

The Correction of Focal Point Displacement Caused by the Refraction of the Beams in High-Intensity Focused Ultrasound

Abstract

Nowadays, high-intensity focused ultrasound (HIFU) as nonionizing radiation is used for cancer treatment. Basically, the function of HIFU is similar to conventional ultrasound. Ultrasound beams are perverted when crossing the border of different environments. This decreases the beam's focus within the tumor and may induce damage to the normal tissues. In this study, we aim to develop appropriate algorithms for correcting the focal point displacement caused by the beam's refraction. First, the level of displacement due to difference in two specific tissues was calculated for one element of the transducer and, then, it extended to all of the elements. Finally, a new focal point was calculated, which is considered as a desired focal point of the transducer in which the maximum temperature occurs. Designed algorithms were implemented in MATLAB software. A HIFU simulator (by the Food and Drug Administration of US) was used to simulate HIFU therapy. The proposed algorithm was tested on four models with two layers of tissue. Results illustrated the use of proposed algorithm results for 78% correction in the focal point displacement. In addition, it was noted that a part of this displacement was caused by the absorption of the beam in the tissues. The proposed algorithm can significantly correct the focal point displacement in HIFU therapy and consequently prevent damage to the normal tissues.

Keywords: Focal depth, HIFU therapy, simulator, refraction correction

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Introduction

High-intensity focused ultrasound (HIFU) has been a topic of interest for biomedical researchers since fifty years. Recently, the HIFU, as a noninvasive surgical technique, is used to treat cancerous tissues of the liver, the kidney, the breast, the prostate, and the pancreas.^[1] In this technique, the high-intensity ultrasound beams are focused on the tumor. Thus, the temperature of the tumor tissue increases to 65°C during a short time, and, consequently, the tumoral cells are destroyed without any damage to the normal adjacent tissues.^[2] However, in the absence of correct settings, it can cause damage to the surrounding normal tissues. To avoid these disadvantages, a transducer of HIFU therapy must be properly designed and implemented. The choice of optimal parameters such as focal depth and frequency for the transducer is important.^[3,4] These parameters should be set in such a way that the bulk transitional of energy focused within the tumor.^[5]

Ultrasound beams are received by the tumor after passing through several different layers of tissues in HIFU therapy. The variation of tissues between the transducer and the tumor causes the beam's refraction, leading to a nonfocused beam within the tumor. A few millimeters shift in the focal depth of beams has been reported in the literature.^[6,7] Liu *et al.*^[8] also reported a turmoil at the beam's focus in the abdomen. Ultrasound beams are deflected owing to the differences of wave velocity in various tissues. Snell's law describes how to create embryos phenomenon, and this is expressed in Eq. (1). According to this rule, the beams that arrive at the border of the two tissues with different characteristics with θ_1 will be refracted if the velocity of sound in the first tissue is c_1 and in the second tissue is c_2 ; the angle of these beams is changed to θ_2 .

$$\frac{\sin(\theta_1)}{\sin(\theta_2)} = \frac{c_1}{c_2} \quad (1)$$

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where θ_1 and θ_2 are, respectively, the angles of incidence and the transmission beam in the first and the second tissue versus vertical axis of the transducer.

Various methods have been proposed to control the displacement due to the beam's refraction. The use of magnetic resonance imaging (MRI) during HIFU therapy is one of these approaches. Methods were proposed for the correction of the transducer parameters as well. These methods mostly were related to the phased array transducers. Ebbini and Cain^[9-12] suggested the usage of the synthesis reversal pattern to calculate the phase of array and the distribution of focus patterns amplitude in the uniform and the nonuniform tissues. Thomas and Fink^[13-17] also applied an inverted time process to correct the arrays phase in transcranial therapies. Nowadays, with the progress of computer science, simulator softwares have been released for HIFU therapy.^[18-20] These are mostly research softwares. The Food and Drug Administration of US (FDA), in a research project, had asked the researchers to use computational methods to assess the safety of HIFU therapy approach and to develop it as well. In this regard, a HIFU simulator was prepared and made available to the researchers.^[19] However, in practice, someone can observe beam refraction with this simulator. Undeniably, this is true for all simulators. The transducer parameters would be set until the beam's focus occurred at the desired location without significant displacement. Can we propose an algorithm to correct the displacement of the focal point?

In this study, the focal point displacement was numerically calculated in a multilayered tissue. Thereafter, the created displacement was corrected by designing an appropriate algorithm and including it in the simulator HIFU. The rest of the paper is organized as follows: the section "Materials and Methods" describes the proposed

method for the correction of the focal point displacement, including mathematical equations and proposed algorithm. Results and discussion are explained in the subsequent sections, and the final section concludes the paper.

Materials and Methods

In this study, MATLAB software was used for implementing the proposed algorithms. The FDA's HIFU simulator was used to simulate HIFU therapy. The spherical type of transducer was selected for computation and simulation. First, the focal point displacement caused by velocity difference in two different tissues was numerically calculated for an element of the transducer with the specified spatial coordinates. Thereafter, this equation was extended to all transducer elements. Next, by obtaining the average displacement of the individual elements, the total displacement was calculated. Because the HIFU simulator is mainly designed for the two layers of tissues, we also considered two layers of tissue in this study. As can be seen in Figure 1, the distance between the transducer and the border of the tissues equals z , and the focal depth equals d . Dotted lines indicate the focal depth of the transducer, and the red area is the actual focal point after the beam's refraction. a and b , respectively, are the external and internal diameters of the transducer, and Δd is the created displacement at the focal point. In addition, θ_1 and θ_2 , respectively, are the beam angles in the first and the second layers.

The focal point displacement of an element was calculated using Snell's law and trigonometric formulas as follows:

$$\begin{cases} \tan(\theta_1) = \frac{x}{d - z} \\ \tan(\theta_2) = \frac{x}{d - z - a} \end{cases} \quad c_1 < c_2 \quad (2)$$

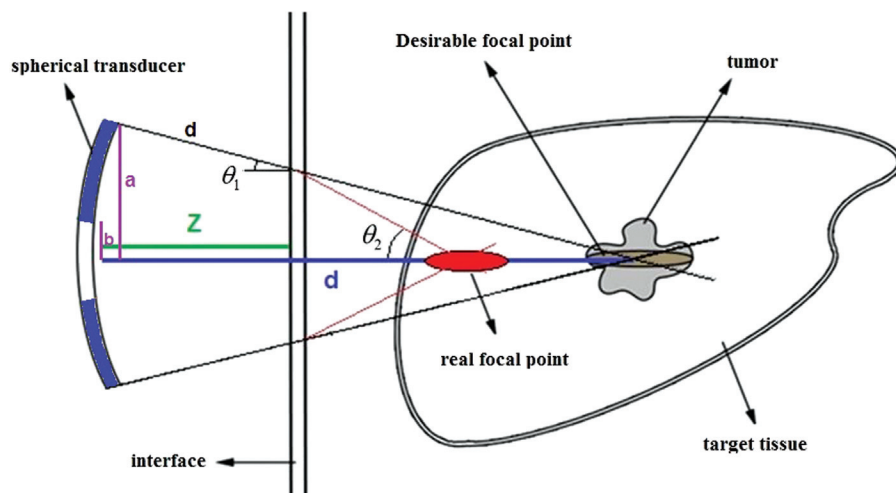


Figure 1: The transducer and emitted beams. The red line shows the refracted beam. d is the desirable focal depth and z is the distance from interface. θ_1 is the beam angle before refraction and θ_2 is the beam angle after refraction

in which a value can be obtained as:

$$a = (d - z) \times \left[1 - \frac{\tan(\theta_1)}{\tan(\theta_2)} \right] \quad (3)$$

If $c_1 < c_2$, then we can write:

$$\begin{cases} \tan(\theta_1) = \frac{x}{d - z} \\ \tan(\theta_2) = \frac{x}{d - z + a} \end{cases} \quad c_1 < c_2 \quad (4)$$

in which a value can be obtained as:

$$a = (d - z) \times \left[\frac{\tan(\theta_1)}{\tan(\theta_2)} - 1 \right] \quad (5)$$

Since θ_2 angle is unknown, this angle should be calculated as follows:

$$\frac{\sin(\theta_1)}{\sin(\theta_2)} = \frac{c_1}{c_2} \Rightarrow \theta_2 = \sin^{-1} \left[\frac{c_2}{c_1} \times \sin(\theta_1) \right]$$

In other words:

$$\tan(\theta_2) = \tan \left(\sin^{-1} \left[\frac{c_2}{c_1} \times \sin(\theta_1) \right] \right) \quad (6)$$

By inserting Eq. (6) in Eqs. (3) and (5), the final formula was obtained as Eq. (7).

$$\Delta d(i) = \begin{cases} a = (d - z) \times \left[1 - \frac{\tan(\theta_1(i))}{\tan \left(\sin^{-1} \left[\frac{c_2}{c_1} \times \sin(\theta_1(i)) \right] \right)} \right] & c_1 < c_2 \\ a = (d - z) \times \left[\frac{\tan(\theta_1(i))}{\tan \left(\sin^{-1} \left[\frac{c_2}{c_1} \times \sin(\theta_1(i)) \right] \right)} - 1 \right] & c_1 > c_2 \end{cases} \quad (7)$$

where $\Delta d(i)$ refers to the focal point displacement of i th element of the transducer.

Figure 2 shows the front view of the transducer. In this transducer, with a given number of elements, the elements in the i th circular rows are placed side by side. If the diameter of each element is equal to L , the difference angle θ_1 of two rows of elements can be shown with Eq. (8). Therefore, the matrix of θ_1 angle of i th rows is shown with Eq. (10).

$$\Delta \theta = \frac{\sin^{-1}(a/d) - \sin^{-1}(b/d)}{i} \quad (8)$$

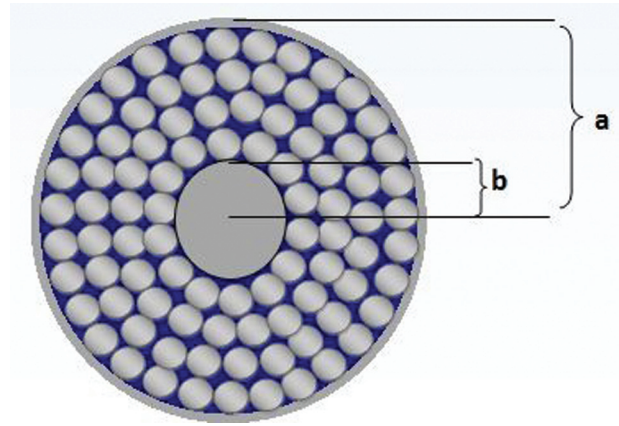


Figure 2: Transducer arrays from the front view shows that it is composed of several elements: a is the outer diameter and b is the inner diameter of the transducer

$$\theta_1(i) = \sin^{-1}(b/d) + (i - 1) * \Delta \theta \quad (9)$$

Therefore, the matrix of θ_1 angle can be written as:

$$[\theta_1]_{1 \times i} = [\sin^{-1}(b/d) : \Delta \theta : \sin^{-1}(a/d)] \quad (10)$$

In addition, because the diameter of each row of elements increases, represented as L , the number of elements increases as $\frac{2\pi L}{L}$ that equals to 2π . This rule is always true. Since the number of increased elements should be integer, the elements matrix of each row is calculated and then rounded. Total elements of this matrix are equal maximum of elements with L diameter that can be used in the design of a transducer with a and b as external and internal diameter, respectively. As a result, the number of elements in each row is related to Eq. (11).

$$N(i) = \frac{2 \times \pi \times b}{L} + (i - 1) \times 2\pi \quad (11)$$

The matrix of elements number is:

$$[N]_{1 \times i} = \left[\frac{2 \times \pi \times b}{L} : 2\pi : \frac{2 \times \pi \times a}{L} \right] \quad (12)$$

Considering Eqs. (7) and (11) and the fact that the focal point displacement is equal for all the elements in each row, the total displacement of all elements can be calculated using Eq. (13).

$$\Delta d_{\text{total}} = \frac{\sum_i \Delta d(i) \cdot N(i)}{\sum_i N(i)} \quad (13)$$

Next, the displacement again was calculated by considering the new focal depth that was obtained using Eq. (14).

$$d_{New} = d + \Delta d_{total} \quad (14)$$

$$\Delta d_{totalNew} = \frac{\sum_i \Delta d_{New}(i) \cdot N(i)}{\sum_i N(i)} \quad (15)$$

Now, it can be said that the maximum temperature after the simulation by considering d_{New} is equivalent to the difference between d_{New} and $\Delta d_{totalNew}$. This is expressed in Eq. (16).

$$d'' = d_{New} - \Delta d_{totalNew} \quad (16)$$

This process will be repeated until d would be equal with the primary focal point by considering the error value of 10^{-5} . Its algorithm is expressed as follows:

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d = 10
dNew = d
for i = 1 to inf
    Δdtotal = (Σi ΔdNew(i) · N(i)) / Σi N(i)
    d' = dNew - Δdtotal
    dNew = dNew + Δdtotal
    if (d - d') < 10-5
        break
    end
end
    
```

The flowchart of the proposed method for the correction of the focal point displacement is shown in Figure 3.

Results

In this study, as the simulator was capable of simulating a two-layer model in maximum, the default model with two layers of water and muscle was used. A thickness of 5 cm was considered for the water layer. Figure 4 shows the results of simulation at 1 MHz frequency and 10 cm focal depth using the transducer with 5 and 2 cm as the external and internal diameters.

Figure 5 shows that the maximum temperature point occurred at 9.32 cm. In addition, it indicates that the displacement of the focal point is 0.68 cm. Although the displacement level is related to factors such as tissue absorption coefficient, however, it is significantly dependent on the beam's refraction. The displacement caused by the beam's refraction was calculated using the designed algorithm, which was equal to 0.557 cm. Moreover, about 0.12 cm of the displacement occurred due to factors such as the beam's absorption in the tissue. After a full run of the designed algorithm, the new focal depth was calculated; by replacing it with desired focal depth, the point of maximum temperature will be less than the initial state, and displacement is corrected as much as 0.557 cm. Finally, the new focal depth was calculated (10.61 cm). Once again, the simulation was performed with a focal depth of 10.61 cm. At this stage also, the new point of maximum temperature was achieved as 9.81 cm, and it represented the displacement correction of 0.48 cm. The reason for inequality of displacement correction with 0.557 cm was the change in absorbance caused by the change in the focal depth. Thus, that in simulation by 10.61 cm of focal depth, 0.12 cm more displacement caused by factors such as beam energy absorption in the tissue. The results of the simulation with 10 and 10.61 cm of focal depths are illustrated in Figure 5.

The designed algorithm was tested on the other four models. The models included the muscle, the liver, the skin, the breast, water, and a phantom. Their profiles are listed in Table 1, and the results are tabulated in Table 2.

Discussion

HIFU therapy is a noninvasive and interesting technique for the treatment of cancerous tumors as well.^[21,22] However, this technique has a most important disadvantage, which is thermal damage to the normal tissues surrounding the tumor tissue. The reason for the damage is the displacement of the focal point depth. Without correcting such displacement, HIFU will not only destroy the tumoral cells, but also the normal tissues surrounding the tumor will be damaged. Many factors are involved in causing the displacement including wrong design of the transducer and also the tissue's acoustic characteristics. Since the transducer is designed by humans, part of a displacement in the focal point can be corrected by optimizing the design. As mentioned, some parts of the displacement, its related to the tissue characteristic that changing of it is not possible for human being. One of these

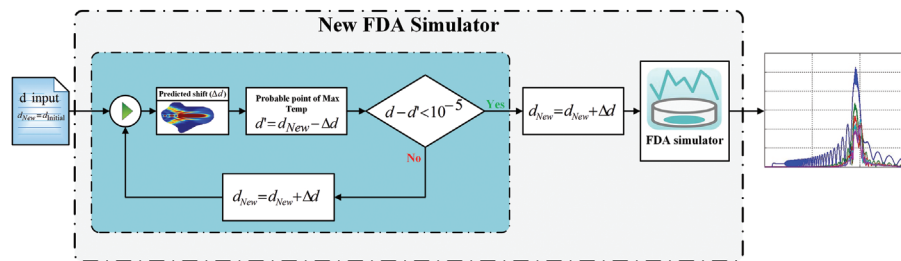


Figure 3: The flowchart of the proposed algorithm. It is composed of two stages: Shift calculating in the focal point and calculating for new focal depth at the first step, and then a new simulation for new focal depth

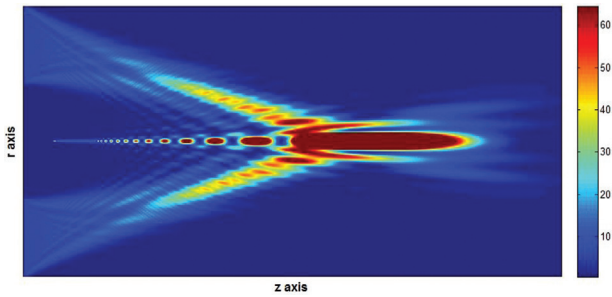


Figure 4: Simulation of ultrasound beam propagation using the HIFU simulator from the Food and Drug Administration of US. This figure shows the thermal effects with a focal depth of 10 cm at 1 MHz of frequency

changes is the velocity in different tissues.^[23] The use of MRI during HIFU treatment as a control technique has been proposed.^[24-27] The use of MRI provides a reliable control with the detection of the temperature map of the treatment location. However, for some reasons, such as nonsimultaneous imaging and treatment processes, the use of other control methods is necessary. Use of computational techniques maybe the other techniques of controlling. The FDA announced a research project to study this field and emphasized on the importance of using computational techniques to increase the safety in HIFU therapy; this study was performed in accompaniment with this goal. Therefore, we used a HIFU simulator that was suggested by the FDA. First, the

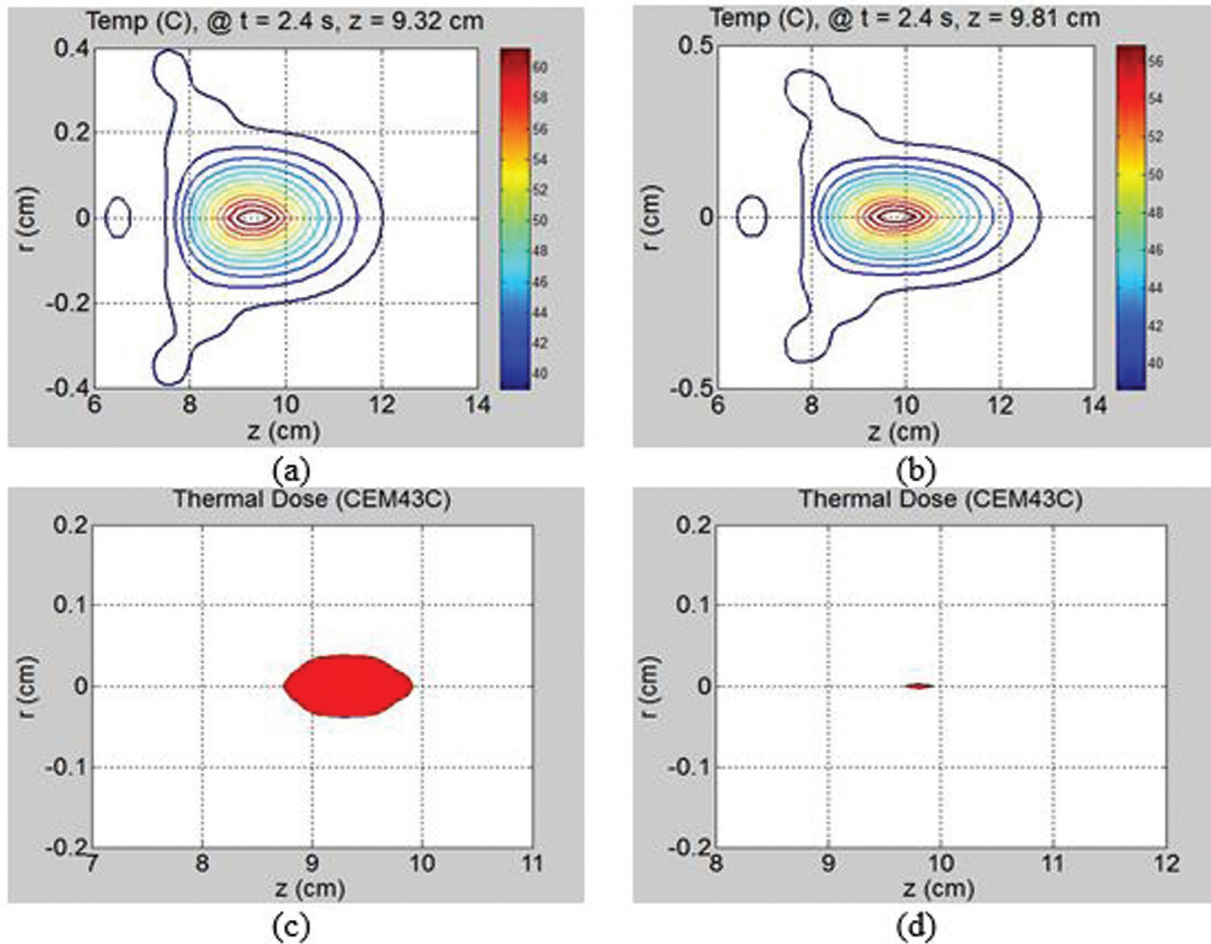


Figure 5: The results of simulation of ultrasound beam propagation in both uncorrected and corrected displacements of the focal point. (a) and (c) show the simulation result and thermal dose without correction of displacement. In addition, (b) and (d) show the simulation result and the thermal dose with correction of displacement

Table 1: Profile of models. Four models in two layers

Model	Velocity in the tissues (m/s)	Thickness of the first tissue (cm)	Operating frequency of the transducer (MHz)	Power (W)
Water-phantom	1482-1629	5	1.5	100
Water-muscle	1482-1580	5	5	100
Water-liver	1482-1578	5	5	500
Skin-breast	1485-1600	0.5	5	100

Table 2: The simulation results for 4 models before and after applying algorithm

Model	Water-phantom	Water-muscle	Water-liver	Skin-breast
Desirable focal depth (cm)	10	10	10	5
Real focal depth (cm)	9.32	9.17	8.92	5.37
The displacement of the focal point (cm)	0.68	0.83	1.08	-0.37
The displacement of the focal point caused	0.557	0.38	0.475	-0.56
New focal depth (cm)	10.61	10.45	10.6	2.8
Focal depth after applying algorithm (cm)	9.81	9.49	9.26	2.25
The correction of the focal point displacement (%)	92	73	72	75

equations were obtained to calculate the displacement of the focal point for an element with a certain incidence angle. Thereafter, the equations extended to all of the transducer elements, and the total displacement caused by velocity differences in the tissue was calculated. Computational algorithms were designed in such a way that both $c_1 < c_2$ and $c_1 > c_2$ were included. Four models of two-layer tissues with different arrangement were studied. In the three models, sound velocity in the first layer was less than that in the second layer, and in another model, velocity in the first layer was more than the second layer. The results show that the designed algorithm in $c_1 < c_2$ situation is more confidence; the effects of factors such as the absorption coefficient of the tissue are the reasons for that. Because of the nature of absorption, it leads to shrinkage of the focal point; however, velocity differences can induce both shrinkage and/or enlargement of the focal point depth of a transducer. Therefore, good results cannot be obtained from applying the algorithm when the velocity differences and absorption coefficient affect the focal point in reverse. However, applying the algorithm in both cases reduces the displacement of the focal point. Although other studies in the field of computational techniques have been conducted, this study is based on the HIFU simulator suggested by the FDA.^[19] Li *et al.*^[28] performed a computational technique similar to this study. Their designed algorithm corrected the displacement of the focal point as much as 73% despite the complexity and strict implementation. However, the results of our study have shown that the designed algorithms can correct the focal point displacement as much as 78% despite its simplicity. In addition, studies have been performed about the thermal effects of HIFU therapy on the tissues.^[29,30] Since all results were based on simulations, we suggest that the algorithm also be evaluated on a real phantom. It should also be considered that the performance of this study on displacement correction contributes to the beam absorption in various tissues for a better estimation of the focal point.

Conclusion

Displacement correction caused by the refraction of the ultrasound beam in HIFU therapy is very important for the

precise treatment of cancerous tumors. Without a correction in the focal point displacement, HIFU would lead to serious damage in the normal tissues. The proposed algorithm in this study can correct the focal point depth and reduce the side effects of HIFU beams in the normal tissues, and consequently, it increases the efficiency of the treatment in HIFU therapy. In this study, it was found that in addition to the beam's refraction, the other factors such as the beam's absorption in the tissue could also contribute to the displacement of the focal point. Applying the developed algorithm significantly resolved the risks of the focal point displacement; however, it is necessary to consider the tissues' absorption parameter for correcting more accurately.

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Conflicts of interest

There are no conflicts of interest.

References

- Kennedy JE, Ter Haar G, Cranston D. High intensity focused ultrasound: Surgery of the future? *Br J Radiol* 2003;76:590-9.
- Kennedy JE. High-intensity focused ultrasound in the treatment of solid tumours. *Nat Rev Cancer* 2005;5:321-7.
- Ergün AS. Analytical and numerical calculations of optimum design frequency for focused ultrasound therapy and acoustic radiation force. *Ultrasonics* 2011;51:786-94.
- Anand A, Byrd L, Kaczkowski PJ, editors. In situ thermal parameter estimation for HIFU therapy planning and treatment monitoring. *Ultrasonics Symposium*. IEEE; 2004.
- Yetik H, Ariyurek C, Bozkurt A, Ergun AS, editors. Frequency optimization in high intensity focused ultrasound. *Ultrasonics Symposium (IUS)*. IEEE International 2014.
- Fan X, Hynynen K. The effect of wave reflection and refraction at soft tissue interfaces during ultrasound hyperthermia treatments. *J Acoust Soc Am* 1992;91:1727-36.
- Fan X, Hynynen K. The effects of curved tissue layers on the power deposition patterns of therapeutic ultrasound beams. *Med Phys* 1994;21:25-34.

8. Liu H-L, McDannold N, Hynynen K. Focal beam distortion and treatment planning in abdominal focused ultrasound surgery. *Med Phys* 2005;32:1270-80.
9. Ebbini ES, Cain CA. Multiple-focus ultrasound phased-array pattern synthesis: Optimal driving-signal distributions for hyperthermia. *IEEE Trans Ultrason Ferroelectr Freq Control* 1989;36:540-8.
10. Ebbini ES, Cain CA. A spherical-section ultrasound phased array applicator for deep localized hyperthermia. *IEEE Trans Biomed Eng* 1991;38:634-43.
11. Ebbini E, Cain C. Optimization of the intensity gain of multiple-focus phased-array heating patterns. *Int J Hyperth* 1991;7:953-73.
12. Botros YY, Volakis JL, VanBaren P, Ebbini ES. A hybrid computational model for ultrasound phased-array heating in presence of strongly scattering obstacles. *IEEE Trans Biomed Eng* 1997;44:1039-50.
13. Thomas J-L., Fink MA. Ultrasonic beam focusing through tissue inhomogeneities with a time reversal mirror: Application to transskull therapy. *IEEE Trans Ultrason Ferroelectr Freq Control* 1996;43:1122-9.
14. Pernot M, Aubry J-F., Tanter M, Boch A-L., Marquet F, Kujas M, *et al.* *In vivo* transcranial brain surgery with an ultrasonic time reversal mirror. *J Neurosurg* 2007;106:1061-6.
15. Aubry J-F., Pernot M, Marquet F, Tanter M, Fink M. Transcostal high-intensity-focused ultrasound: *Ex vivo* adaptive focusing feasibility study. *Phys Med Biol* 2008;53:2937.
16. Marquet F, Pernot M, Aubry J-F, Montaldo G, Tanter M, Fink M, editors. Non-invasive transcranial ultrasound therapy guided by CT-scans. *Engineering in Medicine and Biology Society, 2006 EMBS'06 28th Annual International Conference of the IEEE.* IEEE; 2006.
17. Cochard E, Prada C, Aubry J-F., Fink M. Ultrasonic focusing through the ribs using the DORT method. *Med Phys* 2009;36:3495-503.
18. Howard S, Yuen J, Wegner P, Zanelli CI, editors. Characterization and FEA simulation for a HIFU phantom material. 2003 IEEE Symposium on Ultrasonics. IEEE; 2003.
19. Soneson JE, editor. A user-friendly software package for HIFU simulation. 8th International Symposium on Therapeutic Ultrasound. AIP Publishing; 2009.
20. Tiesler H, Haase S, Schwenke M, Bieberstein J, Preusser T. Software assistance for HIFU therapy planning. *Biomed Tech (Berl)* 2012;57(Suppl 1).
21. Chaussy C, Thüroff S. The status of high-intensity focused ultrasound in the treatment of localized prostate cancer and the impact of a combined resection. *Curr Urol Rep* 2003;4:248-52.
22. Blana A, Walter B, Rogenhofer S, Wieland WF. High-intensity focused ultrasound for the treatment of localized prostate cancer: 5-Year experience. *Urology* 2004;63:297-300.
23. Blackstock DT. *Fundamentals of Physical Acoustics.* John Wiley & Sons; 2000.
24. Grill H, Langereis S. Hyperthermia-triggered drug delivery from temperature-sensitive liposomes using MRI-guided high intensity focused ultrasound. *J Control Release* 2012;161:317-27.
25. Fan T-Y., Zhang L, Chen W, Liu Y, He M, Huang X, *et al.* Feasibility of MRI-guided high intensity focused ultrasound treatment for adenomyosis. *Eur J Radiol* 2012;81:3624-30.
26. Bucknor MD, Rieke V, Do L, Majumdar S, Link TM, Saeed M. MRI-guided high-intensity focused ultrasound ablation of bone: Evaluation of acute findings with MR and CT imaging in a swine model. *J Magn Reson Imaging* 2014;40:1174-80.
27. White PJ, Jolesz FA. MRI-guided focused ultrasound. *Bioelectromagn Subtle Energy Med* 2014: 363.
28. Li D, Shen G, Bai J, Chen Y. Focus shift and phase correction in soft tissues during focused ultrasound surgery. *IEEE Trans Biomed Eng* 2011;58:1621-8.
29. Rangraz P, Behnam H, Shakhssalim N, Tavakkoli J. A feed-forward neural network algorithm to detect thermal lesions induced by high intensity focused ultrasound in tissue. *J Med Signals Sens* 2012;2:192-202.
30. Mobasheri S, Behnam H, Rangraz P, Tavakkoli J. Radio frequency ultrasound time series signal analysis to evaluate high-intensity focused ultrasound lesion formation status in tissue. *J Med Signals Sens* 2016;6:91-8.