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# Reflection Matrix Imaging for Wave Velocity Tomography

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## Abstract

Besides controlling wave trajectory inside complex media, wave velocity constitutes a relevant bio-marker for medical imaging and a crucial monitoring parameter for non-destructive testing. In a transmission configuration, wave-front distortions can be unscrambled to provide a map of the wave velocity landscape  $c(\mathbf{r})$ . However, most in-vivo or in-situ applications correspond to a reflection configuration for which only back-scattered echoes generated by short-scale fluctuations of  $c(\mathbf{r})$  can be harvested. Under a single scattering assumption, this speckle wave-field cannot provide the long-scale variations of  $c(\mathbf{r})$ . In this paper, we go beyond the first Born approximation and show how a map of  $c(\mathbf{r})$  can be retrieved in epi-detection. To that aim, a reflection matrix approach of wave imaging is adopted. While standard reflection imaging methods generally rely on confocal focusing operations, matrix imaging consists in decoupling the location of the incident and received focal spots. Following this principle, a self-portrait of the focusing process can be obtained around each point of the medium. The Gouy phase shift exhibited by each focal spot is leveraged to finely monitor the wave velocity distribution  $c(\mathbf{r})$  inside the medium. Experiment in a tissue-mimicking phantom and numerical simulations are first presented to validate our method. Speed-of-sound tomography is then applied to ultrasound data collected on the liver of a difficult-to-image patient. Beyond paving the way towards quantitative ultrasound, our approach can also be extremely rewarding for standard imaging. Indeed, each echo can be assigned to the actual position of a scatterer. It allows an absolute measurement of distance, an observable often used for diagnosis but generally extremely sensitive to wave velocity fluctuations.

In wave imaging, we aim at characterizing an unknown environment by actively probing it and then recording the waves scattered by the medium. On the one hand, long-scale heterogeneities can induce wave-front distortions that are generally exploited in a transmission configuration to retrieve the wave velocity distribution inside the medium. This is the principle of diffraction tomography, whether it be for light<sup>1</sup>, ultrasound<sup>2</sup>, or seismic waves<sup>3</sup>. Yet, for most in-vivo or in-situ applications, we only have access to the measurement of the wave-field in reflection. In an epi-detection configuration, an image of the medium reflectivity can be generated from the echoes back-scattered by the short-scale heterogeneities of the medium. This is, for instance, the principle of optical coherence tomography, ultrasound imaging or reflection seismology. Nevertheless, the produced image is qualitative and only provides a small fraction of the spatial frequency spectrum of the object<sup>4</sup>. To go beyond and have access to the long-scale fluctuations of the wave velocity, one has to go beyond the Born approximation and exploit multiple scattering. In that perspective, full wave-form inversion<sup>5</sup>, nonlinear image reconstruction methods<sup>6,7</sup> and learning-based approaches<sup>8,9</sup> have been developed with success. However, such mathematical approaches are extremely tedious and computationally expensive.

In this paper, we will take a more physical route towards wave velocity tomography by considering a reflection matrix approach of wave imaging<sup>10-12</sup>. Standard reflection imaging methods generally rely on a confocal focusing operation on each point of the medium to extract the local medium reflectivity. On the contrary, matrix imaging consists in decoupling the location of these transmitted and received focal spots<sup>13</sup>. This process yields a focused reflection matrix that contains the responses between virtual transducers synthesized directly in the medium from the transmitted and received focal spots. The reflection matrix holds much more information on the medium than a conventional image. For instance, we can probe the focusing quality<sup>13,14</sup> and the wave distortions<sup>15,16</sup> undergone by the incident and reflected waves upstream of the focal plane. Wave distortions are the result of the mismatch between the real wave velocity distribution  $c(\mathbf{r})$  and the wave velocity model  $c_0$  used to generate the reflectivity image. Previous works have shown how a minimization of those wave distortions<sup>17-19</sup> or, even better, their inversion<sup>20-22</sup> can lead to a mapping of the wave velocity.

In this paper, an alternative strategy is followed. The focused reflection matrix is first parameterized by the wave velocity model  $c_0$  used in the beamforming process. Then this



matrix is recast into a de-scanned basis with a first dimension stacking image pixels and a second dimension along which the relative position of virtual transducers and the wave velocity model  $c_0$  are concatenated. A singular value decomposition of this de-scanned reflection matrix is shown to provide a self-portrait of the focusing process around each point of the medium. In particular, the Gouy phase shift<sup>23</sup> exhibited by each focal spot allows us to finely monitor the speed-of-sound distribution inside the medium. By optimizing this process for each point of the medium, one can retrieve an estimator of the wave velocity distribution averaged between this point and the probe. A numerical differentiation of the corresponding slowness can then provide a mapping of the local wave velocity  $c(\mathbf{r})$ .

To validate our approach, we will first consider a tissue-mimicking phantom to show how the focusing process can be monitored using random speckle. Then, we validate and outline the limits of our method by considering numerical experiments in synthetic samples in which the speed-of-sound distribution is known. Then, to demonstrate its potential for medical imaging, we will apply it to speed-of-sound measurement in the liver for a difficult-to-image patient. A quantitative measurement of the speed-of-sound in liver is particularly important for the early detection of liver disease, such as hepatic steatosis<sup>18</sup>. This disease consists in an accumulation of fat droplets that results in a low speed-of-sound ( $c \sim 1480 \text{ m.s}^{-1}$ ) compared to its usual value in liver ( $c \sim 1600 \text{ m.s}^{-1}$ ). The effectiveness of ultrasound for diagnosing hepatic steatosis is reduced in obese patients<sup>24</sup>. Indeed, because the ultrasonic waves must travel through successive layers of skin, fat, and muscle tissue before reaching the liver, both the incident and reflected wave-fronts undergo strong aberrations<sup>25,26</sup> and multiple scattering (clutter noise)<sup>27</sup>. The estimation of the speed-of-sound in liver is thus particularly difficult for such patients. Despite an ultrasound image degraded by scattering, our matrix approach will reveal coherent variations of the speed-of-sound across fat, muscles and liver. A particularly low value will be found for the sound speed in liver, which is in agreement with the steatosis diagnosis.

Beyond providing a new contrast to ultrasound imaging, the knowledge of the speed-of-sound is also extremely rewarding for the standard ultrasound image. The reassignment of each scatterer to its true depth allows a direct compensation of axial distortions on the ultrasound image and a clear gain of its contrast. The absolute measurement of distances is also possible since the axial dimension of the ultrasound is no longer dictated by the echo time but rescaled as a function of depth<sup>28</sup>. This rescaling is anything but trivial, since

numerous diagnosis protocols are based on distance measurement<sup>29</sup>. In the last part of the paper, we will discuss the merits and limits of our approach compared with state-of-the-art methods<sup>9,18–20,22,30</sup>. The potential extension of our approach to other fields of wave physics will also be discussed.

## RESULTS

### Reflection matrix acquisition

Ultrasound matrix imaging (UMI) begins with the acquisition of the reflection matrix using an ultrasound array of transducers (Figs. 1A,B and Methods). The first sample under study is a tissue mimicking phantom with a speed-of-sound  $c = 1542 \pm 10$  m/s (Fig. 1C). It is composed of a random distribution of unresolved scatterers which generate an ultrasonic speckle characteristic of human tissue (Fig. 1D). The reflection matrix is captured by sending a series of plane waves into the medium (Methods). Each plane wave is identified with its angle of incidence  $\theta_{\text{in}}$  (Fig. 1A). For each illumination, the reflected waves are recorded by the transducers of the probe, each element being identified by its lateral position  $u_{\text{out}}$  (Fig. 1B). The recorded wave-fronts are noted  $R(u_{\text{out}}, \theta_{\text{in}}, t)$ , with  $t$  the echo time. They are stored in a reflection matrix  $\mathbf{R}_{\mathbf{u}\theta}(t) = [R(u_{\text{out}}, \theta_{\text{in}}, t)]$ .

### Confocal imaging

The first post-processing step is to build a confocal image  $\mathcal{I}$  from the recorded reflection matrix. To do so, a delay-and-sum beamforming process is applied to the coefficients of  $\mathbf{R}_{\mathbf{u}\theta}(t)$ . Physically equivalent to a confocal focusing process (Fig. 1B), this procedure writes mathematically as follows:

$$\mathcal{I}(x, z_0 = c_0 t / 2) = \sum_{\theta_{\text{in}}} \sum_{u_{\text{out}}} A(u_{\text{out}}, \theta_{\text{in}}, x, t, c_0) \quad (1)$$

$$R(u_{\text{out}}, \theta_{\text{in}}, \tau_{\text{out}}(u_{\text{out}}, x, t, c_0) + \tau_{\text{in}}(\theta_{\text{in}}, x, t, c_0)).$$

$c_0$  is the wave velocity model considered in the beamforming process.  $\tau_{\text{in}}$  is the time-of-flight expected for the incident plane wave to reach the target point of coordinates  $(x, z_0)$ .  $\tau_{\text{out}}$  is the time-of-flight expected for the reflected wave to travel from the same target point to

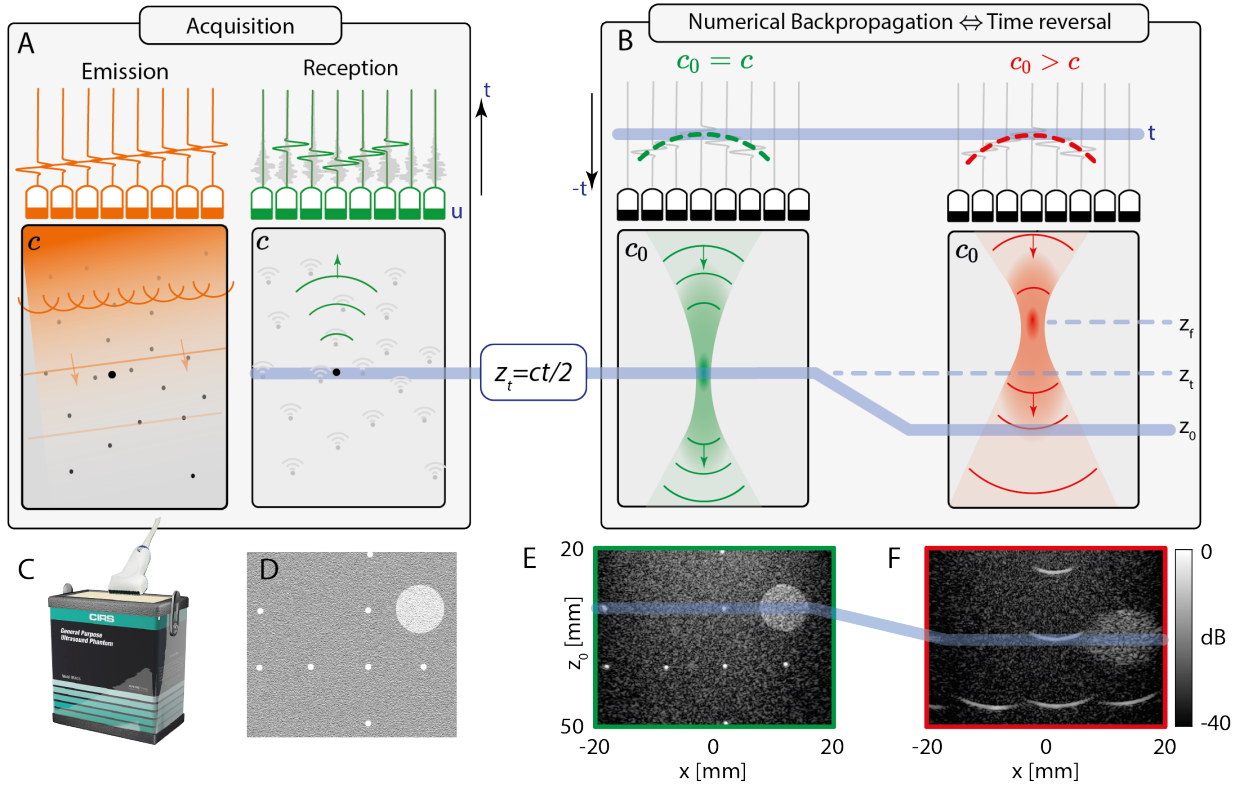


FIG. 1. **Impact of an incorrect speed-of-sound model in ultrasound imaging.** (A) The acquisition of the reflection matrix consists in insonifying the medium with a set of plane waves emitted by the ultrasonic probe. The recorded wave-fronts are stored in the reflection matrix. The contribution of one scatterer located at depth  $z_t$  is highlighted in green. For sake of simplicity, the wave velocity  $c$  is considered as homogeneous. (B) The numerical focusing process can be seen as a fictive time reversal experiment in a medium of wave velocity  $c_0$ . If  $c_0 = c$ , the time-reversed wave-front back-focuses exactly at the initial scatterer location. If  $c_0 \neq c$ , a mismatch exists between the focusing plane ( $z_f = cz_t/c_0$ ), the isochronous plane ( $z_t = ct/2$ ) and the imaging plane ( $z_0 = c_0t/2$ ). (C) Experimental configuration: A linear array of transducers is placed on top of an ultrasound phantom. (D) Scheme of the phantom with nylon rods (white), random distribution of unresolved scatterers (gray) and a more echogene cylinder displaying a stronger concentration of scatterers (light gray). (E, F) Corresponding ultrasound image for  $c = c_0 = 1540 \text{ m.s}^{-1}$  and  $c \neq c_0 = 1800 \text{ m.s}^{-1}$ , respectively.

each transducer.  $A$  is a normalization and apodization factor that limits the extent of the receive synthetic aperture.  $z_0 = c_0t/2$  is the expected position of the isochronous volume, which is defined as the ensemble of points that contribute to the ultrasound signal at time

$t$ . If the wave velocity model is correct ( $c_0 = c$ ),  $z_0$  is a relevant estimator of the scatterers' depth and the ultrasound image is a satisfactory image of the medium reflectivity (Fig. 1E). On the contrary, if the wave velocity model is incorrect ( $c_0 \neq c$ ), each detected scatterer at depth  $z_t = ct/2$  is assigned to a false depth  $z_0$  (Fig. 1F):  $z_0 = (c/c_0)z_t$ . Moreover, the beamformed image is drastically affected by the mismatch between the isochronous volume at  $z_t$  and the focusing plane at  $z_f$  (Fig. 1B) since  $z_f = (c/c_0)z_t$  (SI Appendix, Section S2). This non-coincidence result in axial aberrations on the ultrasound image (Fig. 1F) that manifest as: (i) an axial shift of the scatterers with respect to their true depth; (ii) a degradation of the transverse resolution. The search for the optimum speed-of-sound  $c$  for a particular point therefore consists of bringing the imaging plane into coincidence with the focal plane<sup>31</sup>. If such an optimization seems trivial when considering a bright spot, the goal is now to develop a method to find this value in random speckle. Indeed, the speckle statistics seems unaffected by the wave velocity used in the beamforming process (Figs. 1E and F).

### Focused reflection matrix

UMI can provide a solution to this fundamental issue. The focusing quality can be assessed locally in the ultrasound speckle by projecting the reflection matrix in a focused basis<sup>13</sup>. In the time domain, this operation can be performed by decoupling the input and output focal spots in the beamforming process<sup>16</sup>:

$$R(x_{\text{out}}, x_{\text{in}}, t, c_0) = \sum_{\theta_{\text{in}}} \sum_{u_{\text{out}}} A(u_{\text{out}}, \theta_{\text{in}}, x_{\text{out}}, t, c_0) \quad (2)$$

$$R(u_{\text{out}}, \theta_{\text{in}}, \tau_{\text{out}}(u_{\text{out}}, x_{\text{out}}, t, c_0) + \tau_{\text{in}}(\theta_{\text{in}}, x_{\text{in}}, t, c_0)),$$

At each echo time  $t$ , the focused reflection matrix  $\mathbf{R}_{xx}(t, c_0)$  contains the response  $R(x_{\text{out}}, x_{\text{in}}, t, c_0)$  between virtual transducers at  $\mathbf{r}_{\text{in}} = (x_{\text{in}}, t)$  and  $\mathbf{r}_{\text{out}} = (x_{\text{out}}, t)$  (Fig. 2A) whose axial positions corresponds to the depth  $z_t$  of the isochronous volume and thus dictated by the time-of-flight  $t$ . The diagonal elements of each matrix  $\mathbf{R}_{xx}(t, c_0)$  considered at the ballistic time  $t = 2z_0/c_0$  directly correspond to the confocal image that we previously introduced. However,  $\mathbf{R}_{xx}(t, c_0)$  contains much more information than the confocal image: The spreading of energy over its off-diagonal elements is an indicator of the focusing quality in speckle by probing the cross-talk between distinct virtual transducers<sup>13,14</sup>.

### De-scan reflection matrix

To investigate this cross-talk, the focused reflection matrix can be expressed in a de-scanned frame (SI Appendix, Figure S1). Mathematically, it consists in re-arranging the ultrasound data using the following change of variables:

$$R_D(\mathbf{\Delta}, \mathbf{r}_{\text{in}}) = R(x_{\text{out}}, x_{\text{in}}, t, c_0) \quad (3)$$

with  $\mathbf{\Delta} = (\Delta x, c_0)$  and  $\Delta x = x_{\text{out}} - x_{\text{in}}$ , the relative lateral distance between virtual transducers. Each column of the resulting de-scan matrix  $\mathbf{R}_D$  shows the reflected wave-field in the imaging plane re-centered around each input focusing point  $\mathbf{r}_{\text{in}}$ . We will refer to this quantity as the reflection point spread function (RPSF)<sup>13</sup>. Each RPSF is identified by its transverse position  $x_{\text{in}}$  and echo time  $t$ . The lateral extension  $\Delta x$  of the RPSF is investigated as a function of the wave velocity model  $c_0$ .

Figure 2B shows three realizations of RPSFs obtained for different speckle grains  $\mathbf{r}_{\text{in}}$  displayed in Figure 2C. These RPSFs display a focal spot whose spatial extension is minimized for  $c = c_0$ . However, each RPSF is modulated by the random reflectivity of the sample. To get rid of this problem, the solution is to perform a local average of the focal spots in order to unscramble the effect of wave propagation from the sample reflectivity. To that aim, the field of view shall be truncated into overlapping spatial windows  $\mathcal{P}(\mathbf{r}_{\text{in}} - \mathbf{r}_p)$  defined by their center  $\mathbf{r}_p$  and their spatio-temporal extent  $\mathbf{p} = (p_x, p_t)$ , where  $p_x$  and  $p_t$  denote the lateral and axial extent of each window, respectively. A local reflection matrix  $\mathbf{R}_L(\mathbf{r}_p)$  can then be defined for each point  $\mathbf{r}_p = (x_p, t_p)$  in the field-of-view. Its coefficients write

$$R_L(\mathbf{\Delta}, \mathbf{r}, \mathbf{r}_p) = R_D(\mathbf{\Delta}, \mathbf{r})\mathcal{P}(\mathbf{r} - \mathbf{r}_p), \quad (4)$$

with  $\mathcal{P}(\mathbf{r} - \mathbf{r}_p) = 1$  for  $|x - x_p| < p_x/2$  and  $|t - t_p| < p_t/2$ , and zero otherwise.

### Incoherent Reflection Point Spread Function

The most direct way for probing the focusing quality is to perform a local and incoherent average of each RPSF:

$$RPSF_{\text{inc}}(\mathbf{\Delta}, \mathbf{r}_p) = \sqrt{\langle |R_L(\mathbf{\Delta}, \mathbf{r}, \mathbf{r}_p)|^2 \rangle_{\mathbf{r}}}, \quad (5)$$

where  $\langle \dots \rangle$  denotes a spatial average over the different speckle grains  $\mathbf{r}$ . The result is displayed in Figure 2D for the area  $\mathcal{P}$  indicated in Fig. 2B. As expected, spatial averaging tends to smooth out reflectivity fluctuations. More quantitatively, its intensity provides, in the speckle regime, an estimation of the auto-convolution of the transmit and receive PSFs,  $h_{\text{in}}$  and  $h_{\text{out}}$ , respectively<sup>13</sup> (see SI Appendix, Section S4):

$$RPSF_{\text{inc}}^2(\Delta x, c_0, \mathbf{r}_p) \propto |h_{\text{in}}|^2 \overset{\Delta x}{\otimes} |h_{\text{out}}|^2(\Delta x, c_0, \mathbf{r}_p). \quad (6)$$

A direct estimation of the speed-of-sound can be obtained by considering the value of  $c_0$  that maximizes the amplitude of this incoherent RPSF (black line in Fig. 2H):

$$\hat{c}_{\text{inc}}(\mathbf{r}_p) = \underset{\Delta}{\text{argmax}} (RPSF_{\text{inc}}(\Delta, \mathbf{r}_p)). \quad (7)$$

The estimated speed-of-sound is  $\hat{c}_{\text{inc}} = 1543$  m/s, which is within the uncertainty margin provided by the manufacturer. Nevertheless, the incoherent RPSF also displays a strong background induced by multiple scattering events that can hamper the estimation of the speed-of-sound in more complex situations. Under a Gaussian beam approximation, the uncertainty of this measurement can actually be expressed as follows (SI Appendix, Section S8):

$$\delta c_{\text{inc}} = \frac{2}{\sqrt{3}} \frac{1}{\beta^{1/2} N_{\mathcal{P}}^{1/4}} \frac{z_R}{t} \quad (8)$$

with  $\beta$ , the signal-to-noise ratio,  $z_R \sim 2\lambda/NA^2$ , the depth-of-field (or Rayleigh range),  $NA$ , the numerical aperture and  $N_{\mathcal{P}}$ , the number of independent speckle grains in each area  $\mathcal{P}$ . This last equation points out the main parameters that control the error of our wave speed estimator. Not surprisingly,  $\delta c_{\text{inc}}$  is directly impacted by the signal-to-noise ratio and decreases as  $\beta^{-1/2}$ . An inverse scaling is observed with the time-of-flight  $t$ , which reflects the fact that the precision on the speed-of-sound measurement improves with the travel path length. Interestingly, the linear dependence of  $\delta c_{\text{inc}}$  with  $z_R$  implies a sharper measurement at high numerical aperture (SI Appendix, Figure S3). Through the scaling of  $\delta c_{\text{inc}}$  as  $N_{\mathcal{P}}^{-1/4}$ , Eq. 8 also highlights the compromise we will have to make further for wave velocity tomography. On the one hand, each patch  $\mathcal{P}$  should encompass a sufficient number of resolution cells in order to reduce the bias of the speed-of-sound estimator. On the other hand, the size of each patch will control the spatial resolution of the sound speed map.

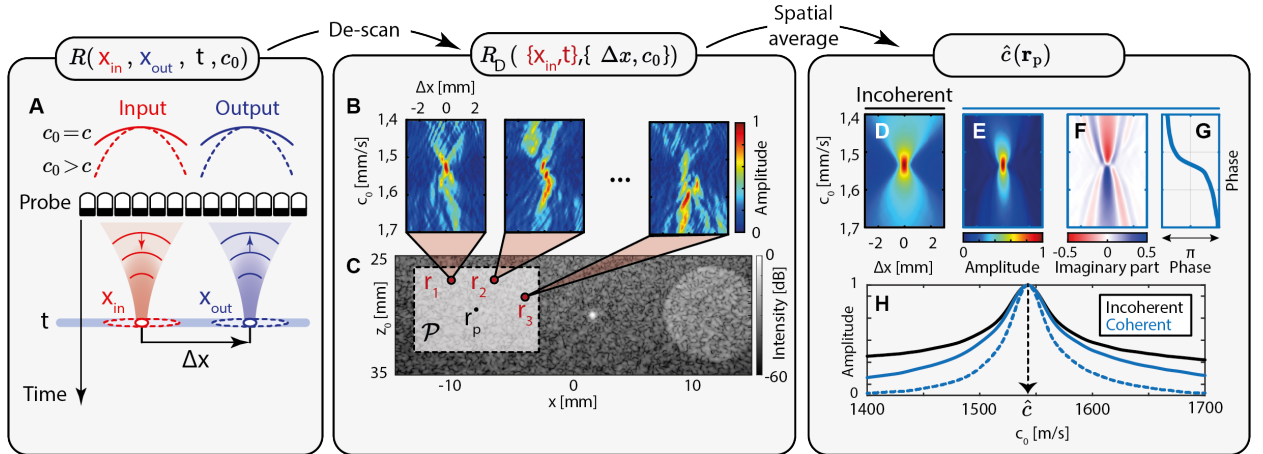


FIG. 2. **Self-portrait of the focusing process.** (A) Matrix imaging consists in splitting the input and the output focusing points during the beamforming process. The focused reflection matrix allows the monitoring of the focusing process with respect to the wave velocity model  $c_0$ . (B) Such a matrix can be expressed in a de-scanned basis in order to provide the dependence of the RPSF shown here in amplitude for three speckle spots of the ultrasound image. (C) The three speckle grains considered in panel B and the area  $\mathcal{P}$  considered for the local averaging of the RPSF in panels D-H are superimposed to the ultrasound image of the phantom. (D) Incoherent RPSF. (E) Amplitude of the coherent RPSF. (F) Imaginary part of the coherent RPSF. (G) Phase of the coherent RPSF as a function of  $c_0$  at  $\Delta x = 0$ . (H) Magnitude of the incoherent RPSF (black line), of the coherent RPSF (blue line) and its real part (dashed blue) as a function of  $c_0$  at  $\Delta x = 0$ . Spatial averaging is here performed with a window of size  $(p_x, p_t) = (10 \text{ mm}, 1.3 \mu\text{s})$  centered around  $(x, t) = (0 \text{ mm}, 43 \mu\text{s})$ .

### Revealing the coherent wave

To reduce the uncertainty, a coherent RPSF can be extracted through a singular value decomposition of the local matrix  $\mathbf{R}_L(\mathbf{r}_p)$ :

$$\mathbf{R}_L(\mathbf{r}_p) = \mathbf{U} \times \mathbf{\Sigma} \times \mathbf{V}^\dagger \quad (9)$$

where  $\mathbf{\Sigma}$  is a diagonal matrix containing the singular values  $\sigma_i$  in descending order:  $\sigma_1 > \sigma_2 > \dots > \sigma_N$ .  $\mathbf{U}$  and  $\mathbf{V}$  are unitary matrices that contain the orthonormal set of eigenvectors,  $\mathbf{U}_i = [U_i(\Delta x, c_0)]$  and  $\mathbf{V}_i = [V_i(\mathbf{r})]$ . In first approximation, the de-scanned matrix is of rank 1 (SI Appendix, Section S5). The first singular vector  $\mathbf{U}_1$ , directly provides a coherent RPSF,

which is a direct estimator of the output PSF weighted by the confocal value of the input PSF (SI Appendix, Section S5):

$$RPSF_{\text{coh}}(\Delta x, c_0, \mathbf{r}_p) \propto h_{\text{in}}(0, c_0, \mathbf{r}_p)h_{\text{out}}(\Delta x, c_0, \mathbf{r}_p). \quad (10)$$

The amplitude of the coherent RPSF obtained in the ultrasound phantom is displayed in Fig. 2E for the area  $\mathcal{P}$  indicated in Fig. 2B. Compared to its incoherent counterpart (Fig. 2D), the multiple scattering background has been reduced, which provides a more contrasted view of the focusing quality in the phantom (Fig. 2H). A novel estimation of the speed-of-sound can be performed by probing its maximum value (blue curve in Fig. 2H):

$$\hat{c}_{\text{coh}}(\mathbf{r}_p) = \underset{\Delta}{\operatorname{argmax}} (|RPSF_{\text{coh}}(\Delta, \mathbf{r}_p)|); \quad (11)$$

The uncertainty  $\delta c_{\text{coh}}$  of such a measurement is slightly better than its incoherent counterpart (Eq. 8) since  $\delta c_{\text{coh}} = 2\delta c_{\text{inc}}/\sqrt{3}$  (see SI Appendix, Section S8).

### Exploiting the Gouy phase

Interestingly, the uncertainty of Eq. 8 can be again reduced by leveraging the phase of the coherent RPSF (Fig. 2F). A phase jump is actually observed in the vicinity of the optimal wave speed (Fig. 2G). This feature is equivalent to the Gouy phase shift  $\phi_G$  generally exhibited by a focused wave in the focal plane<sup>23</sup>. The originality of our observation here is that it occurs when the model speed-of-sound coincides with the sound velocity of the phantom. While  $\phi_g$  should be of  $\pi/2$  in a 2D configuration, the phase of the coherent RPSF (Fig. 2G) shows a shift of  $2\phi_g = \pi$  due to the confocal nature of the measured RPSF (Eq. 10). The origin of the Gouy phase shift originates from the transverse spatial confinement of the wave-field and can be thus a relevant observable for speed-of-sound estimation.

The information carried by the phase of the coherent RPSF can be exploited by considering the real part of the coherent RPSF,  $\mathcal{R}[RPSF_{\text{coh}}]$ . The maximization of this quantity leads to a new estimator  $\hat{c}_{\text{gouy}}$  of the sound speed:

$$\hat{c}_{\text{gouy}}(\mathbf{r}_p) = \underset{\Delta}{\operatorname{argmax}} (\mathcal{R}[RPSF_{\text{coh}}(\Delta, \mathbf{r}_p)]). \quad (12)$$

$\hat{c}_{\text{gouy}}$  actually exploits the amplitude enhancement and the phase jump of the RPSF to provide a sharper estimation of the speed-of-sound by almost a factor 3 with respect to  $\hat{c}_{\text{inc}}$



(SI Appendix, Section S8):  $\delta c_{\text{gouy}} = \delta c_{\text{coh}}/\sqrt{5}$ . This better precision is highlighted by the steeper peak centered around  $\hat{c}_{\text{gouy}} = 1542.5$  m/s exhibited by the real part of the RPSF in Fig. 2H.

### Local speed-of-sound

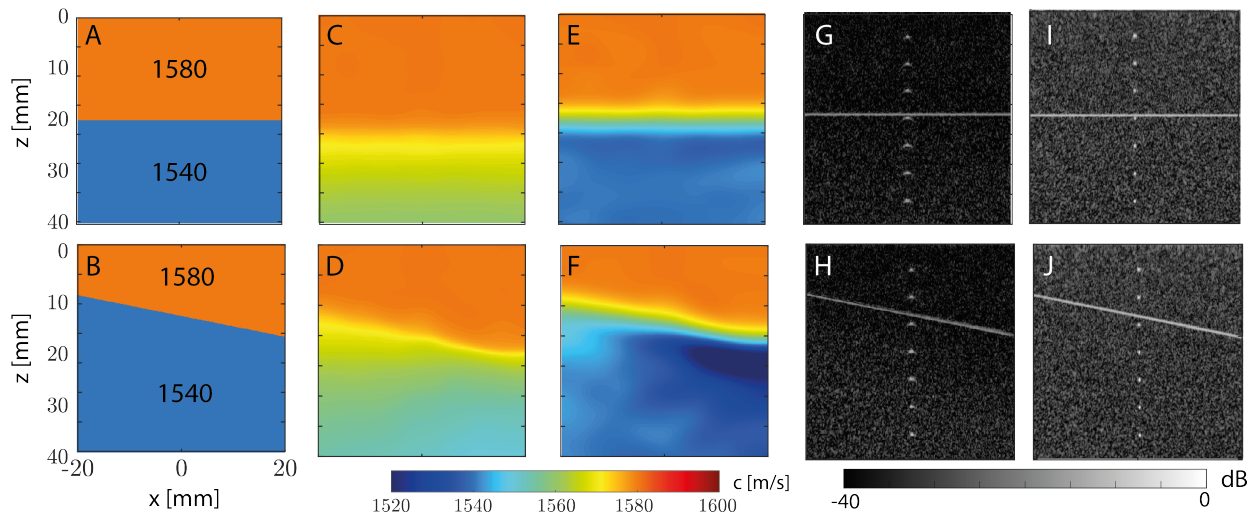


FIG. 3. **Numerical validation of the speed-of-sound tomography in reflection.** (A, B) Simulated speed-of-sound distributions  $c(\mathbf{r})$ . (C, D) Optimized wave velocity  $\hat{c}(\mathbf{r})$ . (E, F) Estimation of the local speed-of-sound map  $c(\mathbf{r})$  with each pixel reassigned to its estimated position. (G, H) Original ultrasound image. (I, J) Corrected image with each pixel reassigned to its estimated position.

To extend and validate our approach for a heterogeneous sound speed distribution, multi-static synthetic aperture datasets have been computed with k-Wave<sup>32</sup> (Methods), a time domain simulation software based on the k-space pseudo-spectral method. The considered speed-of-sound distributions are layered media with parallel (Fig. 3A) and oblique interfaces (Fig. 3B) with respect to the ultrasonic probe. Short-scale fluctuations of density have been superimposed to generate a random speckle characteristic of ultrasound imaging in soft tissues. A set of point-like targets is also included to quantify the spatial resolution at different locations.

Ultrasound images (Eq. 1) are computed from the corresponding reflection matrices by considering a homogeneous wave velocity model  $c_0 = 1540$  m.s<sup>-1</sup> corresponding to the

speed-of-sound in the second layer. The result is displayed in Figs. 3G and H. As expected, the mismatch between  $c(x, z)$  and  $c_0$  results in a shift of the interface and target locations with respect to their true position. The images of the bright targets also shows the impact of an inexact wave velocity model on the spatial resolution, with bright point-like scatterers appearing as curved arches.

On the contrary, as already shown with the phantom experiment, the wrong velocity model has not a clear impact on the speckle grain size. Nevertheless, a coherent RPSF can be determined for each speckle grain  $\mathbf{r}_{\text{in}} = (x_{\text{in}}, t)$  by computing the SVD of the de-scanned matrix (Eqs. 9 and 10) over sliding spatial windows  $\mathcal{P}$  (Methods). An optimized wave velocity  $\hat{c}(x, t)$  is determined for each spatio-temporal point  $(x, t)$  by maximizing the corresponding RPSF. The resulting maps  $\hat{c}(x, z_t)$  are displayed in Figs. 3C and D for each configuration. They are far from the ground truth distributions displayed in Figs. 3A and B. Indeed, the optimized wave velocity is not an estimator for the local speed-of-sound but for the inverse of the mean slowness  $\bar{s}(x, t)$ , averaged between the probe surface and the focusing point  $(x, t)$ :

$$\bar{s}(x, t) = \frac{1}{z_t(x)} \int_0^{z_t(x)} \frac{dz}{c(x, z)}. \quad (13)$$

with  $z_t(x) = \hat{c}(x, t)t/2$ , the depth of the isochronous volume for each echo time  $t$  and lateral position  $x$ . Equation 13 is extremely simplified since it only takes into account vertical paths, thereby neglecting refraction phenomena.

Nevertheless, a numerical inversion of Eq. 13 can be performed to retrieve an estimator of the local speed-of-sound  $c(x, z)$  from  $\hat{c}(x, t)$ <sup>33</sup> (Methods). The resulting speed-of-sound maps are displayed in Figs. 3E and F. They show a close agreement with their ground-truth counterparts (Figs. 3A and B). Not surprisingly, the lateral invariance of the first configuration makes the estimation of  $c(x, z)$  reliable, with a mean error  $\delta c$  in the tissue layer of the order of 10 m.s<sup>-1</sup>. The axial resolution  $\delta z$  can be estimated by investigating the axial dependence of  $c(x, z)$ . In the present case, we find  $\delta z \sim 5$  mm.

Strikingly, our approach remains robust even for an oblique interface between the muscle and tissues behind. The estimated speed-of-sound distribution  $c(x, z)$  (Fig. 3F) is actually in good agreement with the ground truth distribution (Fig. 3B). Nevertheless, more important fluctuations of the speed-of-sound are observed right after the interface. However, beyond  $z = 25$  mm, the mean error  $\delta c$  in the deep tissue layer remains relatively weak ( $\delta c \sim 10$  m/s).

Beyond mapping the wave velocity, our approach also allows a direct compensation of

axial aberrations in the ultrasound images. Indeed, the isochronous volume and each focal plane can be matched by reassigning to each point  $(x, z)$  of the medium a correct echo time based on our estimation of the depth-averaged slowness, such that

$$\mathcal{I}'(x, z) = R(x, x, t = 2z/\hat{c}(x, z), \hat{c}(x, z)) \quad (14)$$

Contrary to the original ultrasound image whose axial dimension was dictated by the echo time and wave velocity assumption  $c_0$ , this new ultrasound image displays the medium as a function of the real depth  $z$ . Moreover, the use of the depth-averaged velocity enables the compensation of defocus. The resulting images are shown in Figs. 3I and J for the numerical experiments described above. Compared to their original versions (Figs. 3G and H), those two images show several striking improvements: *(i)* A drastic contrast enhancement by +6 dB; *(ii)* A drastic gain in transverse resolution highlighted by the images of the bright targets especially at shallow depths. After this numerical validation, the application of the method to a clinical case is presented.

### **Study of a pathological clinical case**

To show the advantages of our method for medical diagnosis, a pathological case is addressed and concerns liver imaging. More precisely, we target a patient liver, which is difficult to image due to an irregular arrangement of adipose and muscle tissues upstream of the liver. As this patient is potentially suffering from steatosis, the measurement of the liver speed-of-sound is critical for diagnosis purpose<sup>18</sup>. Indeed, this disease corresponds to an accumulation of fat droplets in the liver that induces a low speed-of-sound and enhanced scattering. While this disease can manifest as a bright speckle<sup>34,35</sup>, this observable is only qualitative and operator-dependent. The effectiveness of ultrasound for diagnosing hepatic steatosis is reduced in obese patients<sup>24</sup>. Indeed, because the ultrasonic waves must travel through successive layers of skin, fat, and muscle tissue before reaching the liver, both the incident and reflected wave-fronts undergo strong aberrations<sup>25,26</sup> and multiple scattering (clutter noise)<sup>27</sup>. The estimation of the speed-of-sound in liver is thus particularly difficult for such patients. Hence, there is a strong need for a quantitative mapping of the liver speed-of-sound for the early detection of such a disease.

The experimental configuration is described in the Methods section, but the main particu-

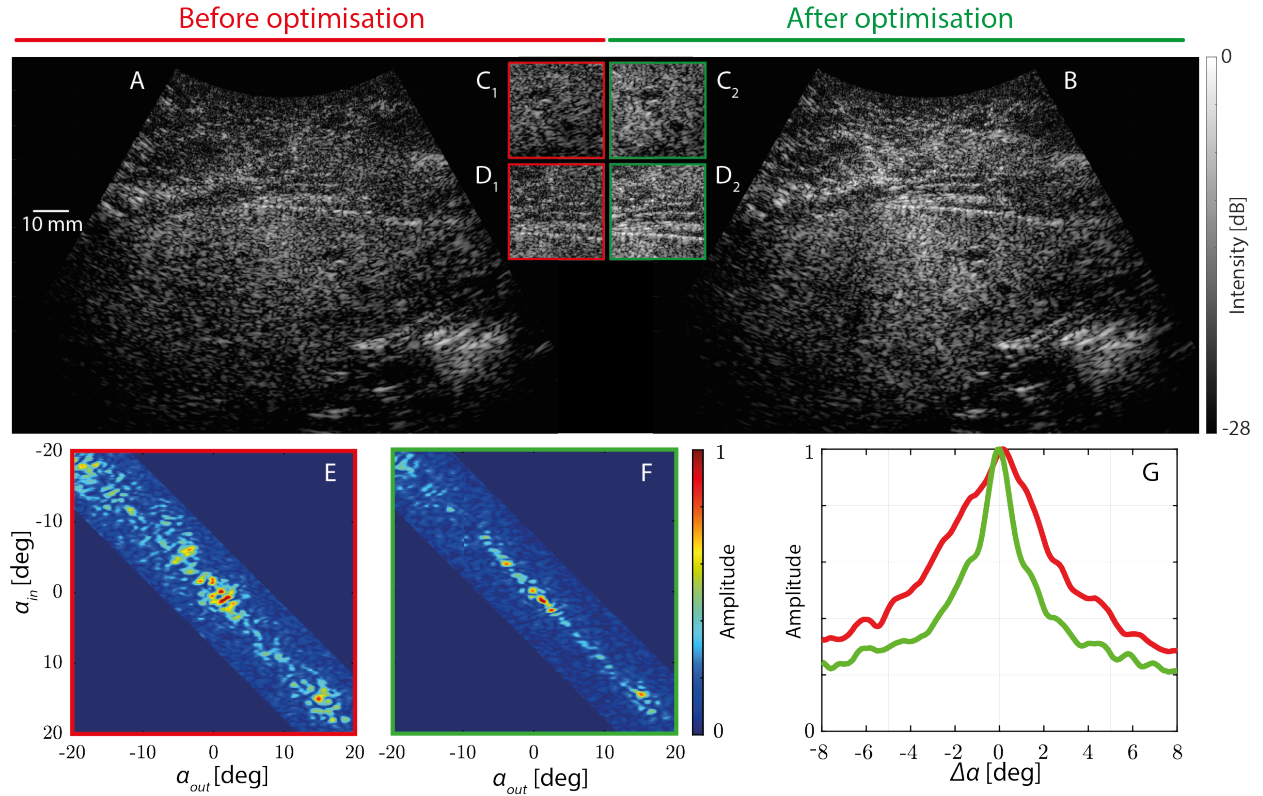


FIG. 4. **Speed of sound optimization in the liver experiment.** (A, B) Original and optimized ultrasound images, respectively. Both images are normalized by the global maximum between the two images and are displayed along the same depth axis, which is estimated with a constant speed of sound ( $c_0 = 1540$  m/s). (b, c) Zoom on specific areas of the field-of-view containing either muscle fibers or veins before and after optimization, respectively. Subscripts “1” and “2” refer to two different areas of the field of view. (e, f) Focused reflection matrix corresponding to  $t = 90.9$   $\mu\text{s}$  ( $\rho_0 = c_0 t / 2 \sim 70\text{mm}$ ) before and after optimization respectively. (g) Incoherent RPSF before (red curve) and after correction (green curve).

larity compared to previous experiments is the use of a curved array. The method is however strictly equivalent except that Cartesian coordinates  $(x, z)$  are replaced by polar ones  $(\alpha, \rho)$ . The conventional image (Eq. 1,  $c_0 = 1540$  m/s) is displayed in Fig. 4A. It shows a poor contrast due to the aberrations induced by the adipose and muscle tissues at shallow depths. This poor image quality is confirmed by investigating the focused reflection matrix at a given echo time  $t = 91$   $\mu\text{s}$  (Fig. 4E). While the focused reflection matrix  $\mathbf{R}_{\alpha\alpha}(z)$  shall be nearly diagonal in an ideal case<sup>13</sup>, it here displays a spreading of the backscattered energy over

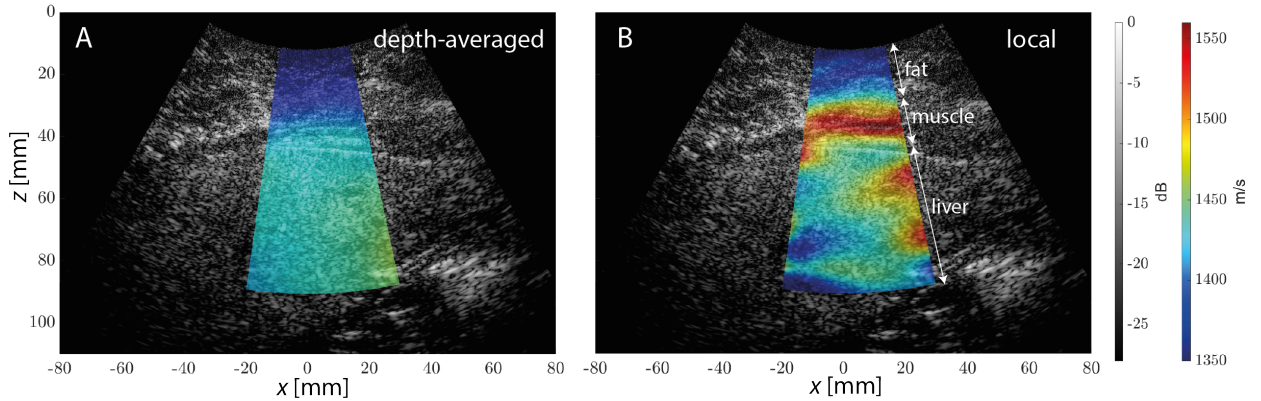


FIG. 5. **Speed-of-sound mapping in the liver experiment.** (A) Depth-averaged and (B) local speed-of-sound reconstruction superimposed onto the standard image of the liver reflectivity. Both images are displayed with an estimated depth axis corresponding to a constant speed-of-sound, such that  $\rho_0 = c_0 t / 2$  with  $c_0 = 1540$  m/s.

off-diagonal coefficients. This feature is a manifestation of: *(i)* aberrations induced by the mismatch between  $c_0$  and  $c(\mathbf{r})$ ; *(ii)* multiple scattering events taking place upstream of the focal plane<sup>13,14</sup>. This observation is confirmed by investigating the transverse dependence of the incoherent PSF shown in Fig. 4G (red curve). This RPSF displays the following shape: A single scattering peak enlarged by aberrations on top of a multiple scattering background whose weight is far from being negligible, since it reaches the value of 20%.

Following the method described above, this observable can be exploited for speed-of-sound tomography by scanning  $c_0$ . An optimized wave velocity  $\hat{c}(x, z_t)$  can be retrieved for each pixel of the ultrasound image, and the resulting map is shown in Fig. 5A. The optimal speed-of-sound  $\hat{c}(x, z_t)$  start from a very low value ( $\sim 1400$  m/s) at shallow depth before suddenly increasing at  $z_t=35$  mm and reaching a plateau ( $\sim 1480$  m/s) beyond  $z_t = 40$  mm. If such a map can be useful to improve the ultrasound image, as we will see further, it is not directly enlightening for quantitative purposes since the probed velocity is averaged from the probe to each focusing point. As before, an inversion of Eq. 13 is needed (Methods) to provide an estimator of the local speed-of sound. The result is displayed in Fig 5B. It clearly highlights the presence of three tissue layers: *(i)* adipose tissue, from  $z = 0$  to  $30$  mm, with a low speed-of-sound  $c \sim 1400$  m/s; *(ii)* muscle tissue, from  $z = 30$  to  $z = 40$  mm, which induce a sudden increase in the speed-of-sound ( $c \sim 1550$  m/s); *(iii)* the liver, beyond  $z = 40$  mm, which is characterized by a relatively slow speed-of-sound ( $c \sim 1480$  m/s in average).

The speed-of-sound map is coherent with the different features shown by the ultrasound image, with a heterogeneous speckle in the fat layer, muscle fibers in the intermediate region and a homogeneous speckle in the liver. However, this map not only confirms the structural information provided by the ultrasound image, it also provides a quantitative measurement of  $c$  which is extremely slow compare to the standard value in a healthy liver ( $c \sim 1600 \text{ m.s}^{-1}$ ). Our measurement thus indicates that the patient is likely to suffer from steatosis.

Beyond this crucial information, mapping the speed-of-sound leads to a more contrasted ultrasound image  $\mathcal{I}'$  (Fig. 4B), as shown by the large improvement of the speckle brightness compared to its original version (Fig. 4A). The interfaces between tissues show a much better lateral coherence [see comparison between insets shown in Figs.4C and D]. This is especially the case at shallow depths, where the variations of the sound velocity are the most drastic and their impact on the image the most important. The correction of axial aberrations is also accompanied by a drastic reduction in transverse aberrations, and thus a significant improvement in terms of resolution. Thus, it allows better visualization of structures such as muscle fibers or veins inside the liver. Such resolution enhancement can be quantified by considering the distribution of energy inside the focused reflection matrix. After defocus compensation, most of the back-scattered energy is brought back in the vicinity of the diagonal coefficients [see comparison between Figs. 4E and F]. A resolution enhancement of about a factor of two is highlighted by comparing the transverse spreading of the confocal peak exhibited by the incoherent RPSF before and after defocus correction [Fig. 4G]. The contrast enhancement is also shown by the lower multiple scattering background observed after correction.

Compared with the ultrasound image (Fig. 4A) whose axial dimension is dictated by the echoes' time-of-flight, each pixel in the optimized image is shifted to its real position in depth, thereby giving access to absolute distances. This feature can be a major breakthrough in ultrasound imaging since a lot of diagnoses rely on distance measurements<sup>29</sup> as, for instance, in obstetrics to monitor fetal growth or detect chromosomal abnormality<sup>36,37</sup>. As an example, we consider the distance between two speckle spots at the extremity of the red and green arrows in Fig. 6. The distance between those two points is overestimated by 3 mm in the initial image (Fig. 6A) compared with the optimized image (Fig. 6B). This difference stems from the re-scaling of the depth axis operated under our approach. This observation highlights the benefit that could provide a depth reassignment of pixels for ultrasound diagnosis.



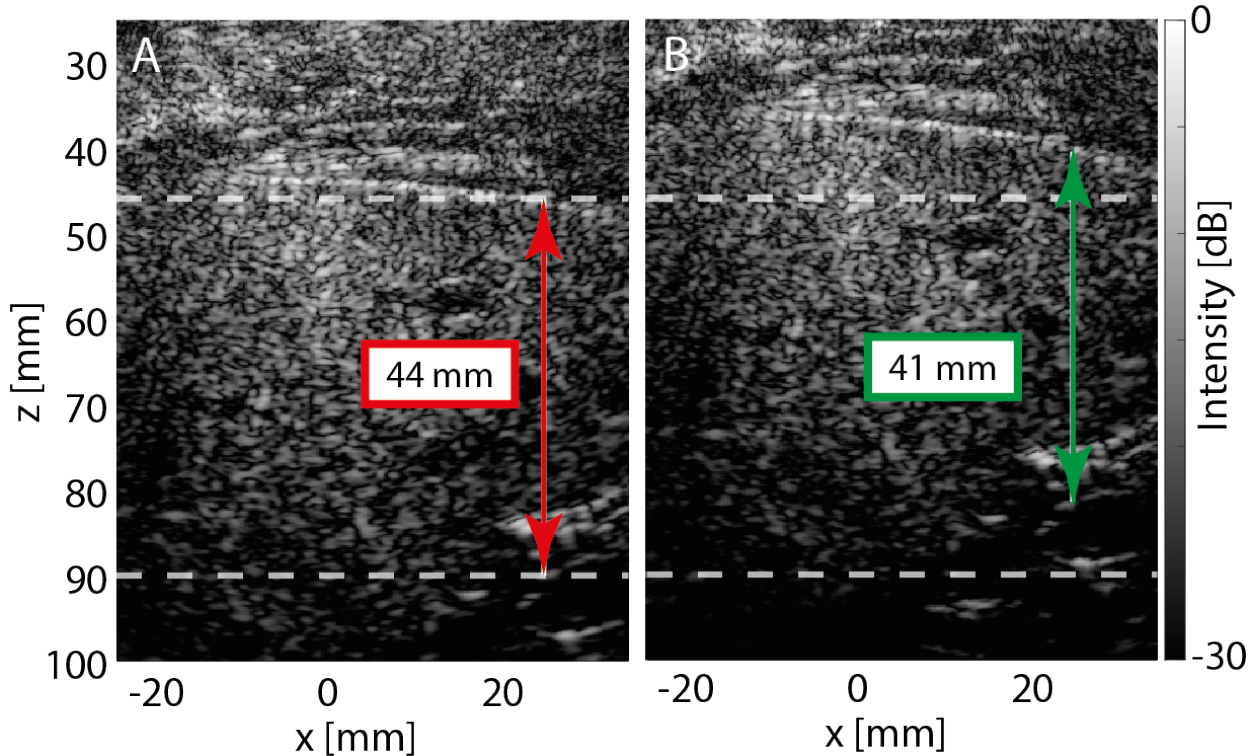


FIG. 6. **Depth axis rescaling of the liver image.** (A) Ultrasound image displayed with a depth axis estimated with a constant speed of sound such that  $\rho_0 = c_0 t/2$  with  $c_0 = 1540$  m/s. (B) Final image (Eq. 14) displayed with a depth axis rescaled by the depth-averaged wave velocity such that the depth  $\rho(x, t)$  of each initial pixel is re-assigned to  $\hat{c}(x, t)t/2$ .

## DISCUSSION AND CONCLUSION

In this experimental proof-of-concept, we demonstrated the capacity of UMI to map the speed-of-sound in reflection. This work is not only an extension of previous studies, since several crucial elements have been introduced to make our approach more robust.

Compared with previous works that relied on a maximization of the image quality<sup>31,38–44</sup>, or parameters such as coherence<sup>18,19,45</sup> or focusing factor<sup>13,16</sup>, our approach is based on a coherent average (SVD) of the focusing process over different speckle grains. Such a process is more robust with multiple scattering and noise that tend to vanish with coherent averaging. Moreover, the access to the Gouy phase allows us to reduce the bias of the speed-of-sound estimator by a factor of about three compared to usual observables relying on an intensity maximization.

Interestingly, our approach is perfectly complementary with a gold standard method called

computed ultrasound tomography in echo mode<sup>20–22</sup>. Inspired by the pioneering work of Kondo *et al.*<sup>46</sup>, this sophisticated approach relies on the measurement of phase mismatches between different couples of incident and reflected beams. It is therefore extremely well suited for probing the lateral variations of the sound speed<sup>47</sup>. However, the axial resolution in CUTE is limited by the depth-of-field of each angular beam. The use of a full aperture can provide direct access to the depth dependence of wave velocity by probing refraction phenomena<sup>30</sup> but this is at the sacrifice of the lateral resolution of the  $c$ -map. On the contrary, our approach provides both an excellent axial and transverse resolution of the speed-of-sound. Moreover, the absolute value of the estimated speed-of-sound in CUTE remains biased by the initial speed-of-sound hypothesis. Here, by scanning the model speed-of-sound  $c_0$ , our approach provides an unbiased estimation of the depth-averaged speed-of-sound. Nevertheless, the current inversion of the local sound velocity map remains largely perfectible.

In the light of Fermat’s principle, such an inverse problem can be viewed as a minimization problem in which the time of flight between any transducer and any focal point must be minimized. However, such a problem is usually ill-posed, since the presence of many local minima can affect the outcome of any gradient descent algorithm. To circumvent this problem, a regularization method must be used to make the loss function convex and find a unique minimum. In this paper, a naive regularization method has been performed with the spatial smoothing of the optimized sound speed map  $\hat{c}$  (Methods). However, strong oscillations can occur with such methods. Other more robust regularization methods could be used<sup>21,48–50</sup> and even combined with a segmentation of the ultrasound image based on the reflectivity image. Furthermore, the need to define a more complex inverse problem that takes into account oblique paths and their distorted trajectories due to refraction<sup>30,51</sup> shall be used to make the inversion process more robust and precise.

Recent advances in applied mathematics, which outperform full-waveform inversion, suggest that an estimate of the local speed of sound can be extracted from the fully sampled reflection matrix<sup>52–54</sup>. In this sense, our method can still help by providing a more accurate starting point for initialization. Such considerations also apply when using artificial intelligence-based methods<sup>9</sup>. In that respect, the inversion problem can be solved iteratively by updating the forward model. As a first step, the estimated sound speed map can actually be used to build a more complex beamforming scheme accounting for refraction phenomena<sup>49,55</sup>. This process can then be iterated using a differential beamformer<sup>56</sup> that



optimizes the sound speed distribution using a variety of physical constraints based on speckle brightness, coherence maximization or RPSF optimization as in the current paper. Such an iterative process can lead to a sharper estimation of the speed-of-sound and a close-to-ideal ultrasound image, not only in terms of transverse and axial resolution but also by a correct positioning of scatterers in depth.

## **Conclusion**

In this paper, we propose a new optimization-based method for mapping the sound velocity of an unknown medium in the speckle regime. Our criterion is based on a self-portrait of the local focusing process provided by ultrasound matrix imaging. Besides directly generating images with better contrast and higher resolution, it allows positioning the depth of each scatterer with greater accuracy and thus to better evaluate the distance across ultrasound images. Even more, the differentiation of the depth-averaged wave velocity allows an estimation of the local speed-of-sound. We have demonstrated its value in a pathological clinical case, a liver of a difficult-to-image patient suffering from steatosis. Beyond this specific example, the sound velocity can be a quantitative bio-marker not only for liver disease but also for tumor assessment<sup>57-59</sup>. Moreover, matrix imaging can apply to any kind of waves for which the multi-element technology exists<sup>60,61</sup>. Mapping the 3D distribution of the optical index in tissues<sup>7</sup> or elastic wave speeds in non-destructive testing<sup>62</sup> and reflection seismology<sup>63</sup> are all examples of relevant applications for the universal method proposed in this paper.

## **MATERIAL AND METHODS**

### **Ultrasound scanner**

In all experiments, the acquisition was performed using a medical ultrafast ultrasound scanner (Aixplorer Mach-30, Supersonic Imagine, Aix-en-Provence, France).

## Phantom experiment

In the phantom experiment, the medium is placed in direct contact of a linear array of transducers (SL15-4, Supersonic Imagine) whose characteristics are provided in Tab. I. The reflection matrix is recorded by emitting a set of plane waves from the probe. The parameters of this emission sequence are also given in Tab. I. Plane waves are generated assuming a constant speed of sound in the medium  $c_{\text{acq}} = 1540$  m/s.

	<b>Phantom</b>	<b>Liver</b>
Type	Linear	Curve
Curvature radius $\mathcal{R}_u$	/	60 mm
Number of transducers $N_{u_{\text{out}}}$	128	192
Transducer pitch $\delta u / \delta \Theta_u$	0.2 mm	0.32°
Central frequency $f_c$	7.5 MHz	3.5 MHz
Bandwidth $\Delta f$	[4 – 15] MHz	[1 – 6] MHz
Plane waves	Maximum $\theta_{\text{in}}^{(\text{max})}$	40°
	Pitch $\delta \theta_{\text{in}}$	1°
	Number $N_{\theta_{\text{in}}}$	81
Sampling frequency $f_s$	30 MHz	26.7 MHz
Recording time $\Delta t$	137 $\mu\text{s}$	235 $\mu\text{s}$

TABLE I. Acquisition parameters in the phantom [Fig. 1 & 2] and liver experiments [Fig. 4, 5 & 6].

## Liver dataset

The in vivo liver ultrasound dataset is extracted from an observational and retrospective, bicentric study (Perpignan Hospital and Angers University Hospital) performed in conformation with the declaration of Helsinki. Between November 2022 and September 2023, 133 patients were consecutively included in this study registered under number (IDRCB) 2022-A00614-39 and that was approved by an ethics committee (EC). Written consent was obtained from patients that underwent liver MRI and abdominal ultrasound on the same day.

The reflection matrix has been recorded with a curved array of transducers (XC 6-1, Supersonic Imagine) whose characteristics are also provided in Tab. I. A set of diverging waves is generated by applying the same time delay that we would apply to generate a plane wave from a linear array. The parameters of the acquisition sequence are also reported in Tab. I. This ultrasound emission sequence meets the FDA Track 3 Recommendations.

### Numerical simulations

Parameters		Value	
<b>Sampling</b>	Spatial grid	Number of points $N_x \times N_z$	$2000 \times 2000$
		Spatial sampling	$\lambda/10 \sim 50 \mu\text{m}$
	Sampling frequency $f_s$	102 MHz	
	Recording time	166 $\mu\text{s}$	
<b>Medium</b>	Speed-of-sound	Figs. 3A,B	
	Density	mean $\langle \rho \rangle$	$1000 \text{ kg.m}^{-3}$
		standard deviation	$3 \text{ kg.m}^{-3}$
<b>Probe</b>	Type	Linear	
	Number of transducers	376	
	Transducer pitch $\delta u$	$\lambda/2 \sim 0.26 \text{ mm}$	
	Central frequency $f_c$	3 MHz	
	Bandwidth $\Delta f$	[2 – 4] MHz	
<b>Acquisition</b>	Speed-of-sound hypothesis $c_0$	1540 m/s	
	Plane wave angles	maximum $\theta_{\text{in}}$	$30^\circ$
		pitch $\delta\theta_{\text{in}}$	$1^\circ$
		number $N_{\theta_{\text{in}}}$	61

TABLE II. Parameters of the k-wave numerical simulations.

Each k-Wave simulation is performed over a two-dimensional grid whose sampling is reported in Tab. II. The simulated speed-of-sound distributions are displayed in Figs. 3A and B. The background density is constant ( $\rho = 1000 \text{ kg.m}^{-3}$ ) but short-scale fluctuations ( $3 \text{ kg.m}^{-3}$  std) have been superimposed to generate a random wave-field characteristic of

ultrasound imaging in soft tissues. Bright targets are point-like threads modeled by a higher density  $\rho_t = 1100 \text{ kg.m}^{-3}$  compared to water.

All simulation parameters such as the probe configuration and acquisition sequence are also described in Tab. II. As in the phantom experiment, the recording of the reflection matrix is performed using a set of incident plane waves. The emitted signal is a 3 MHz two-cycle sinusoidal burst. For each excitation, the back-scattered signal is recorded by the probe and stored in the reflection matrix  $\mathbf{R}_{\mathbf{u}\theta}(t)$ .

### Delay-and-sum algorithm - linear array

For a linear array, the general procedure to build the confocal image and the focused reflection matrix is the delay-and-sum (DAS) algorithm described in Eqs. 1 and 2. The time-of-flight  $\tau_{\text{in}}$  describes the travel time for each incident plane wave  $\theta_{\text{in}}$  from the probe to any targeted focusing point  $(x_{\text{in}}, z_0 = c_0 t/2)$ :

$$\tau_{\text{in}}(\theta_{\text{in}}, x, t, c_0) = \frac{x \sin(\theta_{\text{in}}^0) + (c_0 t/2) \cos(\theta_{\text{in}}^0)}{c_0} + \tau_0(\theta_{\text{in}}, c_{\text{acq}}). \quad (15)$$

with  $\theta_{\text{in}}^0$  the incident angle of the emitted plane wave  $\theta_{\text{in}}$  for a wave velocity model  $c_0$ , such that:

$$\theta_{\text{in}}^0 = \arcsin\left(\frac{c_0}{c_{\text{acq}}} \sin(\theta_{\text{in}})\right). \quad (16)$$

The additional time delay  $\tau_0(\theta_{\text{in}})$  corresponds to the time shift applied to each incident plane wave in order to set the same time origin for each insonification<sup>64</sup>. This time origin corresponds to the time when the incident pulse is emitted by the central element of the array.

The time-of-flight  $\tau_{\text{out}}$  in Eqs. 2 and 1 is the travel time for the reflected wave from the focusing point  $(x_{\text{out}}, z_0 = c_0 t/2)$  to any transducer  $u_{\text{out}}$  of the probe::

$$\tau_{\text{out}}(u_{\text{out}}, x_{\text{out}}, t, c_0) = \frac{\sqrt{(x_{\text{out}} - u_{\text{out}})^2 + (c_0 t/2)^2}}{c_0}. \quad (17)$$

### Delay-and-sum algorithm - curved array

For a curved array, the ultrasound image is expressed in polar coordinates  $(\alpha, \rho)$ . The beamforming process used to build the confocal image displayed in Fig. 4A is expressed as

follows:

$$\begin{aligned} \mathcal{I}(\alpha, r_0 = c_0 t/2) = \sum_{\theta_{\text{in}}} \sum_{\mathbf{u}_{\text{out}}} R(\mathbf{u}_{\text{out}}, \theta_{\text{in}}, \tau_{\text{out}}(\mathbf{u}_{\text{out}}, \alpha, t, c_0)) \\ + \tau_{\text{in}}(\theta_{\text{in}}, \alpha, t, c_0). \end{aligned} \quad (18)$$

with  $\mathbf{u}_{\text{out}} = (v_{\text{out}}, w_{\text{out}})$ , the position vector of each transducer. The input travel times are given by :

$$\tau_{\text{in}}(\theta_{\text{in}}, \alpha, t, c_0) = \frac{D + \mathcal{R}_u \sin(\theta_p) \sin(\theta_{\text{in}})}{c_0} \quad (19)$$

with  $\mathcal{R}_u$ , the curvature radius of the probe and

$$D = \sqrt{\rho'^2 - (\mathcal{R}_u \sin(\theta_{\text{in}}))^2} \quad (20)$$

$$\theta_p = \arcsin((\sin(\alpha)(\mathcal{R}_u + D \cos(\theta_{\text{in}})) - D \cos(\alpha) \sin(\theta_{\text{in}}))/\rho') \quad (21)$$

$$\rho' = \mathcal{R}_u + (c_{\text{acq}} t/2 - \mathcal{R}_u) \frac{c_0}{c_{\text{acq}}} \quad (22)$$

The output travel times are given by :

$$\tau_{\text{out}}(\mathbf{u}_{\text{out}}, \alpha, t, c_0) = \frac{\sqrt{(\rho' \sin(\alpha) - v_{\text{out}})^2 + (\rho' \cos(\alpha) - w_{\text{out}})^2}}{c_0} \quad (23)$$

These travel times are also used to build the focused reflection matrix,  $\mathbf{R}_{\alpha\alpha}(t, c_0)$  whose coefficients are given by:

$$\begin{aligned} R(\alpha_{\text{out}}, \alpha_{\text{in}}, t, c_0) = \sum_{\theta_{\text{in}}} \sum_{\mathbf{u}_{\text{out}}} R(\mathbf{u}_{\text{out}}, \theta_{\text{in}}, \tau_{\text{out}}(\mathbf{u}_{\text{out}}, \alpha_{\text{out}}, t, c_0)) \\ + \tau_{\text{in}}(\theta_{\text{in}}, \alpha_{\text{in}}, t, c_0). \end{aligned} \quad (24)$$

One example of the matrix  $\mathbf{R}_{\alpha\alpha}(t, c_0)$  is given in Fig. 4E.

### Optimal speed-of-sound

The optimal speed-of-sound  $\hat{c}(\mathbf{r}_p)$  is estimated locally by considering the de-scanned matrix over a reduced spatial window  $\mathcal{P}(\mathbf{r} - \mathbf{r}_p)$  (Eq. 4). The choice of this window is dictated by the following compromise: (*i*) encompass a sufficient number of independent speckle points to smooth out speckle fluctuations in the RPSF by spatial averaging; (*ii*) consider a spatial window as small as possible in order to optimize the resolution of the  $\hat{c}$ -map. The size of  $\mathcal{P}$  resulting from this compromise is reported in Tab. III for the experiments and numerical simulations shown in the paper. For computational reasons, the speed-of-sound maps displayed in Figs. 3C and D and Fig.5A have been extracted by optimizing the incoherent RPSF (Eq. 7).

## Local speed of sound

The optimal speed-of-sound map,  $\hat{c}(x, t)$ , can finally be used to estimate a local speed-of-sound map,  $c(x, z)$ . To this end, we take up the method developed by Jakovljevic *et al.*<sup>33</sup> which basically consists in differentiating the first order eikonal equation.

Under a paraxial approximation and assuming that the speed of sound, or equivalently the slowness  $s = 1/c$ , is a piecewise constant function between discretized depths, such as  $z_n = n\delta z$  with  $n \in \{0, 1, \dots, N\}$ , we can write:

$$\underbrace{\int_{z_{n-1}}^{z_n} s(x, z) dz}_{\approx s(x, z_n) \delta z} = \int_0^{z_n} s(x, z) dz - \int_0^{z_{n-1}} s(x, z) dz; \quad (25)$$

which yields

$$s(x, z_n) \delta z = n \bar{s}(x, z_n) \delta z - (n-1) \bar{s}(x, z_{n-1}) \delta z \quad (26)$$

with  $\bar{s}(x, z)$ , the depth-averaged slowness from the probe to the depth  $z$ . The last equation leads to a discretized expression of the local slowness  $s$  as a numerical differentiation of the averaged slowness  $\bar{s}$ :

$$s(x, z_n) = -(n-1) \bar{s}(x, z_{n-1}) + n \bar{s}(x, z_n). \quad (27)$$

The last equation leads to the following system of equations:

$$\begin{cases} s(x, z_1) = \bar{s}(x, z_1); \\ s(x, z_2) = -\bar{s}(x, z_1) + 2\bar{s}(x, z_2); \\ s(x, z_3) = -2\bar{s}(x, z_2) + 3\bar{s}(x, z_3); \\ \dots \\ s(x, z_N) = -(N-1)\bar{s}(x, z_{N-1}) + N\bar{s}(x, z_N). \end{cases} \quad (28)$$

Under a matrix formalism, it writes:

$$\mathbf{S}(x) = \mathbf{A} \times \bar{\mathbf{S}}(x). \quad (29)$$

where  $\mathbf{S}(x) = [s(x, z_i)]_i^\top$  and  $\bar{\mathbf{S}}(x) = [\bar{s}(x, z_i)]_i^\top$  are column vectors containing the discretized values of the local slowness  $s(x, z) = 1/c(x, z)$  and of the depth-averaged slowness  $\bar{s}(x, z_t) =$

$1/\hat{c}(x, t)$  interpolated at each depth  $z_i$ .  $\mathbf{A}$  is the following matrix :

$$\mathbf{A} = \begin{pmatrix} 1 & 0 & 0 & \dots & 0 & 0 \\ -1 & 2 & 0 & \dots & 0 & 0 \\ 0 & -2 & 3 & \dots & 0 & 0 \\ \dots & \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & 0 & \dots & -(N-1) & N \end{pmatrix}. \quad (30)$$

Equation 29 shows how the local velocity  $c(x, z) = 1/s(x, z)$  can be obtained from a numerical differentiation of the depth-averaged slowness  $\bar{s}(x, z_t) = 1/\hat{c}(x, t)$ .

This is, however, an ill-posed problem since our measurement  $\hat{c}(x, t)$  is invariably corrupted by noise. A regularization method is therefore needed and consists in a prior smoothing of the averaged speed-of-sound in order to avoid un-physical short-scale fluctuations of the local speed-of-sound. In practice, the smoothing operation is performed in two steps.

First, the RPSF is smoothed by means of a spatio-temporal Gaussian kernel such that:

$$RPSF_{\text{inc}}(\mathbf{\Delta}, \mathbf{r}_p) = \sqrt{|R(\mathbf{\Delta}, \mathbf{r}_p)|^2 \otimes_{\mathbf{r}_p} \mathcal{K}(\mathbf{r}_p)}, \quad (31)$$

where  $\mathcal{K}$  is a Gaussian kernel such that  $\mathcal{K}(\mathbf{r}) = \mathcal{K}(x, t) = \exp[-x^2/(2l_x^2)] \exp[-t^2/(2l_t^2)]$  for the numerical simulation (Fig. 3, linear array) and  $\mathcal{K}(\mathbf{r}) = \mathcal{K}(\alpha, t) = \exp[-\alpha^2/(2l_\alpha^2)] \exp[-t^2/(2l_t^2)]$  for the liver experiment (Fig. 5, curved array). The values of  $l_x$ ,  $l_\alpha$  and  $l_t$  are provided in Tab. III.

Second, the  $\hat{c}$ -map, extracted from the maximization of  $RPSF_{\text{inc}}$ , is smoothed using an equivalent Gaussian kernel  $\mathcal{K}$ , whose dimension  $(l_{x/\alpha}, l_t)$  is also provided in Tab. III.

Quantity	Direction	Simulations	Liver
RPSF	Lateral	$l_x = 2.5 \text{ mm } (\sim 5\lambda)$	$l_\alpha = 4.5^\circ$
	Axial	$l_t = 1.6 \mu\text{s}$	$l_t = 3.2 \mu\text{s}$
$\hat{c}$ -map	Lateral	$l_x = 2.5 \text{ mm } (\sim 5\lambda)$	$l_\alpha = 2.5^\circ$
	Axial	$l_t = 1.6 \mu\text{s}$	$l_t = 1.0 \mu\text{s}$

TABLE III. Size of the Gaussian kernels used for smoothing the RPSF and  $\hat{c}$ -map prior to the numerical differentiation of Eq. 29.

**Data Availability** Data used in this manuscript have been deposited at Figshare, <https://figshare.com/projects/>.

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**Author Contributions Statement.** A.A. and M.F. initiated the project. A.A. supervised the project. F.B. performed the phantom experiment and the numerical simulations. A.G. and L.C. performed the liver experiment. F.B. and W.L. developed the post-processing tools. F.B. and A.A. analyzed the experimental results. A.A. performed the theoretical study. F.B. prepared the figures. F.B. and A.A. prepared the manuscript. F.B., E.G., A.L.B., W.L., A.G., L.C., M.F., and A.A. discussed the results and contributed to finalizing the manuscript.

**Competing interests.** A.A., M.F., A.L.B, W.L., E.G. and F.B. are inventors of a french patent related to this work filed by the company Supersonic Imagine, CNRS and ESPCI (no. FR2306343). M.F. is cofounder of the SuperSonic Imagine company, which is commercializing the ultrasound platform used in this study. W.L. had his PhD funded by the SuperSonic Imagine company and is now an employee of this company. All authors declare that they have no other competing interests.



# Supplementary Information

## S1. THEORETICAL EXPRESSION OF THE RECORDED REFLECTION MATRIX IN THE TRANSDUCER AND PLANE WAVE BASES

The reflection matrix  $\mathbf{R}_{uu}(t)$  expressed in the transducer basis can be decomposed in the temporal Fourier domain as follows:

$$\mathbf{R}_{uu}(t) = \int d\omega \bar{\mathbf{R}}_{uu}(\omega) \exp(i\omega t) \quad (\text{S1})$$

Under a single scattering assumption, the coefficients of the monochromatic reflection matrix  $\bar{\mathbf{R}}_{uu}(\omega)$  can be expressed as follows:

$$\bar{R}(u_{\text{out}}, u_{\text{in}}, \omega) = \int d\mathbf{r} G_0(\mathbf{u}_{\text{out}}, \mathbf{r}, \omega) \gamma(\mathbf{r}) G_0(\mathbf{u}_{\text{in}}, \mathbf{r}, \omega) \quad (\text{S2})$$

with  $\gamma(\mathbf{r})$ , the medium reflectivity and  $G_0(\mathbf{u}, \mathbf{r})$ , the homogeneous Green's function that accounts for propagation of a monochromatic wave between the transducer located at  $\mathbf{u} = (u, 0)$  and any point  $\mathbf{r} = (x, z)$  inside the medium. In a 2D configuration, the wave equation Green's function reads

$$G_0(\mathbf{u}, \mathbf{r}, \omega) = -\frac{i}{4} \mathcal{H}_0^{(1)} \left( k \sqrt{(x-u)^2 + z^2} \right) \quad (\text{S3})$$

with  $\mathcal{H}_0^{(1)}$  the Hankel function of the first kind and  $k = \omega/c$ , the wave number. In the far-field, the asymptotic expression of the Green's function is:

$$G_0(\mathbf{u}, \mathbf{r}, \omega) \approx \frac{-e^{i\pi/4}}{\sqrt{8\pi k} [(x-u)^2 + z^2]^{1/4}} \exp \left( ik_0 \sqrt{(x-u)^2 + z^2} \right). \quad (\text{S4})$$

A spatial Fourier transform at input and output of  $\mathbf{R}_{uu}(\omega)$  leads to a reflection matrix  $\bar{\mathbf{R}}_{\kappa\kappa}(\omega, z=0)$  expressed in the plane wave basis at the medium surface ( $z=0$ ):

$$\bar{\mathbf{R}}_{\kappa\kappa}(\omega, z=0) = \mathbf{F}_{\kappa u} \times \bar{\mathbf{R}}_{uu}(\omega) \times \mathbf{F}_{\kappa u}^\top \quad (\text{S5})$$

with  $\mathbf{F} = [F(\kappa, u)]$ , the Fourier transform operator, such that

$$F(\kappa, u) = \exp(-i\kappa u) \quad (\text{S6})$$

In the plane wave basis, Eq. S2 becomes:

$$\bar{R}(\boldsymbol{\kappa}_{\text{out}}, \boldsymbol{\kappa}_{\text{in}}, \omega, z = 0) = \int dz P(\boldsymbol{\kappa}_{\text{out}}, z) P(\boldsymbol{\kappa}_{\text{in}}, z) \Gamma(\boldsymbol{\kappa}_{\text{in}} + \boldsymbol{\kappa}_{\text{out}}, z) \quad (\text{S7})$$

with  $\Gamma(\boldsymbol{\kappa}_{\text{in}} + \boldsymbol{\kappa}_{\text{out}}, z) = \int d\boldsymbol{\rho} \gamma(\boldsymbol{\rho}, z) \exp[-i(\boldsymbol{\kappa}_{\text{out}} + \boldsymbol{\kappa}_{\text{in}}) \cdot \boldsymbol{\rho}]$ , the Fourier transform of the object reflectivity.  $\mathbf{P}_{\boldsymbol{\kappa}}(\omega, z, c) = [P(\boldsymbol{\kappa}, \omega, z, c)]$  is the propagator describing plane wave propagation between the probe ( $z = 0$ ) and the plane  $z$  inside the medium, such that

$$P(\boldsymbol{\kappa}, z, c) = \exp(iz\sqrt{k^2 - |\boldsymbol{\kappa}|^2}) \quad (\text{S8})$$

for  $|\boldsymbol{\kappa}| < k$  and zero elsewhere if  $z \gg \lambda$ .

## S2. THEORETICAL EXPRESSION OF THE FOCUSED REFLECTION MATRIX IN THE PLANE WAVE BASIS

The focused reflection matrix  $\mathbf{R}_{xx}(t, c_0)$  defined in Eq. 2 can be decomposed in the temporal Fourier domain as follows:

$$\mathbf{R}_{xx}(t, c_0) = \int_{\omega_-}^{\omega_+} d\omega \bar{\mathbf{R}}_{xx}(\omega, z_0, c_0) \exp(i\omega t) \quad (\text{S9})$$

with  $\omega_{\pm} = \omega_c \pm \delta\omega/2$ ,  $\omega_c$ , the central frequency and  $\delta\omega$ , the frequency bandwidth. Each monochromatic focused reflection matrix  $\bar{\mathbf{R}}_{xx}(\omega, z_0, c_0)$  results from a focusing process at the expected ballistic depth  $z_0 = c_0 t / 2^{13}$ .  $\bar{\mathbf{R}}_{xx}(\omega, z_0, c_0)$  can be projected in the plane wave basis as follows:

$$\bar{\mathbf{R}}_{\boldsymbol{\kappa}\boldsymbol{\kappa}}(z_0, \omega, c_0) = \mathbf{F}_{kx} \times \bar{\mathbf{R}}_{xx}(\omega, z_0, c_0) \times \mathbf{F}_{kx}^{\top}. \quad (\text{S10})$$

Under a matrix formalism, the delay-and-sum beamforming process (Eq. 2) can be expressed in the Fourier domain as the following Hadamard product:

$$\bar{\mathbf{R}}_{\boldsymbol{\kappa}\boldsymbol{\kappa}}(\omega, z_i, c_0) = \exp(2i\omega z_0 / c_0) \mathbf{P}^*(z_0, \omega, c_0) \circ \bar{\mathbf{R}}_{\boldsymbol{\kappa}\boldsymbol{\kappa}}(z = 0, \omega) \circ \mathbf{P}^{\dagger}(z_0, \omega, c_0), \quad (\text{S11})$$

which can be expressed in terms of matrix coefficients as follows:

$$\bar{R}(\boldsymbol{\kappa}_{\text{out}}, \boldsymbol{\kappa}_{\text{in}}, z_0, \omega, c_0) = \exp(2i\omega z_0 / c_0) \quad (\text{S12})$$

$$\times \int dz \Gamma(\boldsymbol{\kappa}_{\text{in}} + \boldsymbol{\kappa}_{\text{out}}, z) O_{\text{out}}(\boldsymbol{\kappa}_{\text{out}}, z) O_{\text{in}}(\boldsymbol{\kappa}_{\text{in}}, z) \quad (\text{S13})$$

$$\times \exp\left(-iz_0 \sqrt{\left(\frac{\omega}{c_0}\right)^2 - |\boldsymbol{\kappa}_{\text{out}}|^2}\right) \exp\left(+iz_0 \sqrt{\left(\frac{\omega}{c_0}\right)^2 - |\boldsymbol{\kappa}_{\text{out}}|^2}\right) \quad (\text{S14})$$

$$\times \exp\left(-iz_0 \sqrt{\left(\frac{\omega}{c_0}\right)^2 - |\boldsymbol{\kappa}_{\text{in}}|^2}\right) \exp\left(+iz_0 \sqrt{\left(\frac{\omega}{c_0}\right)^2 - |\boldsymbol{\kappa}_{\text{out}}|^2}\right), \quad (\text{S15})$$

where the functions  $O_{\text{in}}$  and  $O_{\text{out}}$  account for the angular aperture applied at input and output during the beamforming process, respectively. Under the paraxial approximation, this last equation can be rewritten as follows:

$$\bar{R}(\kappa_{\text{out}}, \kappa_{\text{in}}, z_0, \omega, c_0) = \int dz \exp(2i\omega z/c) \Gamma(\kappa_{\text{in}} + \kappa_{\text{out}}, z) O_{\text{out}}(\kappa_{\text{out}}, z) O_{\text{in}}(\kappa_{\text{in}}, z) \quad (\text{S16})$$

$$\times \exp\left(-i \frac{|\kappa_{\text{out}}|^2 + |\kappa_{\text{in}}|^2}{2\omega} (cz - c_0 z_0)\right). \quad (\text{S17})$$

The last expression can be recast as follows

$$\bar{R}(\kappa_{\text{out}}, \kappa_{\text{in}}, z_0, \omega, c_0) = \int dz \exp(2i\omega z/c) \Gamma(\kappa_{\text{in}} + \kappa_{\text{out}}, z) H_{\text{out}}(\kappa_{\text{out}}, z) H_{\text{in}}(\kappa_{\text{in}}, z). \quad (\text{S18})$$

with  $H_{\text{in}}$  and  $H_{\text{out}}$ , the input and output transfer functions of the imaging process:

$$H_{\text{in/out}}(\kappa, z, z_0, c_0) = O_{\text{in/out}}(\kappa, z) \exp\left(-i \frac{|\kappa|^2}{2\omega} (cz - c_0 z_i)\right). \quad (\text{S19})$$

The cancellation of the phase term defines the position  $z_f$  of the focusing plane, such that

$$z_f = \frac{c_0}{c} z_0. \quad (\text{S20})$$

In first approximation, one can consider the transfer function as relatively constant over the frequency bandwidth and consider its value at the central frequency  $\omega_c$ , such that:

$$H_{\text{in/out}}(\kappa, z, z_0, c_0) \simeq O_{\text{in/out}}(\kappa, z) \exp\left(-i \frac{|\kappa|^2}{2\omega_c} (cz - c_0 z_i)\right) \quad (\text{S21})$$

Injecting Eq. S18 into Eqs. S10 and S9 leads to the following expression for the focused reflection matrix coefficients:

$$R(x_{\text{out}}, x_{\text{in}}, t, c_0) = \int d\omega \int dz \int d\boldsymbol{\rho} \exp[i(\omega t - 2z/c)] h_{\text{out}}(x - x_{\text{out}}, z, z_0, c, c_0) \gamma(\boldsymbol{\rho}, z) h_{\text{in}}(x - x_{\text{in}}, z, z_0, c, c_0) \quad (\text{S22})$$

where  $h_{\text{in/out}}$  is the Fourier transform of the transfer function  $H_{\text{in/out}}$ :

$$h_{\text{in/out}}(x, z, z_0, c_0) = \int d\kappa H_{\text{in/out}}(\kappa, z, z_0, c_0) \exp(-i\kappa x). \quad (\text{S23})$$

$h_{\text{in/out}}(x, z, z_0, c_0)$  corresponds to the point-spread function of the imaging system at depth  $z$  when trying to focus at plane  $z_0$  assuming a wave velocity model  $c_0$ .

Due to the broad spectrum of ultrasound signals, the integral over frequency in Eq. S22 can be simplified in first approximation as follows:

$$R(x_{\text{out}}, x_{\text{in}}, t, c_0) \simeq \int dz \delta(t - 2z/c) \int d\boldsymbol{\rho} h_{\text{out}}(x - x_{\text{out}}, z, z_0, c, c_0) \gamma(x, z) h_{\text{in}}(x - x_{\text{in}}, z, z_0, c, c_0). \quad (\text{S24})$$

The Dirac distribution  $\delta$  in the last expression accounts for the time gating operation and implies that, for a given time-of-flight  $t$ , the contribution of the scattered wave-field is induced by the set of scatterers lying in the vicinity of the isochronous plane located at  $z_t = ct/2$ :

$$R(x_{\text{out}}, x_{\text{in}}, t, c_0) \propto \int dx h_{\text{out}}(x - x_{\text{out}}, z_t, z_0, c_0) \gamma(x, z_t) h_{\text{in}}(x - x_{\text{in}}, z_t, z_0, c_0). \quad (\text{S25})$$

### S3. A “DE-SCAN” REPRESENTATION OF THE FOCUSED R-MATRIX

In previous works<sup>13,65</sup>, the RPSF was extracted in a common mid-point representation, where the input and output focal point were centered around the same common mid-point  $x_{\text{cmp}} = (x_{\text{in}} + x_{\text{out}})/2$ . Here, we extract the RPSF in a “de-scan” representation where the output focal point is simply scanned with respect to the output such that  $x_{\text{out}} = x_{\text{in}} + \Delta x$ . To that aim, the focused reflection matrix (Fig. S1B) can be re-arranged in a de-scan basis (Fig. S1C), Mathematically, it consists in the following change of variables [Fig. S1A]:

$$\underbrace{\begin{bmatrix} x_{\text{in}} \\ x_{\text{out}} \end{bmatrix}}_{\text{Focused basis}} \rightarrow \underbrace{\begin{bmatrix} x_{\text{in}} \\ \Delta x \end{bmatrix}}_{\text{De-scan basis}} = \begin{bmatrix} x_{\text{in}} \\ x_{\text{out}} - x_{\text{in}} \end{bmatrix}, \quad (\text{S26})$$

with  $\Delta x = x_{\text{out}} - x_{\text{in}}$ . This change of variables applied to Eq. S25 leads to the following expression for the  $\mathbf{R}_D$ -matrix coefficients (Eq. 3 of the accompanying paper)

$$R_D(\{\Delta x, c_0\}, \{x_{\text{in}}, t\}) \propto \int dx' h_{\text{out}}(x' - \Delta x, z_t, z_0, c_0) \gamma(x' + x_{\text{in}}, z_t) h_{\text{in}}(x', z_t, z_0, c_0). \quad (\text{S27})$$

It can be emphasised that such a de-scan representation optimises the storage of the focused reflection matrix. Indeed, the latter matrix is a sparse matrix whose signal is located around the confocal signal ( $x_{\text{in}} = x_{\text{out}} \Leftrightarrow \Delta x = 0$ ). So instead of storing the responses between all pairs  $(x_{\text{in}}, x_{\text{out}})$ , only the responses between neighbouring focusing points  $(x_{\text{in}}, \Delta x)$  can be considered, which is much less data intensive.

### S4. INCOHERENT RPSF

In the accompanying paper, the focusing quality is first assessed by considering an incoherent average of each column of  $\mathbf{R}_D$ . Using Eq. S27, the incoherent intensity,  $RPSF_{\text{inc}}^2(\Delta x, c_0) =$

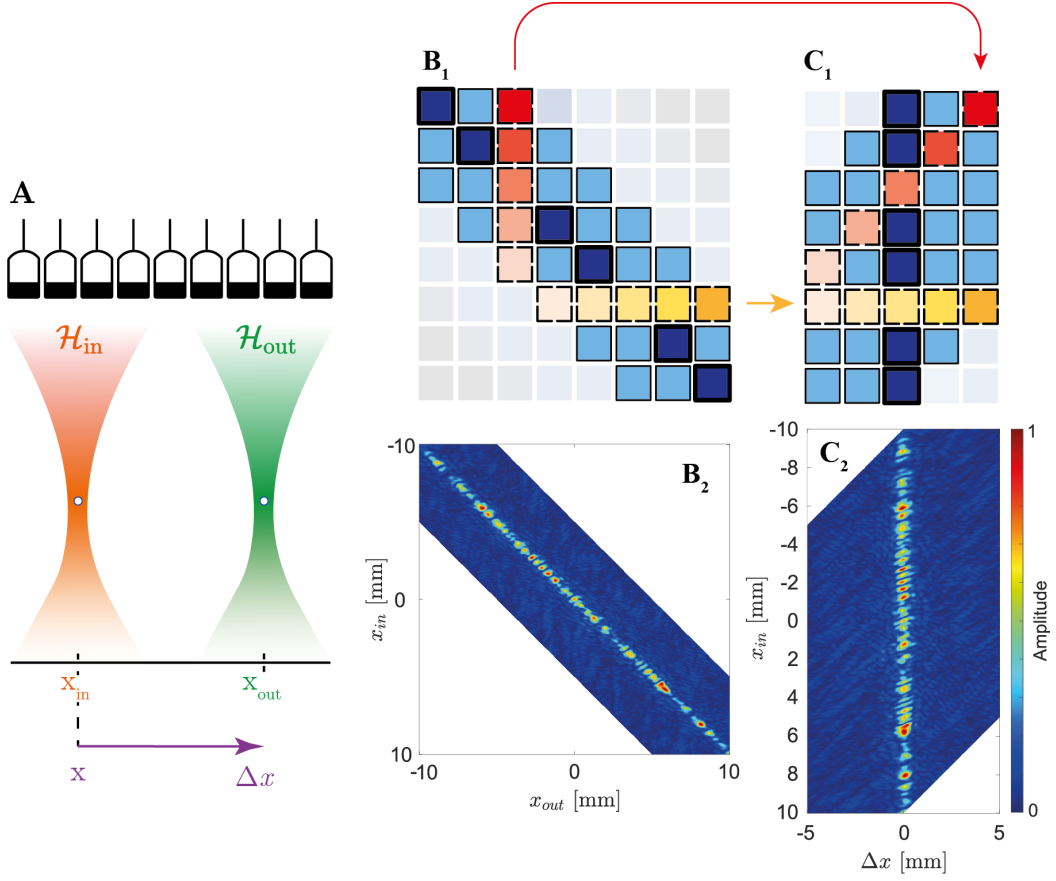


FIG. S1. **The de-scan focused basis.** (A) Schematic view of the input and output focal spots. (B) Reflection matrix  $\mathbf{R} = [R(x_{in}, x_{out}, t, c_0)]$  expressed in the conventional focused basis. (C) Reflection matrix  $\mathbf{R}_D = [R(x_{in}, t, \Delta x, c_0)]$  expressed in the de-scanned basis, with  $\Delta x = x_{out} - x_{in}$ . The sub-panels  $\mathbf{B}_2$  and  $\mathbf{C}_2$  are examples of reflection matrices sketched in sub-panels  $\mathbf{B}_1$  and  $\mathbf{C}_1$ , respectively. They correspond to the tissue mimicking phantom experiment (Table 1) for time  $t = 32\mu\text{s}$  and speed-of-sound  $c_0 = 1540 \text{ m}\cdot\text{s}^{-1}$ .

$\langle |R_D(\{\Delta x, c_0\}, \{x_{in}, t\})|^2 \rangle$ , can be expressed as follows:

$$\begin{aligned}
 RPSF_{inc}^2(\Delta x, c_0) &\propto \left\langle \int dx' \int dx'' \right. && h_{out}(x' - \Delta x, z_t, z_0, c_0) \\
 & && \gamma(x' + x_{in}, z_t) \gamma^*(x'' + \\
 &\propto \int dx' \int dx'' h_{out}(x' - \Delta x, z_t, z_0, c_0) h_{out}^*(x'' - \Delta x, z_t, z_0, c_0) && \langle \gamma(x' + x_{in}, z_t) \gamma^*(x'' +
 \end{aligned}$$

Assuming a random speckle,

$$\langle \gamma(x, z_t) \gamma^*(x', z_t) \rangle = \langle |\gamma|^2 \rangle \delta(x - x'), \quad (\text{S29})$$

Eq. S28 becomes:

$$RPSF_{\text{inc}}^2(\Delta x, c_0) \propto \int dx' \int |h_{\text{out}}(x' - \Delta x, z_t, z_0, c_0)|^2 |h_{\text{in}}(x', z_t, z_0, c_0)|^2 \quad (\text{S30})$$

$$\propto |h_{\text{out}}|^2 \overset{\Delta x}{\circledast} |h_{\text{in}}|^2(\Delta x, c_0). \quad (\text{S31})$$

The incoherent RPSF therefore provides the auto-convolution of the input and output PSF intensities.

## S5. COHERENT RPSF

A second option is to extract a coherent RPSF from the singular value decomposition (SVD) of  $\mathbf{R}_D$ . The result of the SVD can be understood if we assume, in first approximation, a point-like input PSF in Eq. S27 [ $h_{\text{in}}(x', z_t, z_0, c_0) \propto \delta(x')$ ]. Under this assumption, the  $\mathbf{R}_D$ -matrix coefficients can be expressed as follows:

$$R_D^{(1)}(\{\Delta x, c_0\}, \{x_{\text{in}}, t\}) = h_{\text{out}}(-\Delta x, c_0) \gamma(x_{\text{in}}, z_t) \quad (\text{S32})$$

where the superscript (1) stands for the first-order approximation under which this expression has been derived. In this ideal case, Eq. S32 indicates that the  $\mathbf{R}_D$ -matrix is of rank 1. The corresponding eigenstate then directly provides the output PSF in the de-scanned basis,  $U_1^{(1)}(\Delta x, c_0) = h_{\text{out}}(-\Delta x, c_0)$ , and the phase conjugate of the medium reflectivity in the pixel basis,  $\mathbf{V}_1^{(1)} = \gamma^*(x_{\text{in}}, t)$ .

These expressions result from a first-order approximation but can be improved using the relation that links the two singular vectors:  $\lambda_1 \mathbf{U}_1 = \mathbf{R}_D \times \mathbf{V}_1$ . A second-order estimation of  $\mathbf{U}_1$  can therefore be obtained by considering between matrix product between the exact matrix  $\mathbf{R}_D$  and the zero-order estimation of  $\mathbf{V}_1$ , such that:

$$U_1(\Delta x, c_0) \propto \sum_{\{x_{\text{in}}, t\}} R_D(\{\Delta x, c_0\}, \{x_{\text{in}}, t\}) \gamma(x_{\text{in}}, z_t). \quad (\text{S33})$$

Injecting Eq. S27 into the last equation leads to

$$U_1(\Delta x, c_0) \propto \sum_{\{x_{\text{in}}, t\}} \int dx' h_{\text{out}}(x' - \Delta x, z_t, z_0, c_0) h_{\text{in}}(x', z_t, z_0, c_0) \gamma(x' + x_{\text{in}}, z_t) \gamma^*(x_{\text{in}}, z_t). \quad (\text{S34})$$

If the number of pixels in the considered spatial window is sufficiently large, the sum over  $\{x_{\text{in}}, t\}$  in the last equation can be replaced by an ensemble average, such that

$$U_1(\Delta x, c_0) \propto \int dx' h_{\text{out}}(x' - \Delta x, z_t, z_0, c_0) h_{\text{in}}(x', z_t, z_0, c_0) \langle \gamma(x' + x_{\text{in}}, z_t) \gamma^*(x_{\text{in}}, z_t) \rangle, \quad (\text{S35})$$

where the symbol  $\langle \dots \rangle$  stands for the ensemble average. Assuming a random speckle ( $\langle \gamma(x, z_t) \gamma^*(x', z_t) \rangle = \langle |\gamma|^2 \rangle \delta(x - x')$ ), Eq. S35 finally yields to the following expression of  $\mathbf{U}_1$ :

$$U_1(\Delta x, c_0) \propto h_{\text{out}}(-\Delta x, z_t, z_0, c_0) h_{\text{in}}(0, z_t, z_0, c_0). \quad (\text{S36})$$

The first singular vector therefore yields the amplitude distribution of the output focal spot,  $h_{\text{out}}(-\Delta x, z_t, z_0, c_0)$ , weighted by the confocal value of the input focal spot  $h_{\text{in}}(0, z_t, z_0, c_0)$ .

## S6. ANALYTICAL EXPRESSIONS OF THE RPSFS FOR A GAUSSIAN APERTURE FUNCTION

For analytical tractability, a Gaussian aperture function can be assumed in the expression of the transfer function  $H(\kappa, z, \omega, c_0)$  (Eq. S21) such that:

$$O_{\text{in/out}}(\kappa, z) = \exp \left[ -\kappa^2 / (2A^2) \right] \quad (\text{S37})$$

For this Gaussian aperture, the resulting PSF  $h$  (Eq. S23) is a Gaussian beam:

$$h_{\text{in/out}}(x, c_0) = \sqrt{\frac{w_0}{w(c_0)}} \exp \left( -\frac{x^2}{w^2(c_0)} - j \frac{\omega_c}{c} z - j \frac{x^2}{R^2(c_0)} + j \eta(c_0) \right) \quad (\text{S38})$$

with

$$w(c_0) = w_0 \sqrt{1 + \frac{(c^2 - c_0^2)^2}{v^4}}, \quad (\text{S39})$$

the width of the Gaussian beam,

$$R(c_0) = w_0 \sqrt{\frac{v^2}{c^2 - c_0^2} + \frac{c^2 - c_0^2}{v^2}}, \quad (\text{S40})$$

its radius of curvature, and

$$\eta(c_0) = \frac{1}{2} \arctan \left[ \frac{c^2 - c_0^2}{v^2} \right], \quad (\text{S41})$$

the Gouy phase which implies a phase jump of  $\pi/2$  in a 2D configuration. The beam waist,  $w_0 = \sqrt{2}/A$ , and the characteristic velocity  $v$  are related as follows:

$$v^2 = \frac{w_0^2 \omega_c}{t}. \quad (\text{S42})$$

If we assume the input/output PSFs of Eq. S36 as Gaussian beams, the incoherent RPSF (Eq. S31) can be expressed as follows:

$$RPSF_{\text{inc}}(\Delta x, c_0) \propto \left( \frac{w_0}{w(c_0)} \right)^{3/4} \exp \left( -\frac{\Delta x^2}{2w^2(c_0)} \right). \quad (\text{S43})$$

As to the coherent RPSF (Eq. S36), the Gaussian approximation leads to the following expression:

$$RPSF_{\text{coh}}(\Delta x, c_0) \propto \frac{w_0}{w(c_0)} \exp \left( -\frac{\Delta x^2}{w^2(c_0)} - j \frac{\Delta x^2}{R^2(c_0)} + 2j\eta(c_0) \right). \quad (\text{S44})$$

## S7. GOUY PHASE SHIFT

Equation S44 shows that the coherent RPSF exhibits a double Gouy phase jump due to the confocal nature of our measurement. In a 2D configuration, this implies a  $\pi$ -phase jump when going through the optimal wave speed, as observed experimentally in Fig. 2G of the accompanying paper. Figure S2 shows the RPSF estimated in a tissue mimicking phantom in a 3D configuration with a  $32 \times 32$  matrix probe. The experimental configuration and the acquisition parameters are described in Ref.<sup>65</sup>. Figure S2 shows the imaginary part of the 2D coherent RPSF extracted by means of the SVD of de-scanned reflection matrix as described by Eqs. 8 and 9 in the accompanying manuscript. Figs. S2B<sub>1</sub> and B<sub>2</sub> shows the two lateral cross-sections of the RPSF that exhibit a rapid phase jump at focus. Figs. S2D displays the evolution of the RPSF phase at  $\Delta \boldsymbol{\rho} = \mathbf{0}$ . In contrast with a 2D configuration, a  $2\pi$ -shape shift is here observed and results from the accumulation of the  $\pi$ -Gouy phase shifts exhibited by the three-dimensional incident and reflected focal spots. The magnitude of the RPSF also shows a maximal value at an optimal speed-of-sound  $\hat{c}_{\text{coh}} = 1575 \text{ m}\cdot\text{s}^{-1}$  (Fig. S2D). The optimized RPSF shows a characteristic Airy beam profile in the focal plane (Figs. S2E). This experiment illustrates the generality of the method which is, of course, not limited to a 2D configuration. Although it requires a larger number of channels (here 1024), a three-dimensional control of the wave-field allows a more efficient focusing process<sup>65</sup> and thus, in theory, a much sharper estimation of the speed-of-sound.



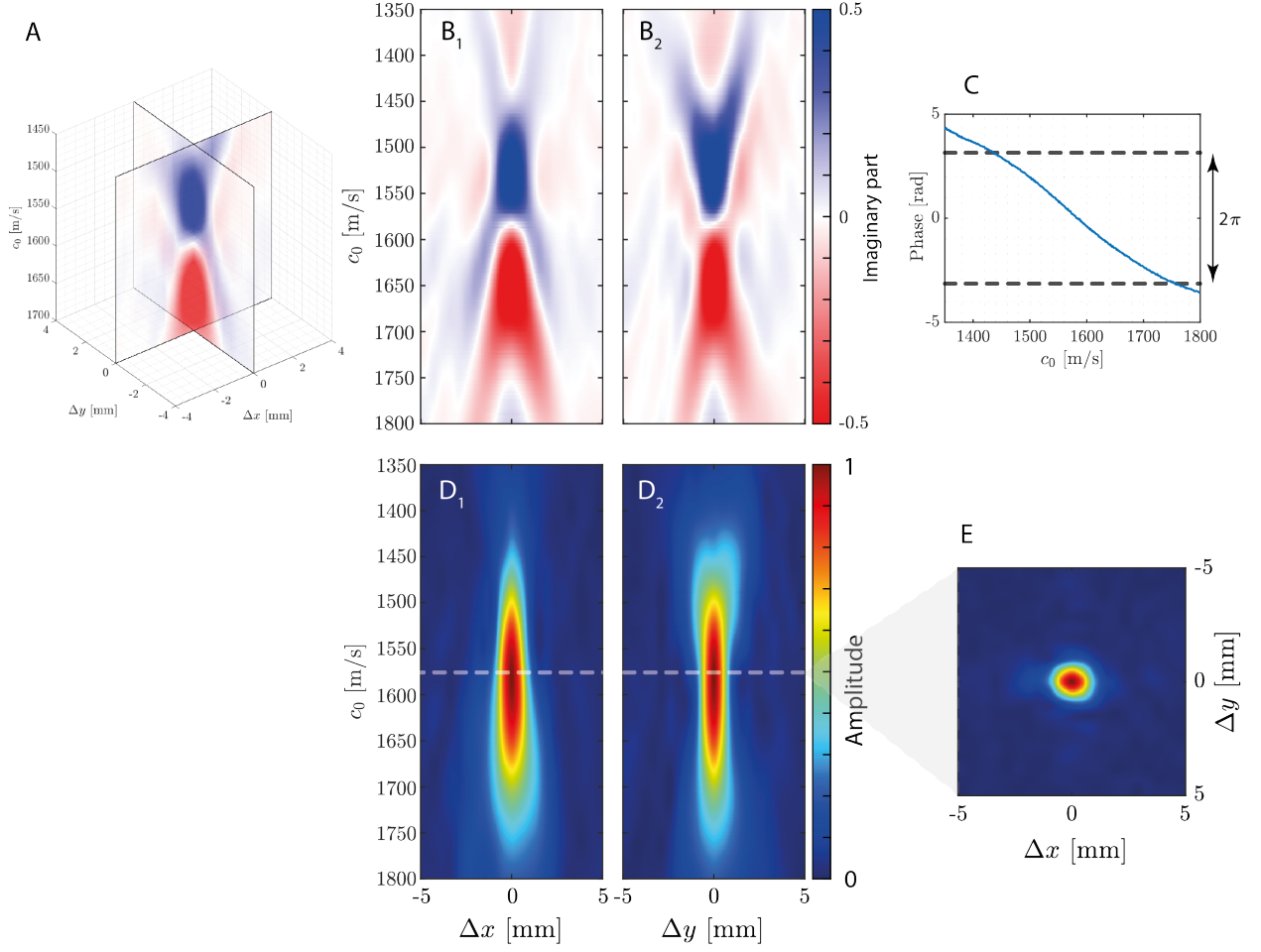


FIG. S2. **Coherent RPSF extracted from speckle in a 3D imaging configuration** (Tissue mimicking phantom experiment). **(A)** 3D view and **(B)** cross-sections of the imaginary part of the coherent RPSF as a function of the wave velocity model  $c_0$ . **(C)** Phase of the coherent RPSF at focus ( $\Delta \rho = 0$ ) as a function of  $c_0$ . **(D)** Cross-sections of the absolute value of the coherent RPSF as a function of the wave velocity model  $c_0$ . **(E)** Transverse cross-section of the RPSF at the optimal wave velocity  $\hat{c}_{\text{coh}} = 1575 \text{ m.s}^{-1}$ .

## S8. UNCERTAINTY

To estimate the uncertainty of our speed-of-sound estimators, a Taylor development can be written around the RPSF maximum at  $\Delta x = 0$ , such that

$$RPSF(c_0) = RPSF(c_0 = c) + \frac{1}{2}(c - c_0)^2 \left( \frac{\partial^2 RPSF}{\partial c_0^2} \right)_{c_0=c} \quad (\text{S45})$$

It leads to the following uncertainty relation:

$$\delta c = \sqrt{\frac{\delta RPSF}{\left| (\partial^2 RPSF / \partial c_0^2)_{c_0=c} \right|}} \quad (\text{S46})$$

with  $\delta c$ , the error of the estimator  $\hat{c}$  and  $\delta RPSF$ , the standard deviation of the RPSF. The fluctuations of the RPSF can be expressed as follows

$$\frac{\delta RPSF_{\text{inc}}}{|RPSF_{\text{inc}}|} = \frac{1}{\beta \sqrt{N_{\mathcal{P}}}} \quad (\text{S47})$$

with  $\beta$ , the signal-to-noise ratio and  $N_{\mathcal{P}}$ , the number of resolution cells contained in each spatial window  $\mathcal{P}$  (Eq. [4]). Injecting the last equation into Eq. S46 leads to the following expression for the error  $\delta c_{\text{inc}}$  of a speed-of-sound estimator based on the incoherent RPSF:

$$\delta c = \frac{1}{\beta^{1/2} N_{\mathcal{P}}^{1/4}} \frac{|RPSF|}{\left| (\partial^2 RPSF / \partial c_0^2)_{c_0=c} \right|} \quad (\text{S48})$$

To go further, Gaussian PSFs are again assumed for sake of analytical tractability. If we first consider the incoherent RPSF (Eq. S43), its second order derivative at  $c_0 = c$  is given by

$$\left( \frac{\partial^2 RPSF_{\text{inc}}}{\partial c_0^2} \right)_{c_0=c} = -3 \frac{c^2}{v^4} \quad (\text{S49})$$

Injecting this last result into Eq. S48 and replacing  $v^2$  by its expression (Eq. S42) lead to the following uncertainty on  $\hat{c}_{\text{inc}}$ :

$$\delta c_{\text{inc}} = \frac{2}{\sqrt{3}} \frac{1}{\beta^{1/2} N_{\mathcal{P}}^{1/4}} \frac{z_R}{t} \quad (\text{S50})$$

with  $z_R = kw_0^2/2$ , the Rayleigh range.

As to the modulus of the coherent RPSF, its second order derivative (Eq. S43) at  $c_0 = c$  is given by

$$\left( \frac{\partial^2 RPSF_{\text{coh}}}{\partial c_0^2} \right)_{c_0=c} = -4 \frac{c^2}{v^4} RPSF_{\text{coh}}(c_0 = c) \quad (\text{S51})$$

Injecting this last result into Eq. S48 and again replacing  $v^2$  by its expression (Eq. S42) lead to the following uncertainty on  $\hat{c}_{\text{coh}}$ :

$$\delta c_{\text{coh}} = \frac{1}{\beta^{1/2} N_{\mathcal{P}}^{1/4}} \frac{z_R}{t} \quad (\text{S52})$$

The wave velocity estimator based on the modulus of the coherent RPSF is therefore slightly better than the incoherent one since  $\delta c_{\text{coh}} = \sqrt{3}\delta c_{\text{inc}}/2$ .

Finally, the second order derivative of the real part of the coherent RPSF (Eq. S43) at  $c_0 = c$  is given by

$$\left( \frac{\partial^2 \mathcal{R}\{RPSF_{\text{coh}}\}}{\partial c_0^2} \right)_{c_0=c} = -20 \frac{c^2}{v^4} RPSF_{\text{coh}}(c_0 = c) \quad (\text{S53})$$

Injecting this last result into Eq. S48 leads to the following uncertainty on  $\hat{c}_{\text{gouy}}$ :

$$\delta c_{\text{gouy}} = \frac{1}{\sqrt{5}} \frac{1}{\beta^{1/2} N_{\mathcal{P}}^{1/4}} \frac{z_R}{t}. \quad (\text{S54})$$

## S9. EFFECT OF THE NUMERICAL APERTURE

Equations S50, S52 and S54 show that the uncertainty  $\delta c$  is directly proportional to the Rayleigh range  $z_R \sim \lambda/NA^2$  and therefore decreases with the numerical aperture  $NA = \sin \alpha$ , with  $\alpha$  the aperture angle. This effect is highlighted by Fig. S3 that shows the  $c_0$ -dependence of the incoherent RPSF (Fig. S3A), the absolute value of the coherent RPSF (Fig. S3B), its real part (Fig. S3C) and its phase (Fig. S3D) along the focusing axis ( $\Delta x = 0$ ) and for different angular apertures. Not surprisingly, a sharper peak is observed for the three first curves around the optimized speed-of-sound value  $c_p$  when the numerical aperture increases (Fig. S3C). This effect is even more drastic on the real part of the RPSF since the Gouy phase jump also becomes steeper at large numerical apertures (Fig. S3D). A sharper RPSF peak implies a larger second order derivative of the RPSF at its maximal value and thus a lower uncertainty on our estimation of the speed-of-sound  $c$  (Eq. S48). Fig. S3 is therefore a striking illustration of the uncertainty reduction scaling as  $NA^{-2}$ .

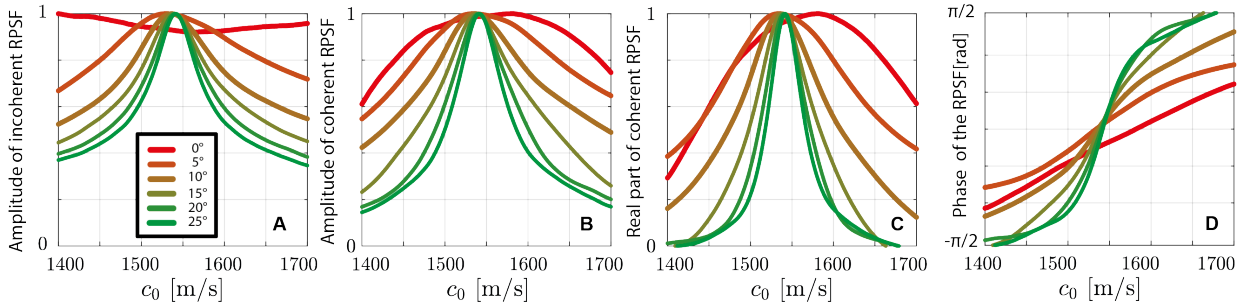


FIG. S3. **Influence of the numerical aperture on the RPSFs.** (A) Amplitude of the confocal component of the incoherent RPSF versus  $c_0$ . (B) Amplitude of the confocal component of the coherent RPSF versus  $c_0$ . (C) Real part of the coherent RPSF versus  $c_0$ . (D) Phase of the coherent RPSF versus  $c_0$ . Each observable is displayed for different numerical apertures from  $\alpha = 0^\circ$  (red) to  $\alpha = 25^\circ$  (green). Results presented here correspond to the tissue mimicking phantom with parameters described in Table 1 of the accompanying paper. The selected point is located at  $\mathbf{r}_p(x_p, t_p) = (0 \text{ mm}, 42.9 \mu\text{s})$  and the average window is  $(p_x, p_t) = (20 \text{ mm}, 2.6 \mu\text{s})$ .

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