Quantification of the CARI breast imaging sensitivity by 2D/3D numerical time-domain ultrasound wave propagation

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Abstract

Breast imaging systems must recognize very small lesions at early stage of detection in order to save lives and reduce costs. The clinical amplitude–velocity reconstruction imaging (CARI), a recent breast imaging technique, is based on the differentiation of velocity and attenuation of ultrasound wave propagating through the breast tissues. Moreover, the method is experimentally verified to have higher sensitivity than conventional ultrasound.

This work is concerned with the numerical study of the CARI technique using a finite element time domain (FETD) ultrasound wave propagation in the breast tissue. The mathematical method consists of a dissipative wave equation incorporating a frequency-dependent attenuation, and supplemented with initial and boundary conditions.

The formulation used provides a good resolution of spatial features, and thus, simulations help in evaluating quantitatively the detection of small lesions in the breast. Three-dimensional (3D) simulations agree with the results obtained for the two-dimensional (2D) model although when the frequency is reduced. In addition, the study shows the effectiveness of the FETD to simulate the CARI modality.

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1. Introduction—medical framework

Early detection and treatment of breast cancer can significantly improve a woman’s chances of surviving. Among breast imaging techniques, ultrasound has proven to be a valuable tool for its wide use and low cost. Most tumors are detected by ultrasound because they produce lower echo than the surrounding tissue. However, the changes of sound velocity in the different breast tissues cannot be assessed in conventional ultrasound. A recent sonography method, called clinical amplitude–velocity reconstruction imaging (CARI), was developed by Dr. K. Richter as a standardized technique [9–11,13] for better detection of breast cancer. In the CARI device, the breast is fixed between two compression plates as

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The aim of this paper is to quantify the sensitivity of the CARI technique according to the tumor parameters by a time domain wave propagation. The paper is organized as follows. A mathematical model based on the wave equation is presented taking into account the two characteristic parameters of the CARI technique. Next, two-dimensional (2D)–three-dimensional (3D) numerical simulations are performed to investigate the CARI sensitivity. Then, remarks and perspectives conclude the paper.

2. Theory—modeling

2.1. Mathematical model

Medical ultrasound is essentially a means of producing visual images based on echoes that occur at acoustic interfaces. This echo contains information that can be used to study the various breast tissues. Hence, a lesion is localized if its echo pattern is different from that of the surrounding medium. A better understanding of ultrasonic wave propagation into human breast tissues is then required.

The hyperbolic equation governing ultrasound pressure fields in lossy attenuated medium consists of a dissipative wave equation incorporating a frequency-dependent attenuation [1]

\[
\frac{1}{c^2} \frac{\partial^2 p(x, t)}{\partial t^2} + \gamma \frac{\partial p(x, t)}{\partial t} = \nabla (\nu \nabla p(x, t)),
\]

(1)
where \( x \) and \( t \) are the space and time variables, respectively, and \( c \) is the sound speed of the traversed tissue. Studies of bioacoustic models have shown that in viscous fluids the absorption coefficient \( \gamma \) is characterized by a power law frequency \([5,14]\)

\[
\gamma = \gamma(f) = \frac{a_0}{c} f^\gamma.
\]  
(2)

Here, \( a_0 \) is a dependent material constant, \( f \) the frequency, and \( \gamma \) the frequency-power exponent varying from 0 to 2 and depending on tissue. The parameters \( a_0 \) and \( \gamma \) are obtained by fitting experimental data with auto-correlation based approach. Note that the damping term models the loss of the wave propagation energy in the tissue.

The breast tissue is initialized with the atmosphere pressure and the condition:

\[
\frac{\partial p}{\partial t}(x, t) = 0.
\]  
(3)

The transducer incident wave is implicitly specified as a Dirichlet boundary condition for the wave equation. A homogeneous Neumann condition is set on the reflecting boundary:

\[
\frac{\partial p}{\partial n} = 0,
\]  
(4)

while first-order absorbing conditions are set on the non-reflecting boundaries:

\[
\frac{\partial p}{\partial n} = -\frac{1}{c} \frac{\partial p}{\partial t}.
\]  
(5)

### 2.2. Discretization

We introduce a time grid \( t_n = n \Delta t \) for \( n = 0, 1, 2, \ldots \) and \( \Delta t \) is the time step size. We set \( p^n(x) = p(x, t_n) \) as the \( n \)th iterate of the pressure at the global point \( x \). The time derivatives in (1) are discretized by centered second-order finite differences, which gives the semi-discrete scheme:

\[
\frac{p^{n+1} - 2p^n + p^{n-1}}{\Delta t^2} + \gamma c^2 \frac{p^{n+1} - p^{n-1}}{2\Delta t} = c^2 \nabla^2 p^n.
\]  
(6)

Let \( p^n = \sum_{j=1}^{N_j} N_j^p p^n_j \) be an expansion of \( p^n(x) \) in a basis functions \( (N_j)_j \). Multiplying (6) by \( N_i \) and integrating second-order derivatives by parts leads to the spatial and temporal discrete problem:

\[
\sum_{j=1}^{N_j} (2 + \gamma c^2 \Delta t)(N_i, N_j)p^{n+1}_j
\]

\[
= 4 \sum_{j=1}^{N_j} (N_i, N_j)p^n_j - 2c^2 \Delta t \sum_{j=1}^{N_j} (\nabla N_i, \nabla N_j)p^n_j - 2 \sum_{j=1}^{N_j} (N_i, N_j)p^{n-1}_j
\]

\[
+ \gamma c^2 \Delta t \sum_{j=1}^{N_j} (N_i, N_j)p^{n-1}_j + 2c^2 \Delta t^2 \int_{\text{stat}} N_i \frac{\partial p^n}{\partial t} \, d\sigma.
\]  
(7)

\( (, ) \) is the \( L^2 \)-inner product and the integration domain is the 2D or 3D breast model configuration. The non-reflecting boundary conditions (5) are inserted in the integral term of (7) and a second-order finite
difference approximation is applied to (3) at $t = 0$. Consequently, (7) is reduced to the matrix form

$$
\left[ (2 + \gamma c^2 \Delta t)M + c \Delta t B \right] p^{n+1} = 4Mp^n - 2c^2 \Delta t^2 Kp^n - 2Mp^{n-1} + \gamma c^2 \Delta t M p^{n-1} + c \Delta t B p^{n-1},
$$

(8)

where $M$ ($M_{ij} = (N_i, N_j)$) and $K$ ($K_{ij} = \langle \nabla N_i, \nabla N_j \rangle$) are the mass and stiffness matrices, respectively. The matrix $B$ is derived from the Neumann condition on the non-reflecting boundaries.

To make the iterative process more computationally efficient, a fictitious iterate $p^{-1}$ is added and verifies:

$$
p^{-1} = p^0 - \frac{1}{2\gamma c^2 \Delta t^2} M^{-1} K p^0.
$$

(9)

The $p^{-1}$ linear system arises from (8) with $n = 0$ and the second-order discrete form of (3). In summary, the ultrasound pressure is calculated by the following algorithm:

1. initialize $p^0$ with the atmosphere pressure;
2. calculate the fictitious iterate $p^{-1}$;
3. compute successively $p^1, p^2, \ldots$ from Eq. (8).

Note that Step 2 and the iterations in Step 3 of the algorithm involve the solution of linear systems which, in this study, are carried out by conjugate gradient method. The simulator is implemented and designed using the finite element and object-oriented programming library Diffpack [4,6]. The matrices of the algorithm are constructed initially once a finite element is chosen. Thanks to the functionalities supplied by this package, the pre- and post-processing are easily handled, and the extension to the 3D case is straightforward.

2.3. On the stability and accuracy of the FETD method

The principal difficulty with biacoustic modeling in real tissue is the back-scattering due to the tissue structure and the long propagation distance. For example, 7.5 MHz waves propagate 200 wavelengths for a round trip along the 2D breast model of Fig. 2. It is well known that at these ranges typical finite element algorithms distort considerably signals because of numerical dispersion, in particular, when low order approximations are used for space and time derivatives.

Simulating the wave propagation at high frequencies requires at least the spatial Nyquist sampling, i.e. two elements per wavelength. However, the experience shows that this choice is insufficient for a good resolution. Our FETD approximation also confirms the numerical instability that could result from low spatial resolution. It is worth noting that the stability of the FETD method can be improved by lumping the mass matrix $M$ (i.e. $M$ can be diagonalized), and the numerical scheme becomes then explicit. Diffpack provides this technique as an option activated (or not) while the mass matrix is formed (cf. [6], Chapter 2).

We will here investigate the accuracy and stability of the suggested scheme from numerical experiments rather than by a mathematical analysis. This last issue needs more attention, and thus will be developed in a separate work.

The simulations in this section are run on the $10 \text{mm} \times 10 \text{mm}$ square, and the transducer incident wave consists of a 7.5 MHz single frequency signal analytically given by:

$$
p_{\text{trsd}}(x, t) = p_{\text{atm}} + K_{\text{trsd}} \sin(\omega t) \cos\left(\frac{\omega t}{6}\right) \quad \text{if } 0 \leq t \leq \frac{3}{f},
$$

(10)
and \( p_{\text{trsd}}(x,t) = p_{\text{atm}} \) elsewhere. \( p_{\text{atm}} \) is the atmosphere pressure, \( \omega = 2\pi f \), and \( K_{\text{trsd}} \) a transducer constant (Fig. 3 and 4).

In order to detect the numerical from the physical damping, preliminary simulations are performed for the wave propagating along the non-attenuated breast tissue. We are then restricted to the linear wave equation. In this case, the suggested method is stable if the condition

\[
p_{\text{atm}}(x,t) = p_{\text{atm}} \quad \text{for} \quad t > 0.6 \mu s.
\]
is fulfilled, with $\Delta x$ and $\Delta y$ are the finite element sizes in the $x$- and $y$-directions, respectively. This stability analysis is treated in [6], Chapter 2.

The first series of tests is presented in Fig. 5. The snapshots show the 3D view of the ultrasound pressure field after reflection with two spatial resolutions: two elements per wavelength in Fig. 5(a) and 10 elements per wavelength in Fig. 5(b). It is clear that a more accurate solution is obtained with high spatial resolution while more oscillations, associated with numerical dispersion, are produced with the Nyquist sampling. Other simulations are run to discuss numerically the stability. The initial condition

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Fig. 6. 3D view of the ultrasound pressure field when the waves propagate are reflected. The simulations are performed on the attenuated and cancerous fatty breast model of size 10 mm × 20 mm using two spatial samplings: (a) two elements per wavelength; and (b) 10 elements per wavelength. The tumor size is 4 mm × 5 mm. Note that the pressure is more stable at high resolution. The attenuation is shown from the colors tones because Fig. 5(a) and (b) have the same color scale.

\[
p(x, t) = p_{\text{atm}} \text{ is perturbed by } \epsilon(p) \text{ and } p_{\epsilon} \text{ denotes the corresponding solution. The numerical results show that the difference } e = (p_{\epsilon} - p) \text{ between the original and perturbed problem solutions is relatively small if } \epsilon(p) \text{ is small. For instance, with two fractions of } p_{\text{atm}}, \text{ namely, } \epsilon(p) = 10^{-3} p_{\text{atm}} \text{ and } \epsilon(p) = 10^{-4} p_{\text{atm}}, \text{ } ||e||/p_{\text{atm}} \text{ is } 10^{-5} \text{ and } 10^{-4}, \text{ respectively.}
\]

The final preliminary numerical experiments are concerned with the attenuated wave equation. Fig. 6 shows that the physical damping cannot easily be identified from the numerical damping when only two elements are resolved per wavelength.

3. Numerical experiments and discussions

3.1. 2D FETD breast model

Simulations of acoustic fields in ultrasound imaging is well treated in the literature [7,8,15]. However, most of these studies are in 2D or pseudo 3D with axial symmetry, which does not give enough quantitative evaluation of acoustic fields. In our study, thanks to the strong geometric flexibility of the finite element method, the numerical formulation can deal with realistic geometries for the breast and the tumor.

For the present work, the tests are limited to simple geometries in order to demonstrate the feasibility of the FETD numerical method. The 2D breast model employed is a 10 mm × 20 mm rectangle as shown in Fig. 2. The tumor is represented by a simple aberration in the tissue. The wave propagates from bottom to top through the 2D configuration. A signal appropriate for exciting high frequency wave, is transmitted from a linear array transducer. More precisely, the input excitation is a broad band signal of 7.5 MHz center frequency, and is explicitly given by:

\[
p_{\text{real}}(x, t) = p_{\text{atm}} \left[ 1 + \frac{\cos(\omega_1 t)}{2} (1 + \cos(\omega_2 t)) \right],
\]  

(12)
Table 1 Sound velocity and coefficients of frequency-dependent power law attenuation of the breast tissue

<table>
<thead>
<tr>
<th>Breast fatty tissue</th>
<th>Breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>$c$ (m/s)</td>
<td>1475</td>
</tr>
<tr>
<td>$a_0$ (dB/MHz$^2$)</td>
<td>15.8</td>
</tr>
<tr>
<td>$y$ (s/m$^2$)</td>
<td>1.7</td>
</tr>
</tbody>
</table>

where $t_1 = t - 0.3 \mu$s, $0 \leq t \leq 0.6 \mu$s, and $p_{pul} (x, t) = p_{atm}$ elsewhere, $t_0 = 0.3 \mu$s, $\omega_1 = 2\pi f$, and $\omega_2 = \omega_1 / 4$ which defines the bandwidth of the signal. The plot of the transducer signal is shown in Fig. 3.

Table 1 displays the sound speeds as well as the power law coefficients of the breast fatty tissue and the cancer. These values result from clinical experiments reported in [5,16]. The 2D breast-tumor model is meshed with a grid of $501 \times 1001$ nodes (or equivalently 500,000 elements) so that 10 elements are resolved per wavelength. For all the simulations, bilinear finite elements are used since the lumping of the mass matrix improves the accuracy when solving the wave equation with this element type. The time stability condition and sampling require a time step size $\Delta t = 9.26 \times 10^{-9}$ s.

3.2. Preliminary

Using the wave propagation speed in tissues, time reflection information can be converted into distance reflection information, and vice versa. For this purpose, we calculate the wave travel times from the transducer to the reflecting line, denoted $T_0$ and $T_1$. They are evaluated when the wave has traversed through the tumor region and when it has not, respectively, by

$$T_0 = \frac{d_0}{c_0}, \quad T_1 = \frac{d_0 - d_1}{c_0} + \frac{d_1}{c_1},$$

where $c_0$ and $c_1$ as given previously, $d_0 = 20$ mm and $d_1$ are, respectively, the distances of the 2D configuration and the lesion in the $z$-direction (see Fig. 2). Note that the expressions (13) are obtained from an approximation based on geometrical acoustics, neglecting diffraction.

3.3. Numerical results

In this section, the simulation of the CARI technique is performed on two breast models: (i) the domain size is $40$ mm $\times$ $20$ mm and the numerical scheme verifies the Nyquist criterion; and (ii) the domain size is $10$ mm $\times$ $10$ mm and 10 elements are resolved per wavelength.

Using the assumptions of the case (i), we compare the ultrasonic pressure for healthy and cancerous breast fatty tissues. The abnormal tissue contains a $5$ mm $\times$ $5$ mm-size lesion. Although a low resolution is used, the snapshots in Fig. 7 show that the tumor causes clearly a change of the echo pattern when the waves are reflected.

Other simulations are run to investigate the sensitivity of the CARI technique to one of the main tumor parameters, i.e., the size. We consider three tumors of sizes $10$ mm $\times$ $10$ mm, $5$ mm $\times$ $5$ mm, and $2$ mm $\times$ $2$ mm, respectively. The ultrasound pressure at the reflecting line, extracted from the 2D simulations, is plotted as function of the lateral distance $x$ (Fig. 8). It is observed in Fig. 9 that the line is straight in the case of a non-cancerous breast tissue, and an elevation shift results for the abnormal
tissues. Note also that the elevation increases with the tumor size. These results show the effect of the tumor size on the pressure at the reference line as well as an acceptable resolution of spatial features with Nyquist sampling (see also [2]).

According to the approximations (13) of the wave time travel along the tissue, the echoes traversing the tumor region arrive sooner at the reflecting line. In Fig. 9, the ultrasound pressure is plotted versus the axial distance $z$, the $x$-position being fixed to the origin ($x = 0$). We remark that the echoes traversing the tissue with $10 \text{ mm} \times 10 \text{ mm}$-lesion arrive earlier than those of the $3 \text{ mm} \times 3 \text{ mm}$-lesion case.
Fig. 9. Comparison of results from simulations in a homogeneous breast tissue (solid line), and in two abnormal ones with a 10 mm × 10 mm-size tumor (dashed line) and a 3 mm × 3 mm-size tumor (dotted–dashed line). The normalized ultrasound pressure is plotted vs. the axial distance $z$ at two time steps: (a) $t = 8 \mu s$, and (b) $t = 13.3 \mu s$. Compared to the non-cancerous tissue, the wave traversing the tissue with 10 mm × 10 mm tumor arrives sooner at the reflecting line, while the arrival delay is reduced for the wave propagating in the tissue with the smaller lesion.

Under the assumptions of the case (ii), other numerical experiments are run for a homogeneous tissue and three tissues with different tumor size. For all the tissues, the results confirm that the waves are well absorbed at the non-reflecting boundaries. Pictures from Fig. 10 show also that the solutions are more stable that those with Nyquist criterion. Moreover, Fig. 10(b) shows the solution with the smallest tumor size, i.e. 1 mm × 1 mm. It can be seen that the waves do not have the same behavior as for the non-cancerous tissue (Fig. 10(a)). The effect of the tumor size can also be identified by the nature of the back-scattering caused with each tumor as illustrated in Fig. 10(c) and (d). The results show, in particular, that using the FETD scheme with high resolution can inform on the sensitivity of the CARI method to the size of the tumor. However, this sensitivity analysis may be improved and evaluated more quantitatively by, for example, inserting other parameters in the model.

### 3.4. 3D FETD breast model

In this section, the study is easily extended to the 3D case thanks to the FETD modeling and the features of the Diffpack library. A 24 mm × 22 mm × 20 mm-3D box is used for a breast tissue-mimicking phantom, and a model is shown in Fig. 4. For simplification, the lesion is a cubic box inside the tissue with the same acoustic properties as for the 2D model. The transducer is a 12 mm × 8 mm-rectangle located on the face down of the 3D breast model. It is known that the finite element time-domain formulation of 3D...
Fig. 10. Sensitivity of the CARI technique to the tumor size via the back-scattering which results from the presence of each tumor in the tissue with size: (b) 1 mm × 1 mm, (c) 2 mm × 2 mm, and (d) 4 mm × 6 mm. The echoes of the three tumors in the cancerous tissue are compared to the (a) healthy breast tissue. The four views are only the part of the pressure field over the upper half of the 10 mm × 20 mm breast model.

Ultrasound wave propagation requires costly computing effort. For this reason, we reduce the frequency to \( f = 5 \text{ MHz} \). But we are still in the frequency range (5–7.5 MHz) used in the CARI clinical breast imaging. In this case, the 3D grid for the breast model and the time step size are, respectively, >1.3 × 10^6 nodes and \( \Delta t = 2 \times 10^{-8} \text{ s} \).
Fig. 11. Ultrasound pressure through a cross-section normal to \( y \)-axis (parallel to the wave direction of propagation) and traversing the tumor region when the wave arrives at the reflecting line: (a) in homogeneous breast fatty tissue; and (b) in tissue with a 5 mm × 5 mm × 5 mm-size tumor.

Fig. 12. Ultrasound pressure through a cross section normal to \( z \)-axis (parallel to the transducer plane) and traversing the tumor region when the wave arrives at the reflecting line: (a) in homogeneous breast fatty tissue; and (b) in tissue with a tumor 5 mm × 5 mm × 5 mm-size tumor. The shape of the tumor is clearly identified in the background medium, and is surrounded by the rectangular transducer.
The simulations are carried out for homogeneous and inhomogeneous breast fatty tissues. The ultrasound pressure is computed over two normal planes acrossing the tumor region. From snapshots in Fig. 11, it is observed that the echo of the beam around the tumor is clearly perturbed. In Fig. 12, the view from the normal plane to the $z$-axis shows instead that the shape of the $5\text{ mm} \times 5\text{ mm} \times 5\text{ mm}$-tumor is well recognizable in the tissue. Therefore, the simulations agree with the quantitative results obtained for the 2D model. In addition, the 3D cross-sections fit well the pictures of the 2D numerical experiments.

4. Concluding remarks and perspectives

This study addresses the problem of large-scale ultrasonic wave propagation in biological media from an application to the CARI breast imaging technique. The mathematical modeling of the CARI modality consists of a damped time-domain wave equation. The model takes into account the change of sound speed and the frequency dependent attenuation, two characteristics of the CARI clinical device. The equations and the corresponding initial and boundary conditions are approximated by a finite element time-domain method. The numerical method is developed, and the stability and accuracy are discussed. The FETD method provides a good resolution of the spatial features when 10 elements are sampled per wavelength. The 2D numerical simulations help in evaluating quantitatively the detection of tumors in the breast tissue. In particular, lesion as small as $2\text{ mm} \times 2\text{ mm}$-size is recognizable in the tissue.

Although the frequency is reduced, which remains in the range of frequency used in the CARI measurements, the 3D numerical experiments still confirm the results obtained for the 2D case.

This study illustrates also the feasibility of using the FETD to model and numerically simulate the CARI technique. Thanks to the functionalities supplied by the Diffpack library, the extension to the 3D breast model is straightforward. Moreover, the simulations can be extended to more realistic geometries of the tumor, for example, an ellipse or ellipsoid which will demonstrate the effectiveness of the FETD method in simulating biacoustic phenomena in breast-mimicking tissues. This issue and that of including some design parameters of the transducer such as focusing and scanning of the beams have been reported in a separate work submitted for publication. Another extension consists in modeling the attenuation by a fractional Laplacian [3], for which a finite element approach has been investigated and numerical experiments are in progress.

References