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1 **FWI-based quantitative ultrasound computed tomography - perspective for imaging of**
2 **musculoskeletal organs in children**

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12

13 1. Abstract

14 B-mode ultrasound has long been a first-line examination tool for the diagnosis of many
15 musculoskeletal diseases in children. Due to the high acoustic impedance contrast between
16 echogenic bone structures and adjacent soft tissue, B-mode ultrasound can only see the outer
17 surface of bone structures, not what lies inside. In this context, linear ultrasound computed
18 tomography can visualize the different morphologies of small organs (bone structures and adjacent
19 soft tissues), but does not provide quantitative, parametric images. This article proposes a non-
20 linear approach to ultrasound computed tomography using a full waveform inversion algorithm,
21 based on a complete numerical modeling of wave propagation in media and on the minimization, in
22 the L^2 -norm sense, of a functional based on the iterative solution of the inverse problem. Our study
23 was performed in two dimensions, as justified by current conventional experimental setups in
24 medical imaging. We used an acoustic modeling for simplification and computational cost
25 reduction. The inverse problem was solved iteratively using a quasi-Newton method known as the
26 memory-limited Broyden-Fletcher-Goldfarb-Shanno method. The gradient of the misfit function
27 was obtained based on the adjoint state method, which required only two simulations of the wave
28 propagation problem per source at each iteration. Experiments were conducted on a newborn arm
29 phantom containing the humerus, radius and ulna, deep radial and ulnar veins, embedded in
30 homogeneous adipose tissue. We show the images obtained for different configurations of
31 initialization and *a priori* information on the medium: without any *a priori* information on the
32 medium, *a priori* information on the initial map of mass densities, and ultrasonic wave velocities.
33 Convergences were of the order of 10 iterations in practice for each frequency band used, typically
34 150 kHz to 600 kHz. The normalized error was limited to less than 11%.

35 2. Keywords

36 Ultrasound computed tomography, Full waveform inversion, Musculoskeletal organ imaging,
37 Children's limbs

38 3. Introduction

39 Today, there is a growing interest in children's musculoskeletal health, firstly because children are
40 concerned by musculoskeletal disorders and damages, and specific infantile osteopathologies (such

41 as fractures, bone infections or tumors), and secondly because musculoskeletal health in childhood
42 is of a great importance for musculoskeletal health in adulthood. Therefore, musculoskeletal
43 development in children is a key issue. For pediatricians, radiologists and orthopedic surgeons, the
44 knowledge of the musculoskeletal disorders and bone quality of the child's limbs remains a major
45 objective, in order to anticipate the evolution of diseases, to guide diagnoses and thus define and
46 follow optimal therapeutic strategies.

47 B-mode ultrasound has long been a first-line examination tool for the diagnosis of many
48 musculoskeletal diseases in adults and children.¹ The other modalities, such as X-ray or magnetic
49 resonance imaging, are often associated with inconveniences of variable importance (cost,
50 irradiation, sedation, accessibility) that are constraining for pediatric applications. B-mode
51 ultrasound is all the more interesting because the functional advantages associated with it are
52 favorable to pediatric use, as the number of procedures can be increased without (known) harmful
53 effects. But the ultrasonic waves are disturbed by the presence of bony structures and have
54 difficulty penetrating bone. In its clinical use, this modality only makes it possible to see the outer
55 surface of a bony structure, and not what lies within. Also, B-mode ultrasound is not a quantitative
56 and parametric modality. The grayscale levels of the map are not linked to any significant physical
57 parameters of the organs. However, the development of a quantitative ultrasound imaging modality,
58 adapted to the musculoskeletal tissues and organs of children's limbs, as a complementary modality,
59 remains a major challenge.

60 The interactions between ultrasonic waves, hyper-echoic bony structures and adjacent hypo-echoic
61 soft tissues, along with the associated propagation problems, have been studied for more than thirty
62 years.² In this context, linear ultrasound computed tomography (USCT) in the orthogonal plane,
63 with several planar projections at different angles, provides images of musculoskeletal organs, at
64 the cost of adapted and time-consuming signal-processing algorithms.^{3,4} For example, linear
65 reflection-mode USCT, with an adapted filtering and wavelet processing algorithm, makes it
66 possible to reach, with a strong contrast-to-noise ratio, the different morphologies of small organs,
67 such as an artificial newborn arm or a chicken drumstick.⁵ With this method one can visualize small
68 X-ray invisible blood vessels in the artificial newborn arm, and, more specifically, muscles, nerves,
69 tibia and the much smaller fibula, fat and skin in the chicken drumstick. But the images obtained are
70 only morphometric, better defined than B-mode ultrasound images, and non-parametric. To

71 quantify the information, it is necessary to change the mathematical paradigm, and deal with the
72 case of non-linear USCT.

73 The approach proposed in this work consists in importing the highly sophisticated nonlinear full
74 waveform inversion (FWI), based on the full numerical modeling of wave propagation in media
75 (the object to be imaged and the background). FWI is at the forefront of the field of geophysics,^{6,7}
76 and has been used in medical imaging for a few years now with relevance (3D imaging, increased
77 resolution, limited computation time, multi-parameterized images, deep learning, programming on
78 *GPU* system). The goal of FWI is to iteratively reconstruct physical and elastic/acoustical
79 parameters in the various media, without having to resort to any of the classical limiting
80 assumptions currently made in USCT, for instance that tissue density is spatially constant. Indeed,
81 FWI is an imaging method for heterogeneous media (objects and/or background) that is based on
82 the full numerical modeling of wave propagation in these media, and on the minimization, in the L^2 -
83 norm sense, of the difference between recorded and simulated waveforms. The term "*full*" refers to
84 the use of the full-time series.⁸⁻¹³

85 FWI has gained in popularity in the medical field because it achieves higher resolution and
86 accuracy than methods that use only part of the information (e.g., the arrival times of the waves) or
87 that are based on approximations (ray tracing, first-order Born approximation, uniform geometrical
88 theory of diffraction, Bojarski's inverse theory, etc.), at the cost of an often high computational
89 burden. The most widely studied application for nonlinear USCT in medicine today is female breast
90 imaging.¹⁴⁻¹⁶ In the presence of bones with surrounding soft tissues and marrow, solutions consist
91 of iterative and adaptive schemes to integrate the induced nonlinear effects, either by retaining the
92 Radon projection-like geometry and variation shapes of the higher-order Born approximation, or by
93 extending the problem to FWI. Indeed, adapted iterative nonlinear methods have been proposed for
94 objects whose acoustic impedance is strongly contrasted against a homogeneous reference (soft
95 tissues, water), such as the Kaczmarz-model based method,¹⁷ the Distorted Born Iterative
96 method,¹⁸⁻²¹ the Phase Shift Migration method,²² or the Full-Matrix Spectrum-Domain method,²³⁻²⁵.
97 Belanger *et al.* have adapted a hybrid algorithm for the mapping of ultrasound velocity in the
98 cortical bone.²⁶ These algorithms have been tested on numerical and experimental data on a bone-
99 mimicking phantom and an *ex vivo* isolated single bone, without surrounding tissues, or by
100 modeling a single layer (muscle tissue for example), and the results are very encouraging. J. Wiskin
101 *et al.*,²⁷⁻²⁹ worked on a complete knee organ (skin, muscle, and bone) using a full wave 3D inverse

102 scattering transmission-based USCT. This approach is appropriate for the anatomical reconstruction
 103 of the bone, but the images do not seem to correctly quantify the wave velocity in the bone.
 104 This article introduces, after the assumptions involved, the forward problem, the adjoint state
 105 method and the Broyden-Fletcher-Goldfarb-Shanno method. Then, the experimental results
 106 obtained on a newborn arm phantom studied with an ultrasound scanner are discussed, for
 107 measurements of mass density and ultrasonic wave velocity, for several frequencies ranging from
 108 150 kHz to 600 kHz, and three configurations for the initial maps: without any *a priori* information
 109 about the phantom, with *a priori* information for the mass density and ultrasonic wave velocity
 110 maps.

111 4. Full waveform inversion

112 4.1. Forward problem and adjoint-state method

113 Let us consider xyz -space \mathbb{R}^3 with the origin O , and a 2D (xy -plan) non-circular cylindrical object to
 114 be imaged with generators parallel to the z -axis, immersed in a continuous surrounding
 115 homogeneous water-like background. The acoustic pressure wave field $p(\mathbf{x}; t)$ [\mathbf{x} , 2D-space vector,
 116 t , time variable] is described by the equation state system:

$$\begin{aligned}
 & \rho(\mathbf{x})\partial_t \mathbf{u}_x(\mathbf{x}; t) = \partial_x p(\mathbf{x}; t), \\
 & \rho(\mathbf{x})\partial_t \mathbf{u}_y(\mathbf{x}; t) = \partial_y p(\mathbf{x}; t), \\
 & \frac{1}{\kappa(\mathbf{x})}\partial_t p(\mathbf{x}; t) = \partial_x \mathbf{u}_x(\mathbf{x}; t) + \partial_y \mathbf{u}_y(\mathbf{x}; t) + f_s(t),
 \end{aligned}$$

117 (1)

118 where $\rho(\mathbf{x})$ and $\kappa(\mathbf{x})$ are the spatially-varying mass density and bulk modulus, respectively. u_x and
 119 u_y are the components of the particle velocity vector. f_s is the point source term.

120 The spatially variable parameters of the medium to be imaged using FWI are obtained by
 121 minimizing the difference between signals recorded at certain positions (receivers) and the
 122 corresponding modeled signals for one or more propagation events (sources) (Figure 1).

123 **Figure 1: Approximately here**

124 Given R recorded signals, $p_r^{\text{obs}}(t) = p^{\text{obs}}(\mathbf{x}_r; t)$, for $r = 1, \dots, R$ receivers, and for a single
 125 source, the cost function to minimize writes:

$$126 \quad (2) \quad \mathcal{C}(\mathbf{m}) = \sum_{r=1}^R \int_0^T [p_r^{\text{obs}}(t) - p_r^{\text{num}}(t; \mathbf{m})]^2 dt,$$

127 with \mathbf{m} the parameters of the object to be estimated, for instance, $\rho(\mathbf{x}), \kappa(\mathbf{x})$, on a spatial grid.
 128 $p_r^{\text{num}}(t; \mathbf{m}) = p^{\text{num}}(\mathbf{x}_r; t; \mathbf{m})$ is the synthetic signal computed numerically in the inversion
 129 process, and T is the recorded time period (or time length of the signal).

130 The main classical difficulties encountered in the minimization of $C(\mathbf{m})$ are its significant
 131 nonlinearity with respect to \mathbf{m} , and thus the presence of numerous local minima. An iterative
 132 method based on the calculation of the gradient of the cost function is generally chosen to minimize
 133 $C(\mathbf{m})$, either a simple gradient descent method or a more sophisticated quasi-Newton technique,
 134 which uses information based on second-order derivatives in order to accelerate convergence. These
 135 methods make it possible to converge to the minimum of the function in a larger or smaller number
 136 of iterations, depending on the method used and on the complexity of the problem. Nevertheless,
 137 the gradient of $C(\mathbf{m})$, i.e., its partial derivatives with respect to each element of \mathbf{m} , cannot easily be
 138 calculated based on a standard and simple finite-difference approach, because this would require
 139 performing as many forward calculations of wave propagation as the number of parameters, and
 140 this for each iteration of the minimization algorithm. The adjoining field method, introduced in the
 141 seismological domain in the 1970s,³⁰ makes it possible to overcome this difficulty. It can be shown
 142 that the gradient of the cost function can be obtained as the convolution product of the forward field
 143 with an adjoint field obtained by calculating the time-reversed wave propagation:

$$144 \quad (3) \quad \mathbf{r}_r(t; \mathbf{m}) = \mathbf{p}_r^{\text{obs}}(-t) - \mathbf{p}_r^{\text{num}}(-t; \mathbf{m}),$$

145 with each receiver acting as a source. Two calculations of the propagation in each medium (object
 146 and background) are then sufficient to obtain the gradient (in the case of multiple sources, two
 147 calculations per source are needed).

148 Minimization algorithms based on the gradient converge to the solution only if they are started
 149 close to the global minimum, i.e., provided that the initial model is already of good quality, which is
 150 of course rarely the case. In practice, this global minimum is unknown and there is therefore a risk
 151 of remaining trapped in a local minimum. In particular, if there is a difference in propagation time
 152 greater than half a period between the computed and real data, the algorithm will attempt to match
 153 different cycles of the signals and will not be able to converge (a problem known as "*cycle*
 154 *skipping*",¹³). A method to reduce this risk is to use an (incremental) "*frequency-hopping*" approach:
 155 first, a low-pass filter is used to retain only the lowest frequencies and then, once a minimum is

156 obtained, the maximum frequency is slightly increased and the process is run again, until all the
 157 frequency information has been included.³¹

158 The FWI method means that the model sought must minimize the mean squared difference between
 159 the numerical synthetic time series and the observed basic time series to be fitted:

$$160 \quad (4) \quad \chi(\mathbf{m}) = \sum_{s=1}^S \sum_{r=1}^R \int_0^T \frac{1}{2} \|\mathbf{p}_{s,r}^{obs}(t) - \mathbf{p}_{s,r}^{num}(t; \mathbf{m})\|^2 dt.$$

161 In other words, the goal is to find a model of the object that can explain a large portion of the
 162 recorded signals. This is basically the reason why drastically-enhanced pictures can be obtained.

163 This functional quantifies the L^2 difference between the observed waveforms, $p_{s,r}^{obs}(t) =$
 164 $p^{obs}(\mathbf{x}_r, \mathbf{x}_s; t)$ at receivers \mathbf{x}_r , $r = 1, \dots, R$, produced by sources at \mathbf{x}_s , $s = 1, \dots, S$, and the
 165 corresponding synthetic time series, $p_{s,r}^{num}(t; \mathbf{m}) = p^{num}(\mathbf{x}_r, \mathbf{x}_s; t; \mathbf{m})$ computed in model \mathbf{m} .

166 In the vicinity of \mathbf{m} , the misfit function can be expanded into a Taylor series:

$$167 \quad (5) \quad \chi(\mathbf{m} + \delta\mathbf{m}) \approx \chi(\mathbf{m}) + \mathbf{g}(\mathbf{m}) \cdot \delta\mathbf{m} + \delta\mathbf{m}^\dagger \cdot \mathbf{H}(\mathbf{m}) \cdot \delta\mathbf{m},$$

168 where $\mathbf{g}(\mathbf{m}) = \frac{\partial\chi(\mathbf{m})}{\partial\mathbf{m}}$ is the gradient of the waveform misfit function, $\mathbf{H}(\mathbf{m}) = \frac{\partial^2\chi(\mathbf{m})}{\partial\mathbf{m}^2}$ the
 169 Hessian, and \dagger denotes the transpose. The nearest minimum of χ in equation (5) with respect to the
 170 model perturbation $\delta\mathbf{m}$ is reached for $\delta\mathbf{m} = -\mathbf{H}^{-1} \cdot \mathbf{g}$. The local minimum of equation (4) is thus
 171 given by perturbing the model in the direction of the gradient preconditioned by the inverse
 172 Hessian. A direct method to compute the gradient is to take the derivative of equation (4) with
 173 respect to model parameters:

$$174 \quad (6) \quad \frac{\partial\chi(\mathbf{m})}{\partial\mathbf{m}} = - \sum_{s=1}^S \sum_{r=1}^R \int_0^T \frac{\partial p_{s,r}^{num}(t; \mathbf{m})}{\partial\mathbf{m}} [\mathbf{p}_{s,r}^{num}(t; \mathbf{m}) - \mathbf{p}_{s,r}^{obs}(t)] dt.$$

175 This equation can be reformulated as the matrix-vector product, $\mathbf{g} = -\mathbf{J}^* \cdot \delta\mathbf{d}$, where \mathbf{J}^* is the
 176 adjoint of the Jacobian matrix of the forward problem that contains the Fréchet derivatives of the
 177 data with respect to model parameters, $\delta\mathbf{d}$ is the vector that contains the data residuals. The
 178 determination of \mathbf{J} would require computing the Fréchet derivatives for each time step in the time
 179 window considered and for all the source-station pairs, which is completely prohibitive on current
 180 computers, even the latest and greatest ones. As mentioned above, it is however, and fortunately,
 181 possible to obtain this gradient without computing the Jacobian matrix explicitly. The idea is to
 182 resort to the adjoint state, which corresponds to the wave field transmitted and back-propagated

183 from the receivers The approach to determine the gradient without computing the Fréchet
 184 derivatives was introduced in nonlinear optimization by Chavent et al. in the 1970s.^{30,32} The
 185 Lagrangian functional is the cost function augmented by the following constraint given by the
 186 equation of state,³³:

187 (7) $\mathcal{L}(\mathbf{u}, \mathbf{u}^a, \rho, \kappa) =$

$$\sum_{s=1}^S \left\{ \sum_{r=1}^R \int_0^T [\mathbf{p}_{s,r}^{num}(t; \mathbf{m}) - \mathbf{p}_{s,r}^{obs}(t)]^2 dt - \int_0^T \int_x \int_y \mathbf{u}^a(\mathbf{x}; t) [\boldsymbol{\sigma}(\rho; \kappa) \partial_t \mathbf{u} - \mathbf{A} \partial_x \mathbf{u} - \mathbf{B} \partial_y \mathbf{u} - \mathbf{F}_s] dy dx dt \right\},$$

188 with $\mathbf{u} = (u_x, u_y, p)^\dagger$, $\boldsymbol{\sigma}(\rho; \kappa) = \begin{pmatrix} \rho & 0 & 0 \\ 0 & \rho & 0 \\ 0 & 0 & 1/\kappa \end{pmatrix}$, $\mathbf{A} = \begin{pmatrix} 0 & 0 & 1 \\ 0 & 0 & 0 \\ 1 & 0 & 0 \end{pmatrix}$, $\mathbf{B} = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 1 \\ 0 & 1 & 0 \end{pmatrix}$,

189 and $\mathbf{F}_s = (0, 0, f_s)^\dagger$.

190 $\mathbf{u}^a(\mathbf{x}; t)$ is the Lagrange multiplier to be found by zeroing the partial derivative of the Lagrangian
 191 functional, equation (7), with respect to the wave field, \mathbf{u} .³⁴

192 By zeroing the misfit function, equation (7), with respect to the model parameters, ρ, κ , the gradient
 193 of the misfit function can then be found:

194 (8) $\partial_{\rho, \kappa} \mathcal{X}(\rho, \kappa) = \frac{1}{2} \sum_{s=1}^S \left\{ \int_0^T \int_x \int_y \mathbf{u}_s^a(t) \partial_{\rho, \kappa} \boldsymbol{\sigma}(\rho, \kappa) \partial_t \mathbf{u}_s(t) \cdot (\delta \rho, \delta \kappa) dy dx dt \right\} = \mathbf{0}$,

195 which gives the expression of the gradient kernels for ρ and κ in terms of direct \mathbf{u} and the adjoint
 196 \mathbf{u}^a field:

197 (9) $\nabla_{\rho} \mathcal{X}(\rho, \kappa) = \sum_{s=1}^S \int_0^T \langle \mathbf{u}_x^a(t) \partial_t \mathbf{u}_x(t) + \mathbf{u}_y^a(t) \partial_t \mathbf{u}_y(t) \rangle_s dt$,

198 (10) $\nabla_{\kappa} \mathcal{X}(\rho, \kappa) = \sum_{s=1}^S \int_0^T \frac{p_s^a(t)}{\kappa(x)^2} \partial_t p_s(t) dt$,

199 with p^a is the adjoint acoustic pressure wave field. As the above equations show, the principle of
 200 the adjoint-state method is to correlate two wave fields: the forward field propagating from the
 201 sources to the receivers, and the adjoint wavefield propagating from the receivers backwards in
 202 time. Calculating the gradient of the misfit function therefore requires only two simulations of the
 203 wave propagation problem per source.

204 4.2. The Limited-memory Broyden-Fletcher-Goldfarb-Shanno method

205 Gradient descent is the most commonly used iterative optimization algorithm for finding the local
206 minimum of a function:

207 (11)
$$\mathbf{m}_{k+1} = \mathbf{m}_k - \alpha \mathbf{g}(\mathbf{m}_k),$$

208 with $\mathbf{m}_k = \begin{pmatrix} \rho_k \\ \kappa_k \end{pmatrix}$ the parameters of the object at iteration k , $\mathbf{g}(\mathbf{m}_k) = \begin{bmatrix} \nabla_{\rho} \chi(\mathbf{m}_k) \\ \nabla_{\kappa} \chi(\mathbf{m}_k) \end{bmatrix}$ the gradient of
209 the cost function at iteration k , and $\alpha \in \mathbb{R}_+$ the step size.

210 The parameter is updated by perturbing its value in the direction opposite to that of the gradient.
211 This method converges slowly and depends on the learning rate of the descent step α . The smaller
212 the step size, the greater the chance of the algorithm converging, which considerably increases
213 convergence time. This method is therefore not recommended for complex problems requiring high
214 computing power to calculate the cost function and its gradient. In contrast to the gradient descent
215 method, the Limited-memory Broyden-Fletcher-Goldfarb-Shanno (L-BFGS) method has a higher
216 convergence speed, and the direction of perturbation is guided by the computation of the Hessian
217 matrix \mathbf{H} , which is the matrix of partial second derivatives. This method is obtained from a second
218 order Taylor series development.

219 The second-order Taylor series expansion of a function χ infinitely differentiable in \mathbf{m}_k is:

220 (12)
$$\chi(\mathbf{m}) = \chi(\mathbf{m}_k) + (\mathbf{m} - \mathbf{m}_k) * \nabla \chi(\mathbf{m}_k) + \frac{1}{2} (\mathbf{m} - \mathbf{m}_k) * \mathbf{H} * (\mathbf{m} - \mathbf{m}_k),$$

221 where $*$ denotes the matrix multiplication. The derivative with respect to \mathbf{m} is then written:

222 (13)
$$\nabla \chi(\mathbf{m}) = \nabla \chi(\mathbf{m}_k) + \mathbf{H} * (\mathbf{m} - \mathbf{m}_k).$$

223 An extremum is reached for $\nabla \chi(\mathbf{m}) = 0$. The final result is:

224 (14)
$$\mathbf{m} = \mathbf{m}_k - \mathbf{H}^{-1} \nabla \chi(\mathbf{m}_k).$$

225 And so, the numerical scheme of the L-BFGS method is defined by:

226 (15)
$$\mathbf{m}_{k+1} = \mathbf{m}_k - \mathbf{H}^{-1}(\mathbf{m}_k) \mathbf{g}(\mathbf{m}_k),$$

227 with \mathbf{H}^{-1} the inverse of the Hessian matrix:

228 (16)
$$\mathbf{H} = \begin{bmatrix} \nabla_{\kappa^2} \chi(\mathbf{m}_k) & \nabla_{\kappa} \nabla_{\rho} \chi(\mathbf{m}_k) \\ \nabla_{\rho} \nabla_{\kappa} \chi(\mathbf{m}_k) & \nabla_{\rho^2} \chi(\mathbf{m}_k) \end{bmatrix}.$$

229 Calculating the inverse of the Hessian matrix requires a large storage capacity (theoretical value,³⁵
 230 of around 600 GB in this work) and is time-consuming. To overcome these difficulties, the matrix
 231 is calculated iteratively, resulting in the calculation of a single matrix, updated at each iteration as
 232 follows:

$$233 \quad (17) \quad \mathbf{H}_k = \mathbf{H}_{k-1} + \frac{\mathbf{y}_{k-1}\mathbf{y}_{k-1}^\dagger}{\mathbf{y}_{k-1}^\dagger\mathbf{d}_{k-1}} - \frac{\mathbf{H}_{k-1}\mathbf{d}_{k-1}\mathbf{d}_{k-1}^\dagger\mathbf{H}_{k-1}}{\mathbf{d}_{k-1}^\dagger\mathbf{H}_{k-1}\mathbf{d}_{k-1}}$$

234 with $\mathbf{d}_{k-1} = \mathbf{m}_k - \mathbf{m}_{k-1}$, $\mathbf{y}_{k-1} = \mathbf{g}(\mathbf{m}_k) - \mathbf{g}(\mathbf{m}_{k-1})$.

235 Using this iterative method ensures that when an extremum is reached, it is a minimum, as it
 236 preserves the symmetry and positivity properties of a matrix. (i.e., $\chi(\mathbf{x}_0)$ is minimum of χ only if
 237 $\nabla\chi(\mathbf{x}_0) = 0$ and $\mathbf{H}[\chi(\mathbf{x}_0)]$ is a positive-definite function).

238 4.3. Discretization

239 For their numerical implementation, the above equations need to be discretized both in time and
 240 space. We resort to a velocity-stress finite-difference approximation of the wave equation, with
 241 explicit conditionally-stable time stepping in a staggered 2D Cartesian grid.³⁶ However, it is
 242 important to note that other numerical approximations could be used, for instance the spectral-
 243 element method.³⁷

244 The time and space coordinates are discretized as follows:

$$245 \quad (18) \quad \mathbf{t} = l\Delta\mathbf{t},$$

$$246 \quad (19) \quad \mathbf{x} = i\mathbf{h},$$

$$247 \quad (20) \quad \mathbf{y} = j\mathbf{h},$$

248 with $\Delta\mathbf{t}$ and h the time and space steps, respectively, and $l = 0, \dots, L - 1$, $i = 0, \dots, I - 1$, and
 249 $j = 0, \dots, J - 1$, temporal and spatial indices such as:

$$250 \quad (21) \quad \mathbf{T} = L\Delta\mathbf{t},$$

$$251 \quad (22) \quad \boldsymbol{\eta}_x = I\mathbf{h},$$

$$252 \quad (23) \quad \boldsymbol{\eta}_y = J\mathbf{h}.$$

253 In the spatial domain, the isotropic grid step h is chosen to obtain smooth, less pixelated images,
 254 according to the criterion of Bernard *et al.*,³⁴:

255 (24)
$$h \approx \frac{\lambda_{\min}}{8},$$

256 λ_{\min} being the smallest wavelength obtained at the highest frequency. In the time domain, the step
 257 Δt must respect the Courant-Friedrichs-Lewy (CFL) stability condition:

258 (25)
$$\Delta t = CFL \frac{h}{\sqrt{2}v_{\max}},$$

259 with $CFL = 0.495$ and V_{\max} the highest velocity of ultrasonic waves in the object.

260 To avoid wave reflection on the domain contours, a Perfectly Matched absorbing Layer (PML),³⁸ is
 261 considered around the simulation grid. It is used to model wave propagation in the infinite domain
 262 by means of PML coefficients, which are zero inside the physical domain and non-zero outside it,
 263 and an integer N_{PML} that is used to set the layer width (Figure 2).

264 **Figure 2: Approximately here**

265 In this discretized framework, the cost function involves a sum over the time steps instead of a time
 266 integral:

267 (26)
$$\nabla_{\rho} \mathcal{X}(\mathbf{m}) = \sum_{s=1}^S \sum_{l=0}^{L-1} \langle \mathbf{u}_x^a(l\Delta t) \partial_t \mathbf{u}_x(l\Delta t) + \mathbf{u}_y^a(l\Delta t) \partial_t \mathbf{u}_y(l\Delta t) \rangle_s,$$

268 (27)
$$\nabla_{\kappa} \mathcal{X}(\mathbf{m}) = - \sum_{s=1}^S \sum_{l=0}^{L-1} \frac{p_s^a(l\Delta t)}{\kappa(x)^2} \partial_t p_s(l\Delta t),$$

269 $p_s, p_s^a, u_x, u_x^a, u_y$ and u_y^a are obtained by simulation of the forward problem at time $l\Delta t$ and points
 270 $(\mathbf{x}, \mathbf{x}_s)$.

271 Using the trivially applied Chain Rule, the previous gradient can be expressed in terms of (ρ, v_p) ,
 272 with v_p the compression wave (ultrasonic wave) velocity (which from now on will be called US
 273 velocity). The parameters to be achieved in this study are:

274 (28)
$$\nabla_{\rho} \mathcal{X}(\rho, v_p) = \nabla_{\kappa} \mathcal{X}(\rho, \kappa) v_p^2(x) + \nabla_{\rho} \mathcal{X}(\rho, \kappa)$$

275 (29)
$$\nabla_{v_p} \mathcal{X}(\rho, v_p) = 2 \nabla_{\kappa} \mathcal{X}(\rho, \kappa) \rho(x) v_p(x)$$

276 $\nabla_{\kappa} \mathcal{X}, \nabla_{\rho} \mathcal{X}$ and v_p are respectively the bulk modulus gradient, the mass density gradient, and the US
 277 velocity map.

278 **4.4. Regularization**

279 The presence of electronic noise (or other noise, such as thermal noise) is handled adding a
 280 regularization term to the cost function. There are several types of regularization, depending on the
 281 assumptions made about the parameter to be optimized. For example, a Tikhonov-type
 282 regularization is suitable for smoothly varying signals, while a total variation (TV) regularization is
 283 suitable for rapidly varying signals. For the purposes of this project, total variation regulation has
 284 been adopted and the regulation term is formulated as follows:

$$285 \quad (30) \quad TV(\mathbf{m}) = \sum_{i=0}^{I-1} \sum_{j=0}^{J-1} \sqrt{\frac{1}{h^2} \left[\left([v_p]_{i+1,j} - [v_p]_{i,j} \right)^2 + \left([v_p]_{i,j+1} - [v_p]_{i,j} \right)^2 \right]} + \epsilon_{TV}$$

$$+ \sqrt{\frac{1}{h^2} \left[\left([\rho]_{i+1,j} - [\rho]_{i,j} \right)^2 + \left([\rho]_{i,j+1} - [\rho]_{i,j} \right)^2 \right]} + \epsilon_{TV}$$

286 with $\epsilon_{TV} = 10^{-8}$.³⁴ The formulation of the forward problem is defined as follows:

$$287 \quad (31) \quad \chi'(\mathbf{m}) = \chi(\mathbf{m}) + \beta TV(\mathbf{m})$$

288 with β a variable for adjusting the weight of the regularization term. After a number of tests, the
 289 value retained for β is 10^{-15} .³⁴

290 **4.5. Precision of the reconstruction**

291 To evaluate the precision of the reconstruction, the Normalized Root Mean Square Error (NRMSE)
 292 is computed to quantify the difference between theoretical US velocity $v_p^{th}(\mathbf{x})$ and mass density
 293 $\rho^{th}(\mathbf{x})$ maps, and estimated ones $[v_p(\mathbf{x})$ and $\rho(\mathbf{x})]$, as follows³⁹:

$$294 \quad (32) \quad NRMSE(v_p) = \sqrt{\frac{1}{IJ} \sum_{i=0}^{I-1} \sum_{j=0}^{J-1} \frac{\left([v_p^{th}]_{i,j} - [v_p]_{i,j} \right)^2}{[v_p^{th}]_{i,j}^2}},$$

$$295 \quad (33) \quad NRMSE(\rho) = \sqrt{\frac{1}{IJ} \sum_{i=0}^{I-1} \sum_{j=0}^{J-1} \frac{\left([\rho^{th}]_{i,j} - [\rho]_{i,j} \right)^2}{[\rho^{th}]_{i,j}^2}}.$$

296 5. Experimental setup and sample

297 5.1. USCT scanner

298 The mechanical ultrasound scanner used consisted of two bistatic arms articulated in the horizontal
299 plane (Figure 3). Each arm carried two transverse carriages allowing the parallel translation of the
300 transducers, for the correct adjustment of the ultrasonic beam to targets. The rotation of the target
301 holder allowed an angular scan. In this work, ($S \times R$) signals were recorded over 360° . All motions
302 were insured by stepper motors sequentially driven by a programmable translator-indexer device
303 fitted with a power multiplexer. The translator-indexer device and power multiplexer were
304 integrated in a control rack that also included other remote controls, such as the distance adjustment
305 of the arms, or the out-of-water setting system.

306 **Figure 3: Approximately here.**

307 5.2. Electro-acoustic devices

308 The transducers were UltratTM transducers with a center frequency of 648 kHz, and the 6dB-
309 bandwidth is 515 kHz (from 375 kHz to 890 kHz) (Figure 4). They were driven using a pulse-
310 receiver generator (Sofranel 5077 PR, Olympus, Waltham, MA 02453, USA). The radio-frequency
311 signals (RF-signals) were conveyed from the 12-bit oscilloscope (Lecroy HDO 6104, Teledyne Inc.,
312 Thousand Oaks, CA, USA) to a personal computer using a USB interface file transfer, and stored.
313 The signal and image processing algorithms were implemented using Matlab[®] (The MathWorks,
314 Inc., Natick, MA, USA).

315 **Figure 4: Approximately here**

316 5.3. Newborn arm phantom

317 The object studied was a phantom of a newborn baby's arm (True Phantom Solutions Inc.,
318 Windsor, Canada). This phantom, initially used for ultrasound guidance training for nurses and
319 doctors, was composed of 3 different materials representing adipose soft tissue, artificial blood
320 vessels and bone. All media were considered isotropic and homogeneous. Only compression waves
321 were propagated (no shear waves). Measurements on the phantom were taken at a distance $H = 10$
322 cm (± 0.2 cm) cm from the tip of the hand (index finger) (Figure 3). The blood vessels were made
323 of a flexible material containing a fluid that mimics blood. The bone part was made of a composite

324 material of urethane reinforced with ceramic powder. It had a mass density similar to that of human
 325 bone, but US velocity was much lower and attenuation higher. Some of the properties of these
 326 materials are presented in Table 1. Data for soft (adipose) tissue, vessels and blood were provided
 327 by the manufacturer. US velocity values in bone were determined using an interferometric
 328 method,⁴⁰ on a block-sample (10 x 10 x 2 cm) of material identical to that constituting the phantom
 329 bone. Mass densities were measured based on Archimedes' principle with a micrometric balance
 330 and a density kit (Voyager 610 GX, Ohaus Corporation, Florham Park, NJ, USA).

331 **Table 1: Approximately here.**

332 5.4. Experimental and numerical parameters

333 The positions of the transmitter and the receiver transducers ($S \times R$) described two concentric circles
 334 with identical centers of rotation, corresponding to the position of the object studied, but with
 335 different diameters (since the transducers cannot be in the same place). The following parameters
 336 correspond to those of the experiment and the numerical simulation:

- 337 • $S = 72$ sources; $R_s = 22.7$ cm
- 338 • $R = 180$ receivers; $R_r = 36.2$ cm
- 339 • CFL = 0.495
- 340 • $N_{\text{PML}} = 16$
- 341 • $h = 0.14$ mm
- 342 • $I = 5447$; $\eta_x = 2R_r + 4 = 76.4$ cm
- 343 • $J = 5447$; $\eta_y = 2R_r + 4 = 76.4$ cm

344 Adding 4 cm allows the model to fully recover the spatial domain.

- 345 • $T = 560$ μs ; $\Delta t = 50$ ns
- 346 • $V_{\text{water}} = 1467$ m/s
- 347 • $\rho_{\text{water}} = 1000$ kg/m
- 348 • $Z_{\text{water}} = 1.47$ MRayls
- 349 • In this work, $V_{\text{max}} = 1600$ m/s $>$ $V_{\text{water}} = 1467$ m/s and $V_{\text{min}} = V_{\text{bone}} = 1129$ m/s
 350 which are respectively US velocity in water and in the material composing the bone.
- 351 • $f_{\text{max}} = 1$ MHz
- 352 • $\lambda_{\text{min}} = \frac{V_{\text{min}}}{f_{\text{max}}} = 1.129$ mm

- 353 • For the incremental frequency-hopping method, the cut-off frequency of the filter was
354 increased in several steps, starting at 150 kHz, then 250 kHz, 400 kHz and finally 600 kHz.

355 5.5. High performance computing resources

356 The inversion was done at the Centre de Calcul Intensif d'Aix-Marseille (Mesocentre), using 32
357 nodes. Each 384 node was a Dell PowerEdge C6420 and contained 32 cores CPU Intel Xeon Gold
358 6142 (Sky Lake) 2.6 GHz and had 192 Gigabytes RAM. The computing was done using multiple
359 cores by dividing the spatial domain into 1024 pieces (32386 x 32) and each piece of the domain
360 was computed with one core. The computation took 12 hours for one 387 frequency, so 2 days in
361 total.

362 6. Results

363 6.1. Methodology

364 The methodology adopted for this work is as follows:

- 365 1. The reference images, which were the objective, were defined by extracting the contours
366 and binarizing the X-ray images of the object.
- 367 2. Initial maps were purely numerical, reconstructed from simulated data derived from
368 previous reference maps.
- 369 3. For reconstructions from experimental data, three tests were carried out: without any *a*
370 *priori* information on the object; by initializing the method with a mapping of *a priori*
371 values for mass density, then another for US velocity.

372 For each configuration, NRMSE were evaluated (Figure 9, Figure 12, Figure 16, Figure 20).

373 6.2. Reference images

374 The first stage of the protocol involved performing X-ray micro-computed tomography (μ CT)
375 (EasyTom XL 150 "Mechanic Ultra", RX Solutions, Chavanod, France) of the newborn arm
376 phantom (Figure 5). Full details of the protocol are presented in Doveri et al..⁵

377 **Figure 5: Approximately here**

378 From the previous X-ray image, two theoretical maps were defined for each of the two properties
379 studied in this work, US velocity, v_p , and mass density, ρ , (Figure 6). These images will be the
380 expected reference images for FWI.

381 **Figure 6: Approximately here**

382 6.3. Reconstructions from simulated data

383 In this section, data inversion was performed (Figure 7) on simulated data by solving the forward
384 problem for theoretical US velocity and mass density maps, without any initial *a priori* information
385 on the different media. Starting maps were initialized with measured values for water (i.e., $v_p =$
386 1467 m/s and $\rho = 1000$ kg/m³). Figure 8 shows the gradient of the cost function at the last iteration
387 with respect to the US velocity and the mass density.

388 **Figure 7: Approximately here**

389 **Figure 8: Approximately here**

390 **Figure 9: Approximately here**

391 6.4. Reconstruction from experimental data

392 ➤ No *a priori* information on the different media

393 In this section, data inversion was performed (Figure 10) on experimental data without any signal
394 processing, by solving the forward problem for theoretical US velocity and mass density maps,
395 without any initial *a priori* information on the different media. Starting maps were initialized with
396 measured values for water (i.e., $v_p = 1467$ m/s and $\rho = 1000$ kg/m³). Figure 11 shows the gradient
397 of the cost function at the last iteration with respect to the US velocity and the mass density.

398 **Figure 10: Approximately here**

399 **Figure 11: Approximately here**

400 **Figure 12: Approximately here**

401 ➤ *A priori* information on mass densities

402 In this section, data inversion was performed (Figure 14) on experimental data without any signal
403 processing, by solving the forward problem for theoretical US velocity and mass density maps,
404 starting from the theoretical map of mass densities (Figure 13). Starting US velocity map was

405 initialized with measured values for water (i.e., $v_p = 1467$ m/s). Figure 15 shows the gradient of the
406 cost function at the last iteration with respect to the US velocity and the mass density.

407 **Figure 13: Approximately here**

408 **Figure 14: Approximately here**

409 **Figure 15: Approximately here**

410 **Figure 16: Approximately here**

411 ➤ A priori information on US velocities

412 In this section, data inversion was performed (Figure 18) on experimental data by solving the
413 forward problem for theoretical US velocity and mass density maps, starting from the theoretical
414 US velocity map (Figure 17). Starting mass density map was initialized with measured values for
415 water (i.e., $\rho = 1000$ kg/m³). Figure 19 shows the gradient of the cost function at the last iteration
416 with respect to the US velocity and the mass density.

417 **Figure 17: Approximately here**

418 **Figure 18: Approximately here**

419 **Figure 19: Approximately here**

420 **Figure 20: Approximately here**

421 7. Discussion

422 Table 2 shows the normalized root mean square errors (NRMSE) calculated for each of the images
423 presented at the last inversion iteration.

424 **Table 2: Approximately here**

425 The error is more important on the mass density maps than on the US velocity maps. It can be
426 explained by the fact that the US velocity contrasts affect every wave (through time shifts for
427 transmitted waves and through amplitude variations for diffracted waves) while the mass density
428 contrasts only affect reflection coefficients at the interfaces. In linear USCT, this phenomenon is
429 well known, and the transfer functions linked to physical parameters such as mass density,
430 compressibility or acoustic impedance, are a function of the diffraction angle. For example, linear

431 ultrasonic impediography is reflection-mode USCT (backscatter imaging)^{3,5}. In this work, the small
 432 angles of observation (reflected waves) contain information on mass density contrasts³⁴. This can
 433 be clearly seen on the US velocity and mass density maps obtained from the inversion of simulated
 434 data (Figure 6), where the US velocity map is accurate whereas the mass density map is not,
 435 especially in the bone part. The US velocity (~1115 m/s) is closer than the theoretical velocity
 436 (1129 m/s) while the mass density (~1050 kg/m³) is half the theoretical mass density (2160 kg/m³).
 437 This can also be seen on the gradients of the cost function (Figure 8), where the gradient with
 438 respect to the mass density (b) oscillates more than the gradient with respect to the US velocity (a).

439 As explained in the theoretical section, gradient-based minimization algorithms only converge to
 440 the solution if they start close to the global minimum, i.e., provided the initial model is already of
 441 good quality. But we know that this is rarely the case. However, in this work, to improve the
 442 process, *a priori* information was used for the initial mass density map, which is easier to estimate
 443 from the numerous patient X-rays. We used a mass density starting map based on the image
 444 obtained from the binarized X-ray μ CT. Starting the inversion process with a knowledge of the
 445 mass density greatly improves the result: the contours of the bone are well defined and the US
 446 velocity is close to the theoretical velocity (~1250 m/s on the external part of the bone), and the
 447 mass density remains close to the theoretical mass density (~2000 kg/m³ in the bone part).

448 However, starting the inversion with *a priori* information on the US velocity does not help much in
 449 improving the resulting maps. As the iterations progress, the US velocity map diverges from the
 450 theoretical velocity map (the NRMSE increases on Figure 20), while the mass density map remains
 451 close to the one obtained without any *a priori* information. It seems that the inversion falls in a local
 452 minimum: the cost function remains stable after 5 iterations (Figure 20) and it stops decreasing at
 453 the last frequency (600 kHz).

454 The difficulties encountered can also arise from the object in itself, especially the material
 455 composing the bone part of the newborn arm phantom used in this work. On the one hand, this
 456 material greatly attenuates the ultrasonic wave (see Table 1), and the attenuation is not taken into
 457 account in the forward modeling during the inversion. On the other hand, the US velocity contrast
 458 between the material composing the bone and the other materials composing the phantom is
 459 negative and below 1:

460 (34)
$$\frac{V_{bone}-V_{tissues}}{V_{tissues}} = \frac{1129}{1400} - 1 \approx -0.2,$$

461 while for a real bone it would be around 1.5 for a velocity around 3500 m/s. It is difficult to know to
462 what extent this negative contrast is causing the algorithm to fail, but the inversion process remains
463 stuck in a local minimum, where the US velocity is much higher than the theoretical velocity (1129
464 m/s).

465 8. Conclusion

466 For several years now, linear ultrasound computed tomography (or, in clinical terms, B-mode
467 ultrasound) has provided qualitative images of musculoskeletal tissue in children. To go one step
468 further, and offer radiologists parametric images relating to the elastic properties of musculoskeletal
469 tissue, a (diffraction-mode) acoustical imaging method based on a full waveform inversion (FWI)
470 algorithm was introduced in this work. The full waveform inversion is an imaging method for
471 heterogeneous media that is based on full numerical modeling of wave propagation in the
472 heterogeneous medium, and on the minimization of the difference between recorded and simulated
473 waveforms based on the iterative resolution of an inverse problem for the estimation of the
474 parameters of the medium. The results presented in this work on a mimetic newborn arm phantom
475 are quite encouraging, although this object was not initially intended for ultrasonic imaging and its
476 material properties are far from those of a real newborn arm. The reconstruction error can be
477 estimated at less than 11%. However, it would be interesting to test this algorithm on other objects,
478 with more realistic acoustic properties, such as the chicken drumstick used par Doveri *et al.*⁵.
479 Future work should also involve viscoelastic materials, not only acoustic materials, because,
480 especially in the case of bone, compressional and shear wave velocities are of the same order of
481 magnitude. Then, it would be necessary to improve the forward model in order to take shear waves
482 and attenuation into account. However, this would raise some issues regarding the computational
483 cost and the interface hopping between fluid and solid media.

484 Signal acquisition and processing could also be improved. In this work, we used few positions for
485 receivers (72) and transmitters (180), and no processing of the recorded signals. More data would
486 have improved the results by increasing redundant angular information. Similarly, only one
487 frequency was used, using conventional piezoelectric transducers, whereas piezo-composite
488 technology could improve the signal-to-noise ratio by over 30 dB. In parallel, suitable signal

489 processing such as the wavelet-based coded excitation (WCE) method should further improve the
490 initial observed data.

491 When it can be made to work, full waveform inversion offers significantly improved resolution,
492 compared with simpler methods based for example on travel times only or on a linearization of
493 propagation in the object (Born approximation), at the cost of longer calculation time. But the
494 computational cost issue tends to be less limiting nowadays, thanks to the continuous increase in the
495 power of computers, easier access to high-performance computing systems, and significant progress
496 in numerical methods, all of which making it possible to apply elastic or viscoelastic full waveform
497 inversion to real seismic data,⁴¹. Moreover, the understanding of the advantages and disadvantages
498 of the method (especially with regard to the convergence problems discussed above) has increased
499 considerably in recent years.

500 9. References

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592

593 Figure 1: Schematic diagram of the Full Waveform Inversion (FWI).

594 Figure 2: Simulation range with absorbent layer.

595 Figure 3: Transmission- and diffraction-mode USCT of a mimetic newborn arm phantom.

596 Figure 4: Temporal and spectral representation of the impulse response of the transducer (65536
597 samples, $f_0 = 648$ kHz, $F_c = 20$ MHz). The dotted red curve on the temporal representation
598 represents the envelope of the signal (i.e., the modulus of the Hilbert transform).

599 Figure 5: X-ray micro-tomography of the newborn arm phantom. Size of 1840×1456 pixels² and
600 resolution of $30 \mu\text{m}$. Marks No. 1 and 2 identify bone contours, No. 3, 4 and 5 blood vessels, and
601 No. 6 adipose tissue.

602 Figure 6: Theoretical maps defined from X-ray micro-tomography of the newborn arm phantom for
603 (a) the US velocity, v_p^{th} , and (b) the mass density, ρ^{th} .

604 Figure 7: Numerical simulation of the non-linear USCT using FWI algorithm of the newborn arm
605 phantom. (a) US velocity map, (b) mass density map. No a priori information on the different
606 media. Starting maps were initialized with measured values for water (i.e., $v_p = 1467$ m/s and $\rho =$
607 1000 kg/m³).

608 Figure 8: Gradient of the cost function at the last iteration with respect to (a) the US velocity and (b)
609 the mass density, for the inversion of simulated data.

610 Figure 9: (left) NRMSE for the different cut-off frequencies of the low pass filter used during
611 inversion, as a function of the iterations, for the US velocity (in blue) and the mass density (in red);
612 (right) convergence of the algorithm, for the inversion of simulated data.

613 Figure 10: Experimental non-linear USCT using FWI algorithm of the newborn arm phantom. (a)
614 US velocity map, (b) mass density map. No a priori information on the different media: starting
615 maps were initialized with measured values for water (i.e., $v_p = 1467$ m/s and $\rho = 1000$ kg/m³)

616 Figure 11: Gradient of the cost function at the last iteration with respect to (a) the US velocity and
617 (b) the mass density, for the inversion of experimental data without any a priori information.

618 Figure 12: (left) NRMSE for the different cut-off frequencies of the low pass filter used during
619 inversion, as a function of the iterations, for the US velocity (in blue) and the mass density (in red);

620 (right) convergence of the algorithm, for the inversion of experimental data without any a priori
621 information.

622 Figure 13: Starting maps used for the first iteration of the non-linear USCT using FWI algorithm of
623 the newborn arm phantom. (a) US velocity starting map initialized with US velocity measured in
624 water ($v_p = 1467$ m/s), (b) theoretical density starting map obtained from the binarized X-ray μ CT.

625 Figure 14: Experimental non-linear USCT using FWI algorithm of the newborn arm phantom. (a)
626 US velocity map, (b) mass density map. A priori information for the mass density starting map
627 obtained from the binarized X-ray μ CT.

628 Figure 15: Gradient of the cost function at the last iteration with respect to (a) the US velocity and
629 (b) the mass density, for the inversion of experimental data with a priori information for the mass
630 density starting map obtained from the binarized X-ray μ CT.

631 Figure 16: (left) NRMSE for the different cut-off frequencies of the low pass filter used during
632 inversion, as a function of the iterations, for the US velocity (in blue) and the mass density (in red);
633 (right) convergence of the algorithm, for the inversion of experimental data with a priori
634 information for the mass density starting map obtained from the binarized X-ray μ CT.

635 Figure 17: Starting maps used for the first iteration of the non-linear USCT using FWI algorithm of
636 the newborn arm phantom. (a) theoretical US velocity starting map obtained from the binarized X-
637 ray μ CT, (b) mass density map initialized with the mass density of water ($\rho = 1000$ kg/m³)

638 Figure 18: Experimental non-linear USCT using FWI algorithm of the newborn arm phantom. (a)
639 US velocity map, (b) mass density map. A priori information for the US velocity starting map
640 obtained from the binarized X-ray μ CT.

641 Figure 19: Gradient of the cost function at the last iteration with respect to (a) the US velocity and
642 (b) the mass density, for the inversion of experimental data with a priori information for the US
643 velocity starting map obtained from the binarized X-ray μ CT.

644 Figure 20: (left) NRMSE for the different cut-off frequencies of the low pass filter used during
645 inversion, as a function of the iterations, for the US velocity (in blue) and the mass density (in red);
646 (right) convergence of the algorithm, for the inversion of experimental data with a priori
647 information for the US velocity starting map obtained from the binarized X-ray μ CT.

649

Material/Medium	Mass density, ρ^{th} [kg/m ³]	US velocity, v_p^{th} [m/s]	Acoustic impedance, Z [MRayls]	Attenuation coefficient [dB/cm]
Water (15.3°C)	1000	1467	1.47	0.011
Adipose tissue	1000	1423 ± 10	1.42	1.1 ± 0.2
Blood vessel	1020	1400 ± 10	1.43	1.7 ± 0.2
Blood	999	1400 ± 10	1.40	1.0 ± 0.2
Bone	2160	1129 ± 5	2.44	21 ± 2.0

650 Table 1: Acoustic mean properties of water and materials in the newborn arm phantom (True
651 Phantom Solutions Inc., Windsor, Canada).

	Methods	US velocity, v_p	Mass density, ρ
1	Simulated data (no <i>a priori</i> information)	2.2%	10.6%
2	Experimental data (no <i>a priori</i> information)	7%	11.2%
3	Experimental data (<i>a priori</i> mass density map)	6.6%	7.7%
4	Experimental data (<i>a priori</i> US velocity map)	6.8%	10.4%

652 Table 2: Summary of the normalized root mean square errors (NRMSE) calculated for each of the
653 images presented at the last iteration.

654

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