom study can be done with an error of about 2.5% [10].

Daniels et al. investigated ultrasound-based temperature estimation during RF ablation using tissue-mimicking phantom experiments. In their study, temperature-dependent echo time shifts were analyzed using different signal processing approaches. While the 2D block matching method provided temperature estimates with a maximum error of approximately 5%, the simpler 1D cross-correlation approach resulted in errors exceeding 30%, highlighting the importance of algorithm selection in ultrasound-based thermometry [11].

Although numerous ultrasound-based temperature estimation techniques have been proposed and validated under study-specific or controlled conditions, their general applicability remains limited. Tissue heterogeneity, motion artifacts, and simplifying model assumptions continue to hinder widespread clinical implementation. Therefore, further experimental investigations are needed to clarify the relationship between temperature variations and ultrasonic signal behavior. In this context, the present study investigates the effect of temperature on ultrasonic signals using a tissue-mimicking phantom.

2. Methodology

2.1. Phantom preparation

Tissue-mimicking material (TMM) is a type of material commonly used in medical ultrasonic applications and research because of its ability to simulate biological soft tissues. Some of the phantoms developed for imaging and diagnostics can also be used in hyperthermia experiments. Gel phantoms based on polyacrylamide, agar, gelatin, and gellan gum are widely used. Besides the fact that the acoustic properties indicate the tissue properties, the following features are also taken into consideration while determining the type of phantom: reproducibility, non-toxicity, ease of production, and stability at high temperatures. A tissue-mimicking phantom was prepared by mixing agar with ZnCl2 and adding scatterers, including silica gel and TiO2 particles.

The agar phantom was prepared by creating a 250 ml solution with 0.4 M ZnCl2 and 2% agar by weight in a rectangular prism container with dimensions of 95 mm (width), 95 mm (length), and 25 mm (height) [12]. The agar melts when heated above 90°C - 95°C. The temperature of the solution was monitored using a thermocouple. The beaker on the magnetic stirrer was filled with 2% agar and 0.4 M ZnCl2 by weight, as measured on a precision scale. The heating feature of the magnetic stirrer was used to dissolve the agar. The phantom was later poured into the mold and polymerized in a very short time.

As is known, different scattering occurs due to the characteristic properties of real tissue. In this context, silica gel and TiO2 were included as scattering agents. Titanium dioxide was prepared at a concentration of 2%. Another scatterer, silica gel, which acts as a moisture absorbent in the form of beads with a diameter of about 2 mm, was added during the gelling process to prevent precipitation.

Figure 1. Agar phantom with silica gel

Small samples were taken from the phantoms for the density measurement, and the masses were measured using a precision balance. The volume was calculated by observing the change in water level in the burette after each sample was added. Using the mass and volume values, the density of the phantom was calculated. At 21.8°C, mass density is 1.168 g/ml± 0.02 g/ml, and at 50°C, mass density is 1.011 g/ml ± 0.02 g/ml.

2.2. Experimental setup

An experimental setup was used to measure the speed of sound at different temperatures. The setup included a pulser-receiver, an oscilloscope, and ultrasonic immersion probes. Ultrasonic signals were transmitted through the phantom, and the reflected signals were analyzed.

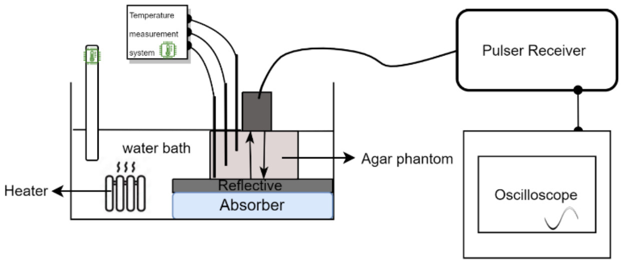

Figure 2. Illustration of the experimental setup

NTC-type thermistors and a five-channel PC-based temperature data acquisition and monitoring system were used to measure and save the temperatures. Three NTC-type thermistor temperature sensors were inserted into the phantom at different depths (approximately 5 mm intervals) with a holder before the phantom was completely frozen. The temperature uncertainty of NTC-type temperature sensors is 0.94°C.

During the tests, the water was heated and stirred continuously to reach the desired temperature. The phantom was allowed to wait until it reached a stable temperature. The general view of the tests is shown in Figure 3.

Figure 3. The experimental set-up for sound velocity measurement in an agar phantom

2.3. Change of sound signals through the phantom at different tests

The sound wave graphs were recorded from agar phantoms with and without scatterers at different test temperatures. The tests were conducted using either a reflective or an absorber back plate to observe the effects on sound signals. The tests are repeated for various types of phantoms at different temperatures. The characteristics of the tests are summarized in Table 1. Four distinct test setups were used to investigate these changes:

a) Group 1: Involved a 20 mm agar phantom containing silica gel particles placed on a reflective plate. These experiments were repeated at 3 different initial and final temperatures.
b) Group 2: A 34 mm agar phantom containing 2% TiO_2 particles was also placed on a reflective plate. For this case, the change in the signals was recorded only for one temperature pair.
c) Group 3: Investigated a 30 mm agar phantom containing silica gel particles placed on an absorber. This group of experiments was conducted for two different starting and ending temperatures.
d) Group 4: Investigated a 25 mm non-scattering agar phantom placed on a reflective plate. In this group of experiments, signal changes were recorded at 3 different return temperatures.

Table 1. Test summary table

Experiment Group	Experiment No	Phantom Composition	Reflector Type	Phantom Thickness	Initial and final temperatures
1	1.1	Agar + Silica Gel	Reflective	20 mm	21.6°C 40.6°C
1	1.2	Agar + Silica Gel	Reflective	20 mm	21.6°C 35°C
1	1.3	Agar + Silica Gel	Reflective	20 mm	32°C 36°C
2	2.1	Agar + 2% TiO_2	Reflective	34 mm	33.6°C 38°C
3	3.1	Agar + Silica Gel	Absorber	30 mm	24°C 37°C
3	3.2	Agar + Silica Gel	Absorber	30 mm	28°C 38°C
4	4.1	Non-Scattering Agar	Reflective	25 mm	21°C 50°C
4	4.2	Non-Scattering Agar	Reflective	25 mm	21°C 40°C
4	4.3	Non-Scattering Agar	Reflective	25 mm	21°C 30°C

In Group 1, where silica particles were used as scatterers and a reflective plate was placed at the back surface of the phantom, an increase in temperature resulted in an acceleration of the echo signal and a noticeable leftward shift along the time axis, as shown in Figures 4, 5, and 6. The reflection from the back surface is observed as peak regions, but scattering from the particles is also visible.

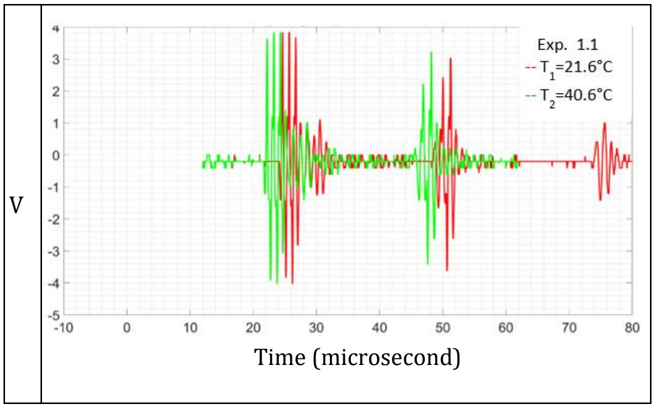

Figure 4. Signal map at different temperatures from a 20 mm agar phantom containing silica gel particles and placed on a reflective plate.

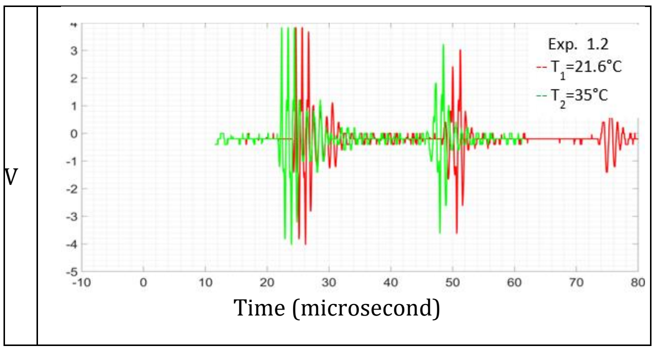

Figure 5. Signal map at different temperatures from a 20 mm agar phantom containing silica gel particles, and placed on a reflective plate.

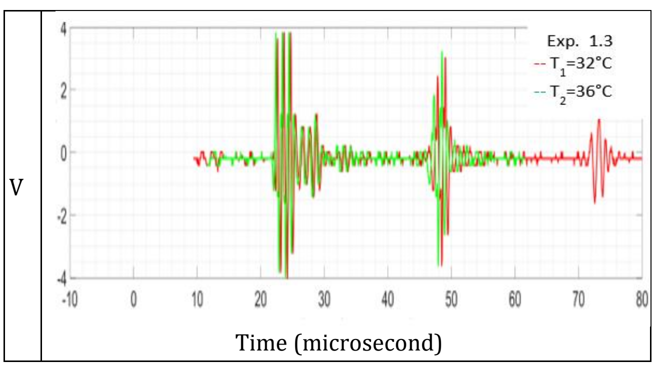

Figure 6. Signal map at different temperatures from a 20 mm agar phantom containing silica gel particles, and placed on a reflective plate.

Figure 7 shows the test with titanium dioxide particles. It is seen that the scattering of titanium dioxide is weaker.

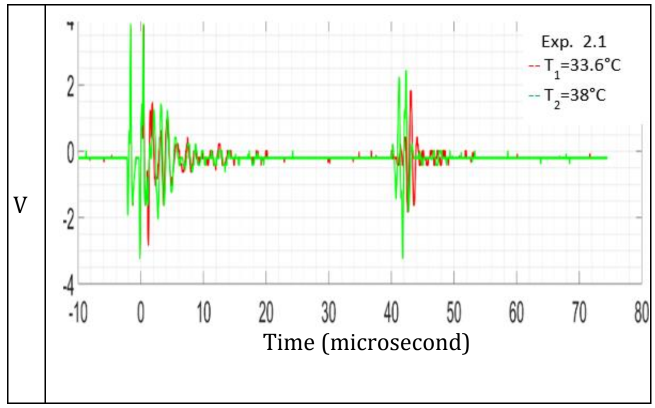

Figure 7. Signal map at different temperatures from a 34 mm agar phantom containing 2% TiO_2 particles, and placed on a reflective plate.

In the third group of tests, the reflective plate was removed, and only the absorber was used. The aim was for the return signals to come from the internal structure. Figures 8 and 9 show the results of these tests. The first signal is the pulse signal. The other signals are reflected back from the internal structure.

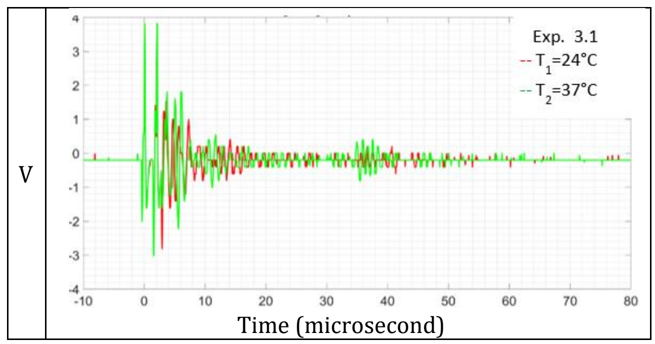

Figure 8. Signal map at different temperatures from a 30 mm agar phantom containing silica gel particles, and placed on an absorber.

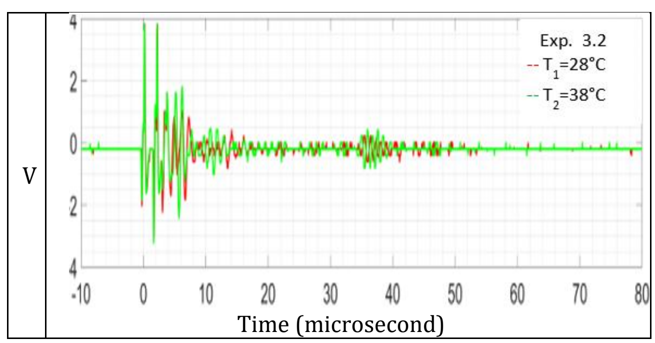

Figure 9. Signal map at different temperatures from a 30 mm agar phantom containing silica gel particles, and placed on an absorber.

The results shown in Figures 10, 11, and 12 represent measurements taken from a non-scatterer agar phantom at different temperatures. A reflective surface was used during the experiment.

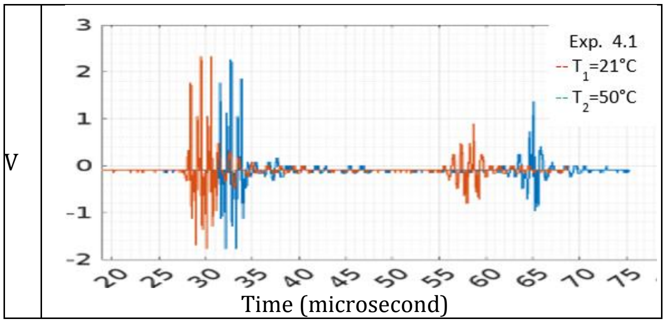

Figure 10. Signal map at different temperatures from a 25 mm agar phantom placed on a reflective plate.

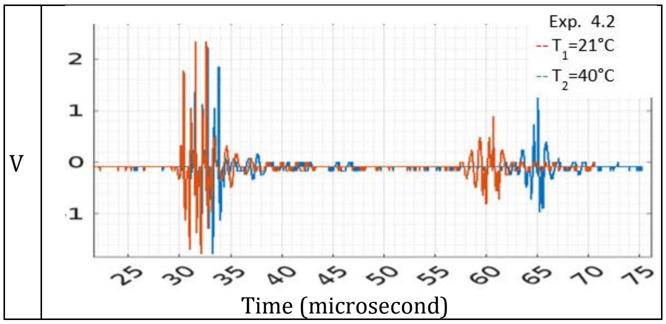

Figure 11. Signal map at different temperatures from a 25 mm agar phantom placed on a reflective plate.

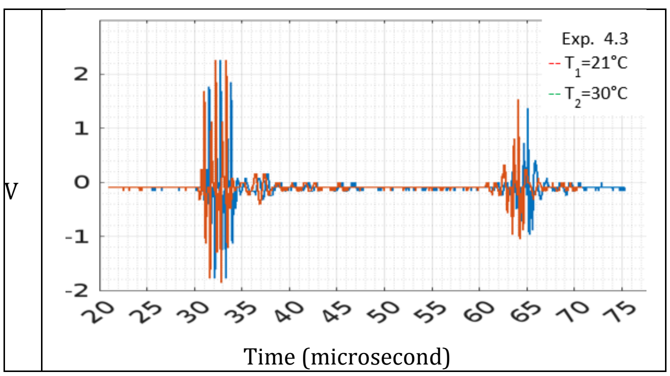

Figure 12. Signal map at different temperatures from a 25 mm agar phantom placed on a reflective plate.

3. Sound Velocity and Temperature Change

3.1. Determination of sound velocity

When sound waves reach the reflective plate, they create a strong signal. The duration of the echo signals is determined by analyzing the waveform on the oscilloscope. Subsequently, the speed of sound was calculated using the echo time, as given in Equation 1.

$$C = \frac{2 \cdot X_p \cdot 10^{-3}}{\Delta t \cdot 10^{-6}} \qquad (1)$$

Here, “C” is sound velocity, m/s; Δt is the returning time of the main echo signal, μs; and X_p is the distance between the ultrasound probe and reflective surface, mm.

The desired phantom temperature was set via the heater system, as shown in Figure 3. The phantom was expected to reach a homogeneous temperature with continuous stirring, and the echo signals were recorded at the temperatures of 21.8°C, 30°C, 40°C, and 50°C, respectively. The return signals at 21.8°C and 50°C are shown on the same time scale in Figure 13. Here, the phase shift for two different temperatures is obvious.

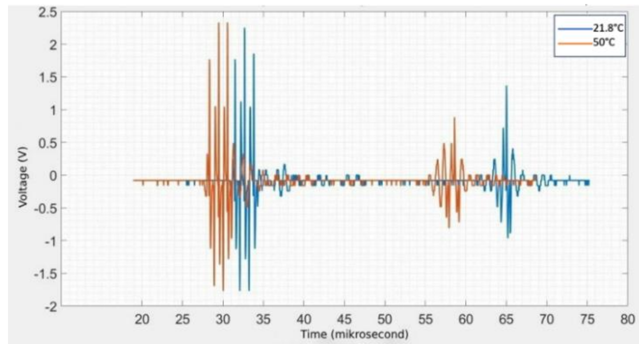

Figure 13. Time shift at different temperatures

The sound velocities at these temperatures are calculated and presented in Table 2, and are also illustrated graphically in Figure 14. The path length of the sound waves was taken as 50 mm, which is twice the distance between the probe and the reflective plate, as shown in Figure 3.

Table 2. The changing of sound speed with temperature in the agar phantom

Average temperature of the phantom (°C)	The time of flight (μs)	Speed of sound (m/s)
21,8	30.85	1621
30	30.23	1654
40	29.23	1711
50	27.5	1818

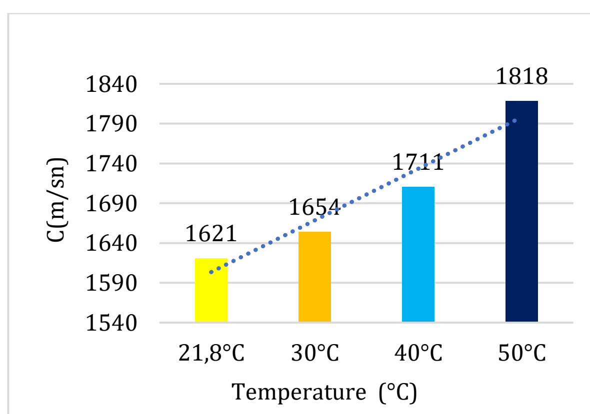

Figure 14. Change of sound speed with temperature

As shown in Figure 14, the speed of sound increased approximately linearly with temperature. The variation of the speed is calculated as shown below:

$$C = C_0 \cdot (1 + \beta(T\text{-}T_0)) \quad (2)$$

Using the values at 21.8°C and 40°C, the coefficient of β, the change in sound velocity with temperature, is calculated as 0.003051 1/°C.

3.2. Estimation of temperature change

The time shift of the signals is used to estimate temperature changes in association with the measurement of changes in the speed of sound. In this context, the distance between the top and bottom surfaces of the phantom is assumed to be constant, so the effect of the thermal expansion of the phantom is not included in the calculation [13]. In this situation, the tissue thermal strain coefficient "k" is defined based on the variation of the time of flight:

$$k = -c_0 \frac{dT}{dc} = -\frac{1}{\beta} \quad (3)$$

The tissue coefficient was calculated as -327.8°C. The change in the average temperature of the medium is calculated as in Eq. 4:

$$\Delta T = k \frac{\Delta t}{t} \quad (4)$$

The times of flight in different tests are given in Table 2. Using the tissue coefficient, the temperature difference between the second and first tests was calculated in the following lines:

$$\Delta t = 30.23 \cdot 10^{-6} - 30.85 \cdot 10^{-6} = -0.62 \cdot 10^{-6} s$$

$$\Delta T = -327.8 \cdot \frac{-0{,}62 \cdot 10^{-6}}{30.23 \cdot 10^{-6}} = 6.72°C$$

The measured and calculated temperature differences for other tests are given in Table 3.

Table 3. The change in the time of flight and temperature differences

Temperature Range (°C)	21.8 to 30	21.8 to 40	21.8 to 50
Time of flight, Δt (μs)	-0.62	-1.62	-3.35
Measured Temperature Difference (°C)	8.2	18.2	28.2
Calculated Temperature Difference (°C)	6.72	18.17	39.93

4. Discussion and Conclusion

In this study, the effect of temperature on ultrasonic signal propagation was experimentally investigated using tissue-mimicking agar phantoms. The results showed a clear relationship between temperature increase and reduction in ultrasonic time-of-flight. The observed trends were repeatable across different phantom configurations, indicating that ultrasonic time-of-flight analysis can be used to estimate temperature changes under controlled experimental conditions. This method has potential applications in real-time temperature monitoring during thermal therapies such as high-intensity focused ultrasound (HIFU), where accurate temperature control is important for treatment precision and safety.

The findings of this study are consistent with previous phantom-based ultrasonic thermometry studies reported in the literature. For example, Georg and Wilkens (2017) demonstrated that echo-shift–based ultrasonic thermometry closely matches thermocouple measurements during the heating phase in an agar phantom, with deviations on the order of 1 °C. Consistent with these findings, the present study shows that temperature estimation based on ultrasonic time-of-flight variations is feasible with a simplified experimental setup. In this context, the response of ultrasonic signals to temperature changes was further evaluated in detail through phantom experiments.

Ultrasonic signals can be used as an effective tool to determine temperature changes. In the experiments with a phantom structure at different temperatures, noticeable changes in ultrasonic signals were observed. The echo signal from the reflecting plate changed with the sound velocity in the phantom. Similar changes were recorded in the reflection signals produced by the particles in the phantom. The findings highlight the feasibility of using ultrasound waves for non-invasive temperature monitoring to estimate changes in tissue temperature. While these results support the potential of ultrasonic signals to detect temperature changes, further research is needed to precisely determine signal variations and reduce noise in measurements.

Phantom experiments and measurements on tissues show how temperature affects the propagation speed and characteristics of ultrasonic signals. These findings shed light on significant applications in medical imaging. Specifically, determining the tissue origin of echo signals plays a crucial role in diagnosing and treating diseases. This method enables a more detailed examination of tissues and facilitates the more precise detection of pathologies.

Future studies should focus on further deepening research in this field. Conducting more extensive experiments on different tissue types and pathological conditions can help us better understand how the method can be integrated into broader medical applications.

However, the limitations of this study should also be recognized. For example, the materials used in phantom experiments are not exactly representative of biological tissues. The thermal properties and behavior of real biological tissues may differ from those of phantoms. Therefore, the applicability of this study's findings directly to the human body requires further investigation.

Overall, this study focuses on analyzing temperature-dependent changes in ultrasonic signal propagation using time-of-flight measurements in different tissue-mimicking phantoms. Although the experiments are limited to controlled phantom conditions, the results demonstrate that direct analysis of ultrasonic signal variations can provide valuable insight into the relationship between temperature change and ultrasonic signal behavior.

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