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Three-Dimensional Ultrasound Matrix Imaging

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Abstract

Matrix imaging paves the way towards a next revolution in wave physics. Based on the response matrix recorded between a set of sensors, it enables an optimized compensation of aberration phenomena and multiple scattering events that usually drastically hinder the focusing process in heterogeneous media. Although it gave rise to spectacular results in optical microscopy or seismic imaging, the success of matrix imaging has been so far relatively limited with ultrasonic waves because wave control is generally only performed with a linear array of transducers. In this paper, we extend ultrasound matrix imaging to a 3D geometry. Switching from a 1D to a 2D probe enables a much sharper estimation of the transmission matrix that links each transducer and each medium voxel. Here, we first present an experimental proof of concept on a tissue-mimicking phantom through ex-vivo tissues and then, show the potential of 3D matrix imaging for transcranial applications.

9 Introduction

10 The resolution of a wave imaging system can be defined as the ability to dis-
11 cern small details of an object. In conventional imaging, this resolution cannot
12 overcome the diffraction limit of a half wavelength and may be further limited
13 by the maximum collection angle of the imaging device. However, even with a
14 perfect imaging system, the image quality is affected by the inhomogeneities of
15 the propagation medium. Large-scale spatial variations of the wave velocity in-
16 troduce aberrations as the wave passes through the medium of interest. Strong
17 concentration of scatterers also induces multiple scattering events that randomize
18 the directions of wave propagation, leading to a strong degradation of the image
19 resolution and contrast. Such problems are encountered in all domains of wave
20 physics, in particular for the inspection of biological tissues, whether it be by ul-
21 trasound imaging¹ or optical microscopy², or for the probing of natural resources
22 or deep structure of the Earth's crust with seismic waves³.

23 To mitigate those problems, the concept of adaptive focusing has been adapted
24 from astronomy where it was developed decades ago^{4,5}. Ultrasound imaging em-
25 ploys array of transducers that allows to control and record the amplitude and
26 phase of broadband wave-fields. Wave-front distortions can be compensated for
27 by adjusting the time-delays added to each emitted and/or detected signal in order
28 to focus ultrasonic waves at a certain position inside the medium⁶⁻⁹. The estima-
29 tion of those time delays implies an iterative time-consuming focusing process that
30 should be ideally repeated for each point in the field-of-view^{10,11}. Such a complex
31 adaptive focusing scheme cannot be implemented in real time since it is extremely
32 sensitive to motion¹² whether induced by the operator holding the probe or by the
33 movement of tissues.

34 Fortunately, this tedious process can now be performed in post-processing^{13,14}
35 thanks to the tremendous progress made in terms of computational power and
36 memory capacity during the last decade. To optimize the focusing process and

37 image formation, a matrix formalism can be fruitful^{15–18}. Indeed, once the reflec-
38 tion matrix \mathbf{R} of the impulse responses between each transducer is known, any
39 physical experiment can be achieved numerically, either in a causal or anti-causal
40 way, for any incident beam and as many times as desired. More specifically, assum-
41 ing that the medium remains fixed during the acquisition, a multi-scale analysis
42 of the wave distortions can be performed to build an estimator of the transmis-
43 sion matrix \mathbf{T} between each transducer of the probe and each voxel inside the
44 medium¹⁹. Once the \mathbf{T} -matrix is known, a local compensation of aberrations can
45 be performed for each voxel, thereby providing a confocal image of the medium
46 with a close to ideal resolution and an optimized contrast everywhere.

47 Although it gave rise to striking results in optical microscopy^{20–24} or seismic
48 imaging^{25,26}, the experimental demonstration of matrix imaging has been, so far,
49 less spectacular with ultrasonic waves^{17,18,27,28}. Indeed, the first proof-of-concept
50 experiments employed a linear array of transducers. Yet, aberrations in the human
51 body are 3D-distributed and a 1D control of the wave-field is not sufficient for a fine
52 compensation of wave-distortions as already shown by previous works^{29–32}. More-
53 over, 2D imaging limits the density of independent speckle grains which controls
54 the spatial resolution of the \mathbf{T} -matrix estimator²⁸.

55 In this work, we extend the ultrasound matrix imaging (UMI) framework to
56 3D using a fully populated matrix array of transducers^{33–35}. The overall method
57 is first validated by means of a well-controlled experiment combining ex-vivo pork
58 tissues as aberrating layer on top of a tissue-mimicking phantom. 3D UMI is
59 then applied to a head phantom whose skull induces a strong attenuation, aber-
60 ration and multiple scattering of the ultrasonic wave-field, phenomena that UMI
61 can quantify independently of each other^{1,19}. Inspired by the CLASS method de-
62 veloped in optical microscopy^{20,22}, aberrations are here compensated by a novel
63 iterative phase reversal algorithm more efficient for 3D UMI than a singular value
64 decomposition^{16–18}. In contrast with previous works, the convergence of this algo-

65 rithm is ensured by investigating the spatial reciprocity between the \mathbf{T} -matrices
66 in transmission and reception. Throughout the paper, we will compare the gain
67 in terms of resolution and contrast provided by 3D UMI with respect to its 2D
68 counterpart. In particular, we will demonstrate how 3D UMI can be a powerful
69 tool for optimizing the focusing process inside the brain through the skull.

70 Results

72 Beamforming the reflection matrix in a focused basis.

73 3D UMI starts with the acquisition of the reflection matrix (see Methods) by
74 means of a 2D array of transducers (32×32 elements, see Fig. 1a,b). It was per-
75 formed first on a tissue-mimicking phantom with nylon rods through a layer of pork
76 tissue of fat and muscle (obtained from a chop rib piece), acting as an aberrating
77 layer [Fig. 2a], and then on a head phantom including brain and skull-mimicking
78 tissue, to reproduce transcranial imaging (see below). In the first experiment, the
79 reflection matrix $\mathbf{R}_{\mathbf{uu}}(t)$ is recorded in the transducer basis [Fig. 1a,c], *i.e.* by
80 acquiring the impulse responses, $R(\mathbf{u}_{\text{in}}, \mathbf{u}_{\text{out}}, t)$, between each transducer (\mathbf{u}) of
81 the probe. In the head phantom experiment, skull attenuation imposes a plane
82 wave insonification sequence [Fig. 1b] to improve the signal-to-noise ratio. The
83 reflection matrix $\mathbf{R}_{\boldsymbol{\theta}\mathbf{u}}$ then contains the reflected wave-field $R(\boldsymbol{\theta}_{\text{in}}, \mathbf{u}_{\text{out}}, t)$ recorded
84 by the transducers \mathbf{u}_{out} [Fig. 1c] for each incident plane wave of angle $\boldsymbol{\theta}_{\text{in}}$.

85 Whatever the illumination sequence, the reflectivity of a medium at a given
86 point \mathbf{r} can be estimated in post-processing by a coherent compound of incident
87 waves delayed to virtually focus on this point, and coherently summing the echoes
88 recorded by the probe coming from that same point [Fig. 1d]. UMI basically
89 consists in decoupling the input (\mathbf{r}_{in}) and output (\mathbf{r}_{out}) focusing points [Fig. 1e]. By
90 applying appropriate time delays to the transmission ($\mathbf{u}_{\text{in}}/\boldsymbol{\theta}_{\text{in}}$) and reception (\mathbf{u}_{out})
91 channels (see Methods), $\mathbf{R}_{\mathbf{uu}}(t)$ and $\mathbf{R}_{\boldsymbol{\theta}\mathbf{u}}(t)$ can be projected at each depth z in a
92 focused basis, thereby forming a broadband focused reflection matrix, $\mathbf{R}_{\boldsymbol{\rho}\boldsymbol{\rho}}(z) \equiv$

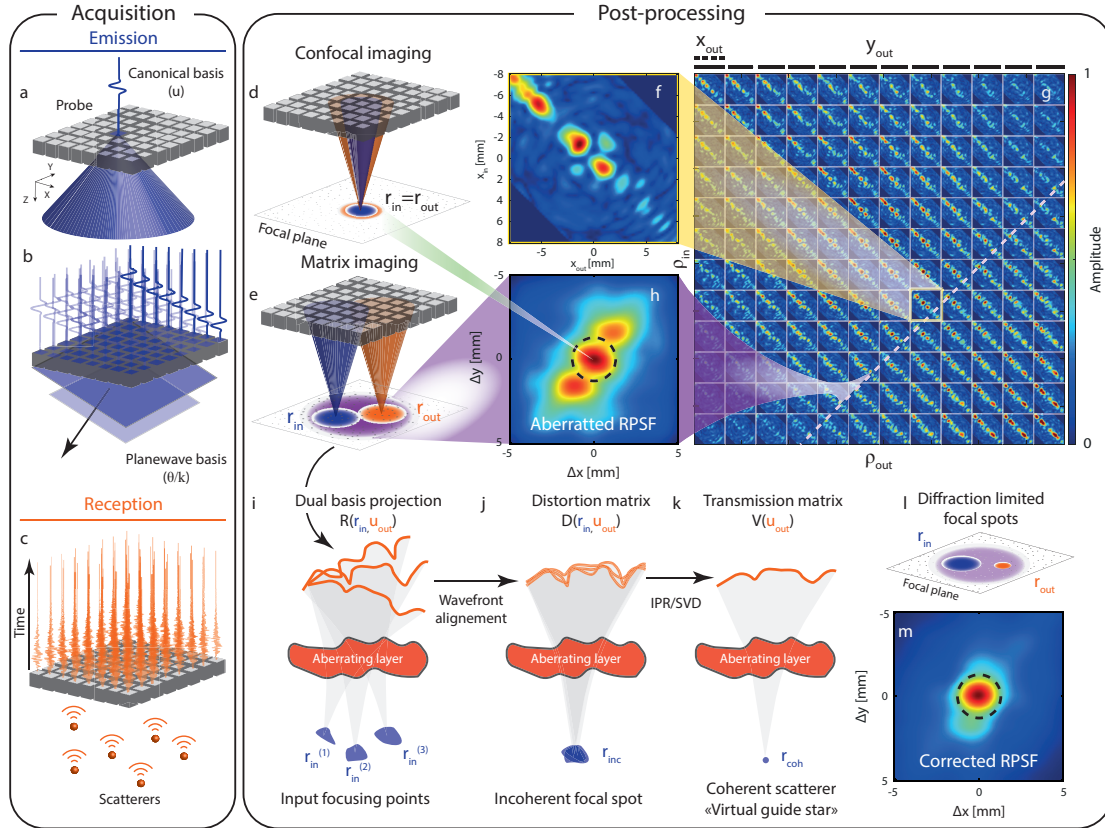


FIG. 1. **3D Ultrasound Matrix Imaging (UMI)**. (a,b) The \mathbf{R} -matrix can be acquired in the transducer (a) or plane-wave (b) basis in transmit and (c) recording the back-scattered wave-field on each transducer in receive. (d) Confocal imaging consists in a simultaneous focusing of waves at input and output. (e) In UMI, the input (r_{in}) and output (r_{out}) focusing points are decoupled. (f) x -cross-section of the (g) focused \mathbf{R} -matrix. (h) UMI enables a quantification of aberrations by extracting a local RPSF (displayed here in amplitude) from each antidiagonal of $\mathbf{R}_{\rho\rho}(z)$. (i) UMI then consists in a projection of the focused \mathbf{R} -matrix in a correction (here transducer) basis at output. The resulting dual \mathbf{R} -matrix connects each focusing point to its reflected wave-front. (j) UMI then consists in realigning those wave-fronts to isolate their distorted component from their geometrical counterpart, thereby forming the \mathbf{D} -matrix. (k) An iterative phase reversal algorithm provides an estimator of the \mathbf{T} -matrix between the correction basis and the mid-point of input focusing points considered in panel g. (l) The phase conjugate of the \mathbf{T} -matrix provides a focusing law that improves the focusing process at output. (m) RPSF amplitude after the output UMI process. The ultrasound data shown in this figure corresponds to the pork tissue experiment at depth $z = 40$ mm.

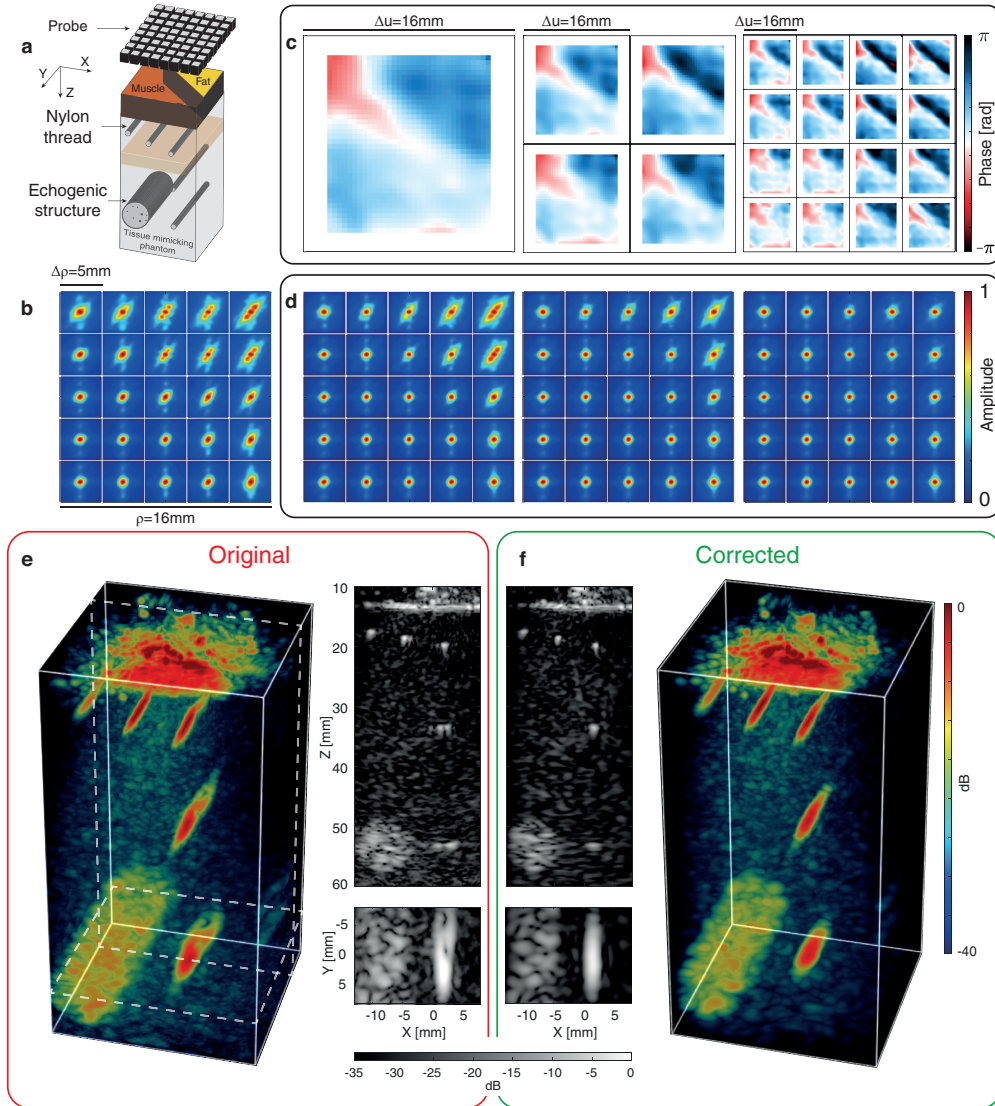


FIG. 2. **Ultrasound matrix imaging of a tissue-mimicking phantom through a pork tissue.** (a) Schematic of the experiment. (b) Maps of original RPSFs (in amplitude) at depth $z = 29$ mm. (c) Aberration phase laws extracted at the different steps of the UMI process. (d) Corresponding RPSFs after aberration compensation at each step. (e,f) 3D confocal and UMI images with one longitudinal and transverse cross-section.

93 $[R(\boldsymbol{\rho}_{\text{in}}, \boldsymbol{\rho}_{\text{out}}, z)]$.

94 Since the focal plane is bi-dimensional, each matrix $\mathbf{R}_{\rho\rho}(z)$ has a four-dimension
 95 structure: $R(\boldsymbol{\rho}_{\text{in}}, \boldsymbol{\rho}_{\text{out}}, z) = R(\{x_{\text{in}}, y_{\text{in}}\}, \{x_{\text{out}}, y_{\text{out}}\}, z)$. $\mathbf{R}_{\rho\rho}(z)$ is thus concate-

96 nated in 2D as a set of block matrices to be represented graphically [Fig. 1g]. In
 97 such a representation, every sub-matrix of \mathbf{R} corresponds to the reflection matrix
 98 between lines of virtual transducers located at y_{in} and y_{out} , whereas every ele-
 99 ment in the given sub-matrix corresponds to a specific couple $(x_{\text{in}}, x_{\text{out}})$ [Fig. 1e].
 100 Each coefficient $R(x_{\text{in}}, y_{\text{in}}, x_{\text{out}}, y_{\text{out}}, z)$ corresponds to the complex amplitude of
 101 the echoes coming from the point $\mathbf{r}_{\text{out}} = (x_{\text{out}}, y_{\text{out}}, z)$ in the focal plane when fo-
 102 cusing at point $\mathbf{r}_{\text{in}} = (x_{\text{in}}, y_{\text{in}}, z)$ (or conversely, since $\mathbf{R}_{\rho\rho}(z)$ is a symmetric matrix
 103 due to spatial reciprocity).

104 As already shown with 2D UMI, the diagonal of $\mathbf{R}_{\rho\rho}(z)$ directly provides the
 105 transverse cross-section of the confocal ultrasound image:

$$\mathcal{I}(\boldsymbol{\rho}, z) = |R(\boldsymbol{\rho}_{\text{in}} = \boldsymbol{\rho}_{\text{out}}, z)|^2 \quad (1)$$

106 where $\boldsymbol{\rho} = \boldsymbol{\rho}_{\text{in}} = \boldsymbol{\rho}_{\text{out}}$ is the transverse coordinate of the confocal point. The
 107 corresponding 3D image is displayed in Fig. 2e for the pork tissue experiment.
 108 Longitudinal and transverse cross-sections illustrate the effect of the aberrations
 109 induced by the pork layer by highlighting the distortion exhibited by the image of
 110 the deepest nylon rod.

111 **Probing the focusing quality.**

112 We now show how to quantify aberrations in ultrasound speckle (without any
 113 guide star) by investigating the antidiagonals of $\mathbf{R}_{\rho\rho}(z)$. In the single scattering
 114 regime, the focused \mathbf{R} -matrix coefficients can be expressed as follows¹:

$$R(\boldsymbol{\rho}_{\text{out}}, \boldsymbol{\rho}_{\text{in}}, z) = \int d\boldsymbol{\rho} H_{\text{out}}(\boldsymbol{\rho} - \boldsymbol{\rho}_{\text{out}}, \boldsymbol{\rho}_{\text{out}}, z) \gamma(\boldsymbol{\rho}, z) H_{\text{in}}(\boldsymbol{\rho} - \boldsymbol{\rho}_{\text{in}}, \boldsymbol{\rho}_{\text{in}}, z) \quad (2)$$

115 with $H_{\text{in/out}}$, the input/output point spread function (PSF); and γ the medium
 116 reflectivity. This last equation shows that each pixel of the ultrasound image (diag-
 117 onal elements of $\mathbf{R}_{\rho\rho}(z)$) results from a convolution between the sample reflectivity
 118 and an imaging PSF, which is itself a product of the input and output PSFs. The

119 off-diagonal points in $\mathbf{R}_{\rho\rho}(z)$ can be exploited for a quantification of the focusing
 120 quality at any pixel of the ultrasound image by extracting each antidiagonal. Such
 121 an operation is mathematically equivalent to a change of variable to express the
 122 focused \mathbf{R} -matrix in a common midpoint basis¹ (see Supplementary Section 2):

$$R_{\mathcal{M}}(\Delta\rho, \mathbf{r}_m) = R\left(\rho_m - \frac{\Delta\rho}{2}, \rho_m + \frac{\Delta\rho}{2}, z\right), \quad (3)$$

123 where the subscript \mathcal{M} stands for the common midpoint basis. $\mathbf{r}_m = \{\rho_m, z\} =$
 124 $\{(\rho_{\text{in}} + \rho_{\text{out}})/2, z\}$ is the common midpoint between the input and output focal
 125 spots, with the two separated by a distance $\Delta\rho = \rho_{\text{out}} - \rho_{\text{in}}$.

126 In the speckle regime (random reflectivity), this quantity probes the local fo-
 127 cusing quality as its ensemble average intensity, which we refer to as the *reflection*
 128 *point spread function* (RPSF), scales as an incoherent convolution between the
 129 input and output PSFs¹:

$$RPSF(\Delta\rho, \mathbf{r}_m) = \langle |R_{\mathcal{M}}(\Delta\rho, \mathbf{r}_m)|^2 \rangle \propto |H_{\text{in}}|^2 \overset{\Delta\rho}{\otimes} |H_{\text{out}}|^2(\Delta\rho, \mathbf{r}_m), \quad (4)$$

130 where $\langle \dots \rangle$ denotes an ensemble average, which, in practice, is performed by a
 131 local spatial average (see Methods).

132 Figure 1h displays the mean RPSF associated with the focused \mathbf{R} -matrix dis-
 133 played in Fig. 1g (pork tissue experiment). It clearly shows a distorted RPSF
 134 which spreads well beyond the diffraction limit (black dashed line in Fig. 1h):

$$\delta\rho_0(z) \sim \frac{\lambda_c}{2 \sin \{\arctan [\Delta u / (2z)]\}} \quad (5)$$

135 with Δu the lateral extension of the probe. The RSPF also exhibits a strong
 136 anisotropy that could not have been grasped by 2D UMI. As we will see in the
 137 next section, this kind of aberrations can only be compensated through a 3D
 138 control of the wave-field.

139 **Adaptive focusing by iterative phase reversal.**

140 Aberration compensation in the UMI framework is performed using the distortion matrix concept. Introduced for 2D UMI^{17,28}, the distortion matrix can be
141 obtained by: (i) projecting the focused \mathbf{R} -matrix either at input or output in
142 a correction basis (here the transducer basis, see Fig. 1i); (ii) extracting wave
143 distortions exhibited by \mathbf{R} when compared to a reference matrix that would have
144 been obtained in an ideal homogeneous medium of wave velocity c_0 [Fig. 1j]. The
145 resulting distortion matrix $\mathbf{D} = [D(\mathbf{u}, \mathbf{r})]$ contains the aberrations induced when
146 focusing on any point \mathbf{r} , expressed in the correction basis.

148 This matrix exhibits long-range correlations that can be understood in light of
149 isoplanicity. If in a first approximation, the pork tissue layer can be considered as
150 a phase screen aberrator, then the input and output PSFs can be considered as
151 spatially invariant: $H_{\text{in/out}}(\boldsymbol{\rho} - \boldsymbol{\rho}_{\text{in/out}}, \mathbf{r}_{\text{in/out}}) = H(\boldsymbol{\rho} - \boldsymbol{\rho}_{\text{in/out}})$. UMI consists in
152 exploiting those correlations to determine the transfer function $T(\mathbf{u})$ of the phase
153 screen. In practice, this is done by considering the correlation matrix $\mathbf{C} = \mathbf{D} \times \mathbf{D}^\dagger$.
154 The correlation between distorted wave-fields enables a virtual reflector synthesized
155 from the set of output focal spots¹⁷ [Fig. 1k]. While, in previous works^{17,19}, an
156 iterative time-reversal process (or equivalently a singular value decomposition of
157 \mathbf{D}) was performed to converge towards the incident wavefront that focuses perfectly
158 through the medium heterogeneities onto this virtual scatterer, here an iterative
159 phase reversal algorithm is employed to build an estimator $\hat{T}(\mathbf{u})$ of the transfer
160 function (see Methods). Supplementary Figure 3 demonstrates the superiority of
161 this algorithm compared to SVD for 3D UMI.

162 Iterative phase reversal provides an estimation of aberration transmittance
163 [Fig. 1k] whose phase conjugate is used to compensate for wave distortions (see
164 Methods). The resulting mean RPSF is displayed in Fig. 1m. Although it shows
165 a clear improvement compared with the initial RPSF, high-order aberrations still
166 subsist. Because of its 3D feature, the pork tissue layer cannot be fully reduced to

167 an aberrating phase screen in the transducer basis.

168 **Spatial reciprocity as a guide star.**

169 The 3D distribution of the speed-of-sound breaks the spatial invariance of input
170 and output PSFs. Figure 2b illustrates this fact by showing a map of local RPSFs
171 (see Methods). The RPSF is more strongly distorted below the fat layer of the
172 pork tissue ($c_f \approx 1480 \pm 10$ m/s³⁶) than below the muscle area ($c_m \approx 1560 \pm 50$
173 m/s). A full-field compensation of aberrations similar to adaptive focusing does
174 not allow a fine compensation of aberrations [Fig. 2d1]. Access to the transmission
175 matrix $\mathbf{T} = [T(\mathbf{u}, \mathbf{r})]$ linking each transducer and each medium voxel is required
176 rather than just a simple aberration transmittance $T(\mathbf{u})$.

177 To that aim, a local correlation matrix $\mathbf{C}(\mathbf{r}_p)$ should be considered around each
178 point \mathbf{r}_p over a sliding box $\mathcal{W}(\mathbf{r} - \mathbf{r}_p)$ (see Methods), commonly called patches,
179 whose choice of spatial extent w is subject to the following dilemma: On the
180 one hand, the spatial window should be as small as possible to grasp the rapid
181 variations of the PSFs across the field of view; on the other hand, these areas should
182 be large enough to encompass a sufficient number of independent realizations of
183 disorder^{16,19}. The bias made on our \mathbf{T} -matrix estimator actually scales as (see
184 Supplementary Section 6):

$$|\delta T(\mathbf{u}, \mathbf{r}_p)|^2 \sim \frac{1}{\mathcal{C}^2 N_{\mathcal{W}}}. \quad (6)$$

185 \mathcal{C} is the so-called coherence factor that is a direct indicator of the focusing quality⁸
186 but that also depends on the multiple scattering rate and noise background²⁸. $N_{\mathcal{W}}$
187 is the number of diffraction-limited resolution cells in each spatial window.

188 The validity of the \mathbf{T} -matrix estimator in a region \mathcal{W}_1 (Fig. 3c) is investigated
189 by examining the corrected RPSF in a neighbour region \mathcal{W}_2 (yellow box). \mathcal{W}_1 and
190 \mathcal{W}_2 are sufficiently close to assume, in a first approximation, that they belong to the
191 same isoplanatic patch. If the box is too small (left of Fig. 3d), our estimator has

192 not converged yet and the correction is not valid, as shown by the degraded quality
 193 of the RPSF in \mathcal{W}_2 [left panel of Fig. 3h] compared to its initial value [Fig. 3g]. With
 194 sufficient spatial averaging [third panel of Fig. 3d], a valid aberration law can be
 195 extracted, as shown by a corrected RPSF now close to be only diffraction-limited
 196 [third panel of Fig. 3h].

197 The question that now arises is how we can, in practice, know if the convergence
 198 of $\hat{\mathbf{T}}$ is fulfilled without any *a priori* knowledge on \mathbf{T} . An answer can be found
 199 by comparing the estimated input and output aberration phase laws, $\hat{T}_{\text{in}}(\mathbf{u}, \mathbf{r}_p)$
 200 and $\hat{T}_{\text{out}}(\mathbf{u}, \mathbf{r}_p)$, at a given point \mathbf{r}_p as shown in Figs. 3e and f. Spatial reciprocity
 201 implies that \hat{T}_{in} and \hat{T}_{out} shall be equal when the convergence of the estimator is
 202 reached [third panel of Figs. 3e and f]. Their normalized scalar product, $P_{\text{in/out}} =$
 203 $N_u^{-1} \hat{\mathbf{T}}_{\text{in}} \hat{\mathbf{T}}_{\text{out}}^\dagger$, can thus be used to probe the error made on the aberration phase law
 204 $|\delta T|^2$. Both quantities are actually related as follows (see Supplementary Section
 205 7):

$$|\delta T|^2 \simeq 1 - P_{\text{in/out}}. \quad (7)$$

206 The normalized scalar product $P_{\text{in/out}}$ is displayed as a function of w and shows
 207 the convergence of the IPR process [Fig. 3a]. For a sufficiently large box [third
 208 panel of Fig. 3d], $\hat{\mathbf{T}}$ is supposed to have converged towards \mathbf{T} when $\hat{\mathbf{T}}_{\text{in}}$ and $\hat{\mathbf{T}}_{\text{out}}$
 209 are almost equal [third panel of Fig. 3e,f], while, for a small box [left panel of
 210 Fig. 3d], a large discrepancy can be found between them. In the following, the
 211 parameter $P_{\text{in/out}}$ will thus be used as a guide star for monitoring the convergence
 212 of the UMI process.

213 The scaling law of Eq. 6 with respect to $N_{\mathcal{W}}$ is checked in Fig. 3b. The in-
 214 verse scaling of the bias with $N_{\mathcal{W}}$ shows the advantage of 3D UMI over 2D UMI,
 215 since $N_{\mathcal{W}} \sim w^d$, with d the imaging dimension. This superiority is evident in
 216 Fig. 3a, which shows a faster convergence with 3D boxes (green curve) than with
 217 2D patches (orange curve). For a given precision, 3D UMI thus provides a better
 218 spatial resolution for our \mathbf{T} -matrix estimator as shown by right panels of Figs. 3f,

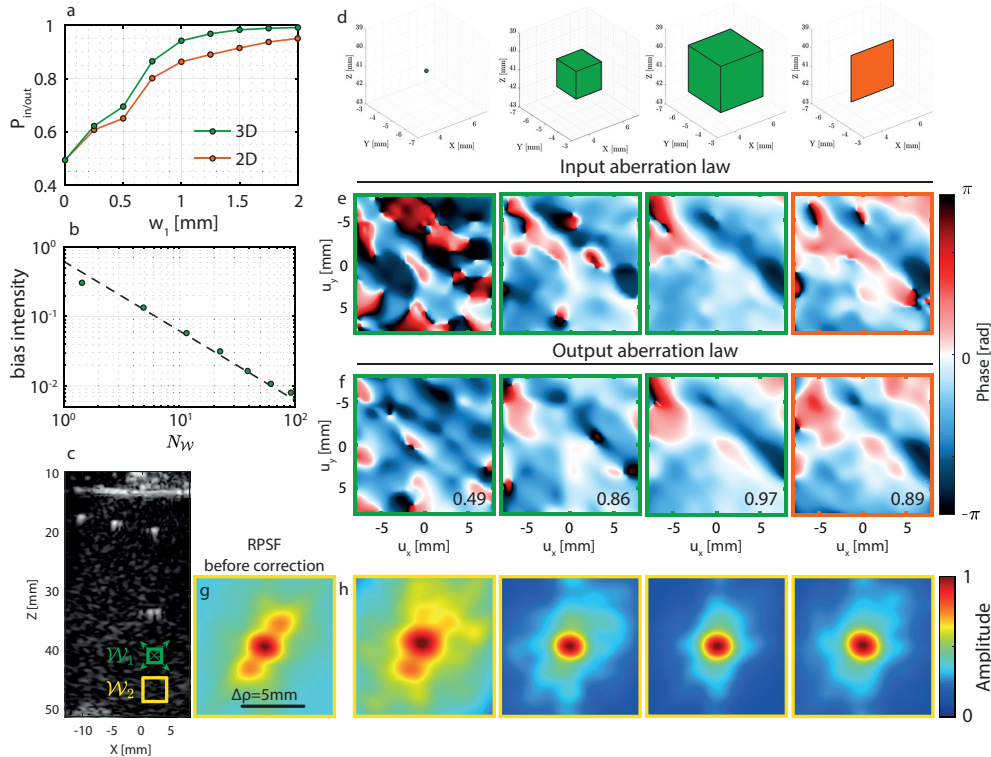


FIG. 3. **Convergence of the UMI process towards the T-matrix.** (a) Normalized scalar product $P_{\text{in/out}}$ extracted at a point \mathbf{r}_1 (c) as a function of the size w_1 of the considered spatial window \mathcal{W}_1 for 2D (orange) and 3D (green) imaging. (b) Corresponding bias intensity estimator, $|\delta T|^2 = 1 - P_{\text{in/out}}$, as a function of the number of resolution cells $N_{\mathcal{W}}$ contained in the window \mathcal{W}_1 . The plot is in log-log scale and the theoretical power law (Eq. 6) is shown with a dashed black line for comparison. (c) Cross-section of the confocal volume showing the location of \mathcal{W}_1 in green and \mathcal{W}_2 in yellow. The green box \mathcal{W}_1 , centered around the point $\mathbf{r}_1 = (5, -5, 41)$ mm, denotes the region where the $\hat{\mathbf{T}}$ -matrix is extracted, while the yellow box \mathcal{W}_2 , of fixed size $w_2 = 2$ mm and centered around the point $\mathbf{r}_2 = (5, -5, 45)$ mm, is the area where the effect of aberration correction is investigated by means of the RPSF. (d) Spatial windows \mathcal{W}_1 considered for the calculation of $\mathbf{C}(\mathbf{r}_1)$. From left to right: Boxes of dimension $w = 0$ mm, $w = 0.75$ mm, $w = 1.25$ mm, rectangle of dimension $w = 1.25$ mm. (e,f) Corresponding input $\hat{\mathbf{T}}_{\text{in}}$ and output $\hat{\mathbf{T}}_{\text{out}}$ aberration laws, respectively. The scalar product $P_{\text{in/out}}$ is displayed in each sub-panel of (f). (g) Original RPSF associated with the yellow box \mathcal{W}_2 before correction and (h) after correction using the corresponding $\hat{\mathbf{T}}$ -matrices displayed in panels (e) and (f).

219 where much better agreement between $\hat{\mathbf{T}}_{\text{in}}$ and $\hat{\mathbf{T}}_{\text{out}}$ is observed for a 3D box [third

220 panel of Fig. 3d] than for a 2D patch [right panel of Fig. 3d] of same dimension w .

221 **Multi-scale compensation of wave distortions.**

222 The scaling of the bias intensity $|\delta T|^2$ with the coherence factor \mathcal{C} has not
223 been discussed yet. This dependence is however crucial since it indicates that a
224 gradual compensation of aberrations shall be favored rather than a direct partition
225 of the field-of-view into small boxes²² (see Supplementary Fig. 4). An optimal
226 UMI process should proceed as follows: first, compensate for input and output
227 wave distortions at a large scale to increase the coherence factor \mathcal{C} ; then, decrease
228 the spatial window \mathcal{W} and improve the resolution of the \mathbf{T} -matrix estimator.
229 The whole process can be iterated, leading to a multi-scale compensation of wave
230 distortions (see Methods). As explained above, the convergence of the process is
231 monitored using spatial reciprocity ($P_{\text{in/out}} > 0.9$).

232 The result of 3D UMI is displayed in Fig. 2. It shows the evolution of the
233 \mathbf{T} -matrix at each step [Fig. 2c] and the corresponding local RPSFs [Fig. 2d].
234 In the most aberrated area (*i.e.* under the fat), the phase fluctuations of the
235 aberration law corresponds to a time delay spread of 56 ns (rms). This value is
236 comparable with past measurements through the human abdominal wall³⁷. The
237 pork tissue layer thus induces a level of aberrations typical of standard ultrasound
238 diagnosis. The comparison with the initial and full-field maps of RPSF highlights
239 the benefit of a local compensation via the \mathbf{T} -matrix, with a diffraction-limited
240 resolution reached everywhere. The local aberration phase laws exhibited by $\hat{\mathbf{T}}$
241 perfectly match with the distribution of muscle and fat in the pork tissue layer.
242 The comparison of the final 3D image [Fig. 2f] and its cross-sections with their
243 initial counterparts [Fig. 2e] show the success of the UMI process, in particular
244 for the deepest nylon rod, which has retrieved its straight shape. The local RPSF
245 on the top right of Fig.2 shows a contrast improvement by 4.2 dB and resolution
246 enhancement by a factor 2 (see Methods and Supplementary Fig. 5).

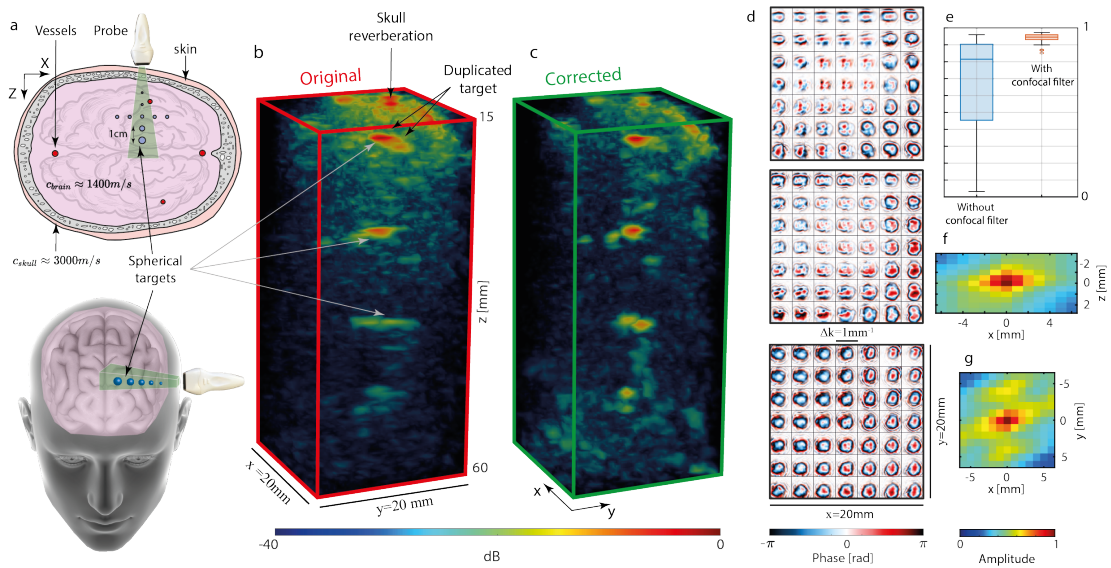


FIG. 4. **Ultrasound Matrix Imaging (UMI) of the head phantom.** (a) Top and oblique views of the experimental configuration. Image credits: Harryarts and kjpargeter on Freepik. (b,c) Original and UMI images, respectively. (d) Aberration laws at 3 different depths. From top to bottom: $z = 20$ mm, $z = 32$ mm, $z = 60$ mm. (e) Reciprocity criterion $P_{in/out}$ with or without the use of a confocal filter: Each box chart displays the median, lower and upper quartiles, and the minimum and maximum values. (f,g). Correlation function of the $\hat{\mathbf{T}}$ -matrix in the (x, z) -plane (f) and (x, y) -plane (g), respectively. We attribute the sidelobes along the y -axis (g) to the inactive rows separating each block of 256 elements of the matrix array.

247 Overcoming multiple scattering for trans-cranial imaging

248 The same UMI process is now applied to the ultrasound data collected on the
 249 head phantom [Fig. 4a]. The parameters of the multi-scale analysis are provided in
 250 the Methods section (see also Supplementary Fig. 6). The first difference with the
 251 pork tissue experiment lies in our choice of correction basis. Given the multi-layer
 252 configuration in this experiment, the \mathbf{D} -matrix is investigated in the plane wave
 253 basis¹⁷.

254 The second difference is that our spatial reciprocity criterion $P_{in/out}$ is very low
 255 [see the blue box plot in Fig. 4e]. This is the manifestation of a bad convergence
 256 of our \mathbf{T} -matrix estimator. The incoherent background exhibited by the original

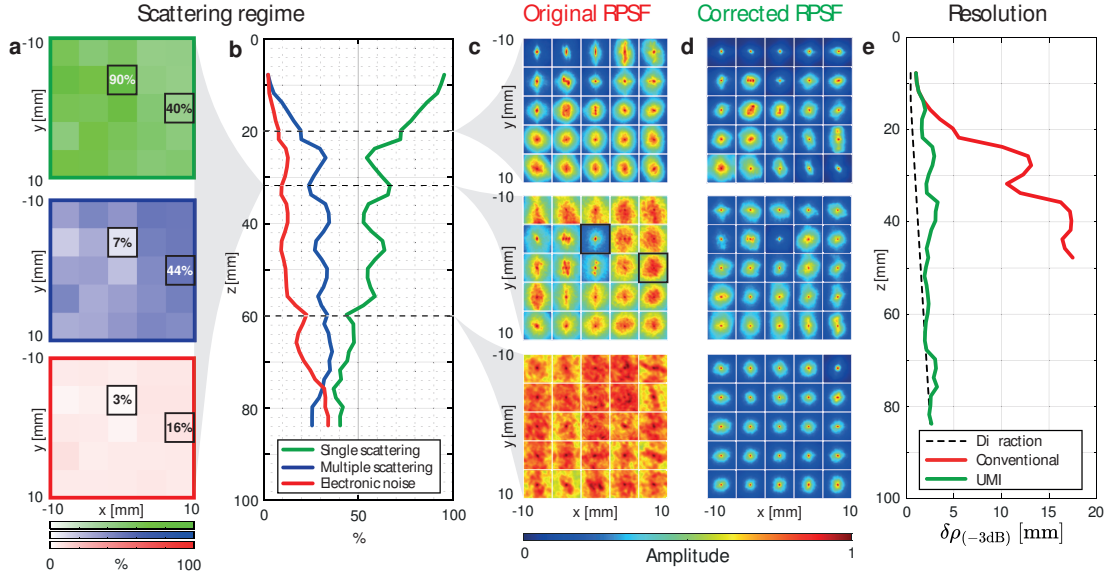


FIG. 5. **Aberrations and multiple scattering quantification.** (a) Single scattering (green), multiple scattering (blue) and noise (red) rate at $z = 32$ mm. (b) Single scattering, multiple scattering, and noise rates as a function of depth. (c,d) Maps of local RPSFs (in amplitude) before and after correction, respectively, at three different depths (From left to right: $z = 20$ mm, 32 mm and 60 mm. Black boxes in panel (a) and (c) corresponds to the same area. (e) Resolution $\delta\rho_{(-3dB)}$ as a function of depth. Initial resolution (red line) and its value after UMI (green line) are compared with the ideal (diffraction-limited) resolution (Eq. 5).

257 PSFs [Fig. 5c] drastically affects the coherence factor \mathcal{C}^{28} , which, in return, gives
 258 rise to a strong bias on the \mathbf{T} -matrix estimator (Eq. 6). The incoherent back-
 259 ground is due to multiple scattering events in the skull and electronic noise, whose
 260 relative weight can be estimated by investigating the spatial reciprocity symmetry
 261 of the \mathbf{R} -matrix (see Methods). Fig. 5b shows the depth evolution of the single
 262 and multiple scattering contributions, as well as electronic noise. While single
 263 scattering dominates at shallow depths ($z < 20$ mm), multiple scattering quickly
 264 reaches 35% and remains relatively constant until electronic noise increases, so
 265 that the three contributions are almost equal at depths of 75 mm.

266 Beyond the depth evolution, 3D imaging even allows the study of multiple
 267 scattering in the transverse plane, as shown in Figure 5a. Two areas are examined,

268 marked with black boxes, corresponding to the RPSFs shown in [Fig. 5c] ($z = 32$
 269 mm). In the center, the RPSFs exhibits a low background due to the presence
 270 of a spherical target, resulting in a single scattering rate of 90%. The second
 271 box on the right, however, is characterized by a much higher background, leading
 272 to a multiple-to-single scattering ratio slightly larger than one. This high level
 273 of multiple scattering highlights the difficult task of trans-cranial imaging with
 274 ultrasonic waves.

275 In order to overcome these detrimental effects, an adaptive confocal filter can
 276 be applied to the focused \mathbf{R} -matrix¹⁹.

$$R'(\boldsymbol{\rho}_{\text{in}}, \boldsymbol{\rho}_{\text{out}}, z) = R(\boldsymbol{\rho}_{\text{in}}, \boldsymbol{\rho}_{\text{out}}, z) \exp\left(-\frac{|\boldsymbol{\rho}_{\text{out}} - \boldsymbol{\rho}_{\text{in}}|^2}{2l_c(z)^2}\right) \quad (8)$$

277 This filter has a Gaussian shape, with a width $l_c(z)$ that scales as $3\delta\rho_0(z)^{19}$. The
 278 application of a confocal filter drastically improves the correlation between input
 279 and output aberration phase laws (see Fig. 4e and Supplementary Fig. 7), proof
 280 that a satisfying convergence towards the \mathbf{T} -matrix is obtained.

281 Figure 4d shows the \mathbf{T} -matrix obtained at different depths in the brain phan-
 282 tom. Its spatial correlation function displayed in Figs. 4f,g provides an estimation
 283 of the isoplanatic patch size: 5 mm in the transverse direction (Fig. 4f) and 2 mm
 284 in depth (Fig. 4g). This rapid variation of the aberration phase law across the
 285 field of view confirms *a posteriori* the necessity of a local compensation of aber-
 286 rations induced by the skull. It also confirms the importance of 3D UMI with a
 287 fully sampled 2D array, as previous work recommended that the array pitch should
 288 be no more than 50% of the aberrator correlation length to properly sample the
 289 corresponding adapted focusing law³⁸.

290 The phase conjugate of the \mathbf{T} -matrix at input and output enables a fine
 291 compensation of aberrations. A set of corrected RPSFs are shown in Fig. 5d.
 292 The comparison with their initial values demonstrates the success of 3D UMI: a

293 diffraction-limited resolution is obtained almost everywhere [Fig. 5e)], whether it
294 be in ultrasound speckle or in the neighborhood of bright targets, at shallow or
295 high depths, which proves the versatility of UMI.

296 The performance of 3D UMI is also striking when comparing the three-
297 dimensional image of the head phantom before and after UMI. [Figs. 4b and
298 c, respectively]. The different targets were initially strongly distorted by the skull,
299 and are now nicely resolved with UMI. In particular, the first target, located at
300 $z = 19$ mm and originally duplicated, has recovered its true shape. In addition,
301 two targets laterally spaced by 10 mm are observed at 42 mm depth, as expected
302 [Fig. 4a]. The image of the target observed at 54 mm depth is also drastically
303 improved in terms of contrast and resolution but is not found at the expected
304 transverse position. One potential explanation is the size of this target (2 mm
305 diameter) larger than the resolution cell. The guide star is thus far from being
306 point-like, which can induce an uncertainty on the absolute transverse position of
307 the target in the corrected image.

308 Finally, an isolated target can be leveraged to highlight the gain in contrast
309 provided by 3D UMI with respect to its 2D counterpart. To that aim, a linear
310 1D array is emulated from the same raw data by collimating the incident beam
311 in the y -direction [Fig. 6]. The ultrasound image is displayed before and after
312 UMI in Figs. 6b and c, respectively. The radial average of the corresponding focal
313 spots is displayed in Figs. 6d. Even though 2D UMI enables a diffraction-limited
314 resolution, the contrast gain G is quite moderate ($G_{2D} \sim 8$ dB) as it scales with the
315 number N of coherence grains exhibited by the 1D aberration phase law [Figs. 6a]:
316 $N_{2D} \sim 6.2$. On the contrary, as expected, 3D UMI provides a strong enhancement
317 of the target echo (see the comparison between Figs. 6e,f and g): $G_{3D} \sim 18$ dB.
318 The 2D aberration phase law actually provides a much larger number of spatial
319 degrees of freedom than its 1D counterpart: $N_{3D} \sim 63$. The gain in contrast is
320 accompanied by a drastic increase of the transverse resolution ($> 8\times$ for $z > 40$

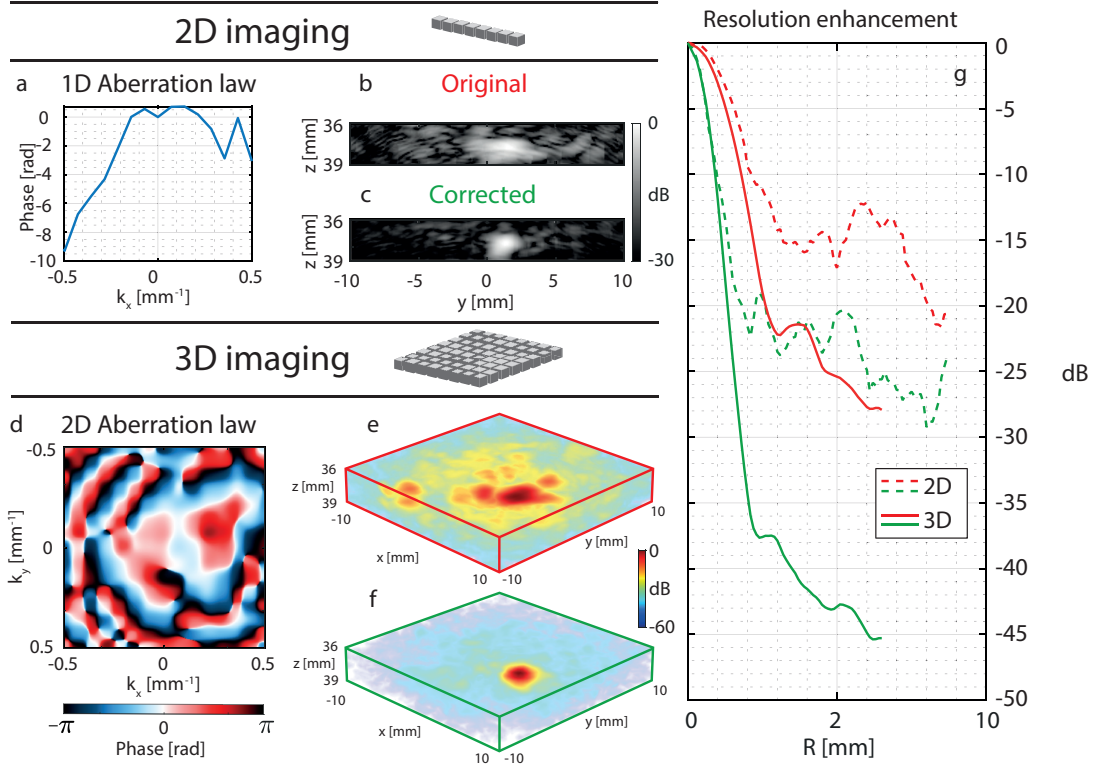


FIG. 6. **2D versus 3D matrix imaging in a head phantom.** (a) Aberration law extracted with 2D UMI. (b,c) Original and corrected images of the same target with 2D UMI, respectively. (d) Aberration law extracted with 3D UMI for a target located at $z = 38$ mm. (e,f) Original and corrected images of the same target with 3D UMI, respectively. (g) Imaging PSF before (red) and after (green) 2D (dotted line) and 3D (solid line) UMI. The depth range considered in each panel corresponds to the echo of the target located at $z = 38$ mm.

321 mm in Fig. 5e). Figure 6 demonstrates the necessity of a 2D ultrasonic probe for
 322 trans-cranial imaging. Indeed, the complexity of wave propagation in the skull can
 323 only be harnessed with a 3D control of the incident and reflected wave fields.

324 Discussion

325 In this experimental proof-of-concept, we demonstrated the capacity of 3D UMI
326 to correct strong aberrations such as those encountered in trans-cranial imaging.
327 This work is not only a 3D extension of previous studies^{17,28} since several crucial
328 elements have been introduced to make UMI more robust.

329 First, the proposed iterative phase reversal algorithm outperforms the SVD
330 for local compensation of aberrations because it can evaluate the aberration law
331 on a larger angular support (see Supplementary Fig. 3), resulting in a sharper
332 compensation of aberrations. Second, the bias of our \mathbf{T} -matrix estimator has been
333 expressed analytically (Eq. 6) as a function of the coherence factor that grasps
334 the detrimental effects of the virtual guide star blurring induced by aberrations,
335 multiple scattering and noise. This led us to define a general strategy for UMI
336 with: (i) a multi-scale compensation of wave distortions to gradually reduce the
337 blurring of the virtual guide star and tackle high-order aberrations associated with
338 small isoplanatic lengths; (ii) the application of an adaptive confocal filter to cope
339 with multiple scattering and noise; (iii) a fine monitoring of the convergence of our
340 estimator by means of spatial reciprocity. The latter is a real asset, as it provides
341 an objective criterion to check the physical significance of the extracted aberration
342 laws and optimize the resolution of our \mathbf{T} -matrix estimator.

343 Although the results presented in this paper are striking, they were obtained *in*
344 *vitro*, and some challenges remain for *in vivo* brain imaging. Until now, UMI has
345 only been applied to a static medium, while biological tissues are usually moving,
346 especially in the case of vascular imaging, where blood flow makes the reflectivity
347 vary quickly over time. A lot of 3D imaging modes are indeed designed to image
348 blood flow, such as transcranial Doppler imaging³⁹ or ULM^{40,41}. These methods
349 are strongly sensitive to aberrations^{42,43} and their coupling with matrix imaging
350 would be rewarding to increase the signal-to-noise ratio and improve the image
351 resolution, not only in the vicinity of bright reflectors⁴⁴ but also in ultrasound

352 speckle.

353 However, due to spatial aliasing, the number of illuminations required for UMI
354 scales with the number of resolution cells covered by the RPSF (see Supplemen-
355 tary Fig. 8). Because the aberration level through the skull is important, the
356 illumination basis should thus be fully sampled. It limits 3D transcranial UMI to
357 a compounded frame rate of only a few hertz, which is much too slow for ultrafast
358 imaging⁴⁵. Moreover, a reduced number of illuminations breaks the symmetry of
359 the reflection matrix. It would therefore also affect the accuracy of our monitoring
360 parameter based on spatial reciprocity.

361 Soft tissues usually exhibit much slower movement, and provide signals several
362 dB higher than blood. Ultrasound imaging of tissues is generally discarded for the
363 brain because of the strong level of aberrations and reverberations. Interestingly,
364 UMI can open a new route towards quantitative brain imaging since a matrix
365 framework can also enable the mapping of physical parameters such as the speed-
366 of-sound^{1,46-48}, attenuation and scattering coefficients^{49,50}, or fiber anisotropy^{51,52}.
367 Those various observables can be extremely enlightening for the characterization
368 of cerebral tissues.

369 Alternatively, a solution to directly implement 3D UMI *in vivo* for ultrafast
370 imaging, would be to design an imaging sequence in which the fully sampled
371 \mathbf{R} -matrix is acquired prior to the ultrafast acquisition itself, where the illumi-
372 nation basis can be drastically downsampled. The $\hat{\mathbf{T}}$ -matrix obtained from \mathbf{R}
373 could then be used to correct the ultrafast images in post-processing.

374 Interestingly, if an ultrafast 3D UMI acquisition is possible (in cases with less
375 aberrations, or at shallow depths), the quickly decorrelating speckle observed in
376 blood flow can be an opportunity since it provides a large number of speckle real-
377 izations in a given voxel. A high resolution \mathbf{T} -matrix could thus be, in principle,
378 extracted without spatial averaging and relying on any isoplanatic assumption^{53,54}.

379 So far, one limit of UMI concerns the strong aberration regime in which extreme

380 time delay fluctuations can occur. Indeed, our approach relies on a broadband
381 focused reflection matrix that consists in a coherent time gating of singly-scattered
382 echoes. If time delay fluctuations are larger than the time resolution δt of our
383 measurement, the angular components of each echo will not necessarily emerge in
384 the same time gate and aberration compensation will be imperfect.

385 Beyond strong aberrations, another issue for transcranial imaging arises from
386 multiple reflections caused by the skull. While such reverberations are not observed
387 in the pork tissue experiment, their detrimental effects are much greater in a
388 transcranial experiment because of the large impedance mismatch between the
389 skull and brain tissues. In this work, such artefacts are not corrected and they
390 drastically pollute the image at shallow depths ($z < 20$ mm).

391 To cope with those issues, a polychromatic approach to matrix imaging is re-
392 quired. Indeed, the aberration compensation scheme proposed in this paper is
393 equivalent to a simple application of time delays on each transmit and receive
394 channel. On the contrary, a full compensation of reverberation requires the tailor-
395 ing of a complex spatio-temporal adaptive (or even inverse) filter. To that aim, 3D
396 UMI provides an adequate framework to exploit, at best, all the spatio-temporal
397 degrees of freedom provided by a high-dimension array of broadband transducers.

398 To conclude, 3D UMI is general and can be applied to any insonification se-
399 quence (plane wave or virtual source illumination) or array configuration (ran-
400 dom or periodic, sparse or dense). Matrix imaging can be also extended to any
401 field of wave physics for which a multi-element technology is available: optical
402 imaging²⁰⁻²², seismic imaging^{25,26} and also radar⁵⁵. All the conclusions raised in
403 that paper can be extended to each of these fields. The matrix formalism is thus
404 a powerful tool for the big data revolution coming in wave imaging.

405 Methods

406 **Description of the pork tissue experiment.** The first sample under investi-
 407 gation is a tissue-mimicking phantom (speed of sound: $c_0 = 1540$ m/s) composed
 408 of random distribution of unresolved scatterers which generate ultrasonic speckle
 409 characteristic of human tissue [Fig. 2a]. The system also contains nylon filaments
 410 placed at regular intervals, with a point-like cross-section, and, at a depth of 40
 411 mm, a 10 mm-diameter hyperechoic cylinder, containing a higher density of unre-
 412 solved scatterers. A 12-mm thick pork tissue layer is placed on top of the phantom.
 413 It is immersed in water to ensure its acoustical contact with the probe and the
 414 phantom. Since the pork layer contains a part of muscle tissue ($c_m \sim 1560$ m/s)
 415 and a part of fat tissue ($c_f \sim 1480$ m/s), it acts as an aberrating layer. This ex-
 416 periment mimics the situation of abdominal *in vivo* imaging, in which layers of fat
 417 and muscle tissues generate strong aberration and scattering at shallow depths.

418 The acquisition of the reflection matrix is performed using a 2D matrix array of
 419 transducers (Vermon) whose characteristics are provided in Tab. I. The electronic
 420 hardware used to drive the probe was developed by Supersonic Imagine (member of
 421 Hologic group) in the context of collaboration agreement with Langevin Institute.

422

Number of transducers	$32 \times 32 = 1024$ (with 6 dead elements)
Geometry (y-axis)	3 inactive rows between each block of 256 elements
Pitch	$\delta u = 0.5$ mm ($\approx \lambda$ at $c = 1540$ m/s)
Aperture	$\Delta \mathbf{u} = \begin{pmatrix} \Delta u_x \\ \Delta u_y \end{pmatrix} = \begin{pmatrix} 16 \text{ mm} \\ 17.5 \text{ mm} \end{pmatrix}$
Central frequency	$f_c = 3$ MHz
Bandwidth (at -6 dB)	$80\% \rightarrow \Delta f = [1.8 - 4.2]$ MHz
Transducer directivity	$\theta_{max} = 28^\circ$ at $c = 1400$ m/s

TABLE I. **Matrix array datasheet.**

423

424

425 The reflection matrix is acquired by recording the impulse response between
 426 each transducer of the probe using IQ modulation with a sampling frequency
 427 $f_s = 6$ MHz. To that aim, each transducer \mathbf{u}_{in} emits successively a sinusoidal

428 burst of three half periods at the central frequency f_c . For each excitation \mathbf{u}_{in} , the
 429 back-scattered wave-field is recorded by all probe elements \mathbf{u}_{out} over a time length
 430 $\Delta t = 139 \mu\text{s}$. This set of impulse responses is stored in the canonical reflection
 431 matrix $\mathbf{R}_{\mathbf{u}\mathbf{u}}(t) = [R(\mathbf{u}_{\text{in}}, \mathbf{u}_{\text{out}}, t)]$.

432 Description of the head phantom experiment.

433 In this second experiment, the same probe [Tab. I] is placed slightly above
 434 the temporal window of a mimicking head phantom, whose characteristics are
 435 described in Tab. II. To investigate the performance of UMI in terms of resolution
 436 and contrast, the manufacturer (True Phantom Solutions) was asked to place small
 437 spherical targets made of bone-mimicking material inside the brain. They are
 438 arranged crosswise, evenly spaced in the 3 directions with a distance of 1 cm
 439 between two consecutive targets, and their diameter increases with depth: 0.2,
 440 0.5, 1, 2, 3 mm [Fig. 4a]. Skull thickness is of ~ 6 mm on average at the position
 441 where the probe is placed and the first spherical target is located at $z \approx 20$ mm
 442 depth, while the center of the cross is at $z \approx 40$ mm depth. The transverse size of
 443 the head is ~ 14 cm.

	Speed-of-sound [m/s]	Density [g/cm ³]	Attenuation @2.25 MHz [dB/cm]
Cortical bone	3000 \pm 30	2.31	6.4 \pm 0.3
Trabecular bone	2800 \pm 50	2.03	21 \pm 2
Brain tissue	1400 \pm 10	0.99	1.0 \pm 0.2
Skin tissue	1400 \pm 10	1.01	1.7 \pm 0.2

TABLE II. Head phantom characteristics.

444 To improve the signal-to-noise ratio, the \mathbf{R} -matrix is here acquired using a set
 445 of plane waves⁵⁶. For each plane wave of angles of incidence $\boldsymbol{\theta}_{\text{in}} = (\theta_x, \theta_y)$, the
 446 time-dependent reflected wave field $R(\boldsymbol{\theta}_{\text{in}}, \mathbf{u}_{\text{out}}, t)$ is recorded by each transducer
 447 \mathbf{u}_{out} . This set of wave-fields forms a reflection matrix acquired in the plane wave
 448 basis, $\mathbf{R}_{\boldsymbol{\theta}\mathbf{u}}(t) = [R(\boldsymbol{\theta}_{\text{in}}, \mathbf{u}_{\text{out}}, t)]$. Since the transducer and plane wave bases are

449 related by a simple Fourier transform at the central frequency, the array pitch
450 δu and probe size Δu dictate the angular pitch $\delta\theta$ and maximum angle θ_{max}
451 necessary to acquire a full reflection matrix in the plane wave basis such that:
452 $\theta_{max} = \arcsin[\lambda_c/(2\delta u)] \approx 28^\circ$; $\delta\theta = \arcsin[\lambda_c/(2\Delta u_y)] \approx 0.8^\circ$, with $\lambda_c = c_0/f_c$ the
453 central wavelength and $c_0 = 1400$ m/s the speed-of-sound in the brain phantom.
454 A set of 1225 plane waves are thus generated by applying appropriate time delays
455 $\Delta\tau(\boldsymbol{\theta}_{in}, \mathbf{u}_{in})$ to each transducer $\mathbf{u}_{in} = (u_x, u_y)$ of the probe:

$$\Delta\tau(\boldsymbol{\theta}_{in}, \mathbf{u}_{in}) = [u_x \sin \theta_x + u_y \sin \theta_y]/c_0. \quad (9)$$

Focused beamforming of the reflection matrix. The focused \mathbf{R} -matrix, $\mathbf{R}_{\rho\rho}(z) = [R(\boldsymbol{\rho}_{in}, \boldsymbol{\rho}_{out}, z)]$, is built in the time domain via a conventional delay-and-sum beamforming scheme that consists in applying appropriate time-delays in order to focus at different points at input $\mathbf{r}_{in} = (\boldsymbol{\rho}_{in}, z) = (\{x_{in}, y_{in}\}, z)$ and output $\mathbf{r}_{out} = (\boldsymbol{\rho}_{out}, z) = (\{x_{out}, y_{out}\}, z)$:

$$R(\boldsymbol{\rho}_{in}, \boldsymbol{\rho}_{out}, z) = \sum_{\mathbf{i}_{in}} \sum_{\mathbf{u}_{out}} A(\{\mathbf{i}_{in}, \mathbf{r}_{in}\}, \{\mathbf{u}_{out}, \mathbf{r}_{out}\}) R(\mathbf{i}_{in}, \mathbf{u}_{out}, \tau(\mathbf{i}_{in}, \mathbf{r}_{in}) + \tau(\mathbf{u}_{out}, \mathbf{r}_{out})) \quad (10)$$

456 where $\mathbf{i} = \mathbf{u}$ or $\boldsymbol{\theta}$ accounts for the illumination basis. A is an apodization factor
457 that limit the extent of the synthetic aperture at emission and reception. This
458 synthetic aperture is dictated by the transducers' directivity $\theta_{max} \sim 28^\circ$ ⁵⁷.

459 In the transducer basis, the time-of-flights, $\tau(\mathbf{u}, \mathbf{r})$, writes:

$$\tau(\mathbf{u}, \mathbf{r}) = \frac{|\mathbf{u} - \mathbf{r}|}{c_0} = \frac{\sqrt{(x - u_x)^2 + (y - u_y)^2 + z^2}}{c_0}. \quad (11)$$

460 In the plane wave basis, $\tau(\boldsymbol{\theta}, \mathbf{r})$ is given by

$$\tau(\boldsymbol{\theta}, \mathbf{r}) = \left[x \sin \theta_x + y \sin \theta_y + z \sqrt{1 - \sin^2 \theta_x - \sin^2 \theta_y} \right] / c_0. \quad (12)$$

461 **Local average of the reflection point spread function.** To probe the local
 462 RPSF, the field-of-view is divided into spatial regions $\mathcal{W}(\mathbf{r}_m - \mathbf{r}_p)$, defined by their
 463 center \mathbf{r}_p and their extent $\mathbf{w} = (w_\rho, w_z)$, where w_ρ and w_z denote the lateral and
 464 axial extent, respectively. A local average of the back-scattered intensity can then
 465 be performed in each region:

$$RPSF(\Delta \boldsymbol{\rho}, \mathbf{r}_p) = \langle |R_{\mathcal{M}}(\Delta \boldsymbol{\rho}, \mathbf{r}_m)|^2 \mathcal{W}(\mathbf{r}_m - \mathbf{r}_p) \rangle_{\mathbf{r}_m} \quad (13)$$

466 where the symbol $\langle \dots \rangle$ denotes here a spatial average over the variable in the
 467 subscript. $\mathcal{W}(\mathbf{r}_m - \mathbf{r}_p) = 1$ for $|\boldsymbol{\rho}_m - \boldsymbol{\rho}_p| < w_\rho/2$ and $|z_m - z_p| < w_z/2$, and zero
 468 otherwise. The dimensions of \mathcal{W} used for [Fig. 2b,d] are: $\mathbf{w} = (w_\rho, w_z) = (3.2, 3)$
 469 mm. The dimensions of \mathcal{W} to obtain [Figs. 5c,d] are: $\mathbf{w} = (w_\rho, w_z) = (4, 5.5)$ mm.

470

471 **Distortion Matrix in 3D UMI.** The first step consists in projecting the focused
 472 \mathbf{R} -matrix $\mathbf{R}_{\boldsymbol{\rho}\boldsymbol{\rho}}(z)$ [Fig. 1e] onto a dual basis \mathbf{c} at output [Fig. 1i]:

$$\mathbf{R}_{\boldsymbol{\rho}\mathbf{c}}(z) = \mathbf{R}_{\boldsymbol{\rho}\boldsymbol{\rho}}(z) \times \mathbf{G}_{\boldsymbol{\rho}\mathbf{c}}(z) \quad (14)$$

473 where the symbol \times stands for the matrix product. $\mathbf{G}_{\boldsymbol{\rho}\mathbf{c}}(z)$ is the propagation
 474 matrix predicted by the homogeneous propagation model between the focused basis
 475 ($\boldsymbol{\rho}$) and the correction basis (\mathbf{c}) at each depth z . \mathbf{c} can be either the plane wave, the
 476 transducer, or any other correction basis suitable for a particular experiment^{23,58,59}.

477 In the transducer basis ($\mathbf{c} = \mathbf{u}$), the coefficients of $\mathbf{G}_{\boldsymbol{\rho}\mathbf{u}}(z)$ correspond to the

478 z -derivative of the Green's function¹⁹:

$$G(\boldsymbol{\rho}, \mathbf{u}, z) = \frac{ze^{ik_c\sqrt{|\mathbf{u}-\boldsymbol{\rho}|^2+z^2}}}{4\pi(|\mathbf{u}-\boldsymbol{\rho}|^2+z^2)} \quad (15)$$

479 where k_c is the wavenumber at the central frequency. In the Fourier basis ($\mathbf{c} = \mathbf{k}$),
480 $\mathbf{G}_{\boldsymbol{\rho}\mathbf{k}}$ simply corresponds to the Fourier transform operator¹⁷:

$$G(\boldsymbol{\rho}, \mathbf{k}) = \exp(j\mathbf{k}\cdot\boldsymbol{\rho}) = \exp(j(k_x x + k_y y)). \quad (16)$$

481 At each depth z , the reflected wave-fronts contained in $\mathbf{R}_{\boldsymbol{\rho}\mathbf{c}}$ are then decomposed
482 into the sum of a geometric component $\mathbf{G}_{\boldsymbol{\rho}\mathbf{c}}$, that would be ideally obtained in
483 absence of aberrations, and a distorted component that corresponds to the gap
484 between the measured wave-fronts and their ideal counterparts [Fig. 1j]^{17,19}:

$$\mathbf{D}_{\boldsymbol{\rho}\mathbf{c}}(z) = \mathbf{G}_{\boldsymbol{\rho}\mathbf{c}}^*(z) \circ \mathbf{R}_{\boldsymbol{\rho}\mathbf{c}}(z) \quad (17)$$

485 where the symbol \circ stands for a Hadamard product. $\mathbf{D}_{\mathbf{rc}} = \mathbf{D}_{\boldsymbol{\rho}\mathbf{c}}(z) = [D(\{\boldsymbol{\rho}_{\text{in}}, z\}, \mathbf{c}_{\text{out}})]$
486 is the so-called distortion matrix, here expressed at the output. Note that the
487 same operations can be performed by exchanging input and output to obtain the
488 input distortion matrix $\mathbf{D}_{\mathbf{cr}} = [D(\mathbf{c}_{\text{in}}, \mathbf{r}_{\text{out}})] = [D(\mathbf{c}_{\text{in}}, \{\boldsymbol{\rho}_{\text{out}}, z\})]$.

489 **Local correlation analysis of the \mathbf{D} -matrix.** The next step is to exploit
490 local correlations in $\mathbf{D}_{\mathbf{rc}}$ to extract the \mathbf{T} -matrix. To that aim, a set of output
491 correlation matrices $\mathbf{C}_{\text{out}}(\mathbf{r}_p)$ shall be considered between distorted wave-fronts in
492 the vicinity of each point \mathbf{r}_p in the field-of-view:

$$C(\mathbf{c}_{\text{out}}, \mathbf{c}'_{\text{out}}, \mathbf{r}_p) = \langle D(\mathbf{r}_{\text{in}}, \mathbf{c}_{\text{out}}) D^*(\mathbf{r}_{\text{in}}, \mathbf{c}'_{\text{out}}) \mathcal{W}(\mathbf{r}_{\text{in}} - \mathbf{r}_p) \rangle_{\mathbf{r}_{\text{in}}} \quad (18)$$

493 An equivalent operation can be performed in input in order to extract a local
494 correlation matrix $\mathbf{C}_{\text{in}}(\mathbf{r}_p)$ from the input distortion matrix $\mathbf{D}_{\mathbf{cr}}$.

495 **Iterative phase reversal algorithm.** The iterative phase reversal algorithm is
 496 a computational process that provides an estimator of the transmission matrix,

$$\mathbf{T}_{\text{out}}(z) = \mathbf{G}_{\rho\mathbf{c}}^{\top}(z) \times \mathbf{H}_{\text{out}}(z), \quad (19)$$

497 where the superscript \top stands for matrix transpose. $\mathbf{T}_{\text{out}} = [\mathbf{T}(\mathbf{c}_{\text{out}}, \mathbf{r}_p)]$ links each
 498 point \mathbf{c}_{out} in the dual basis and each voxel \mathbf{r}_p of the medium to be imaged [Fig. 1k].
 499 Mathematically, the algorithm is based on the following recursive relation:

$$\hat{\mathbf{T}}_{\text{out}}^{(n)}(\mathbf{r}_p) = \exp \left[i \arg \left\{ \mathbf{C}_{\text{out}}(\mathbf{r}_p) \times \hat{\mathbf{T}}_{\text{out}}^{(n-1)}(\mathbf{r}_p) \right\} \right] \quad (20)$$

500 where $\hat{\mathbf{T}}_{\text{out}}^{(n)}$ is the estimator of \mathbf{T}_{out} at the n^{th} iteration of the phase reversal process.
 501 $\hat{\mathbf{T}}_{\text{out}}^{(0)}$ is an arbitrary wave-front that initiates the iterative phase reversal process
 502 (typically a flat phase law) and $\hat{\mathbf{T}}_{\text{out}} = \lim_{n \rightarrow \infty} \hat{\mathbf{T}}_{\text{out}}^{(n)}$ is the result of this iterative
 503 phase reversal process.

504 This iterative phase reversal algorithm, repeated for each point \mathbf{r}_p , yields an
 505 estimator $\hat{\mathbf{T}}_{\text{out}}$ of the \mathbf{T} -matrix. Its digital phase conjugation enables a local
 506 compensation of aberrations [Fig. 1l]. The focused \mathbf{R} -matrix can be updated as
 507 follows:

$$\mathbf{R}_{\rho\rho}^{(\text{corr})}(z) = \left[\mathbf{D}_{\rho\mathbf{c}}(z) \circ \hat{\mathbf{T}}_{\text{out}}^{\dagger}(z) \right] \times \mathbf{G}_{\rho\mathbf{c}}^{\dagger}(z) \quad (21)$$

508 where the symbol \dagger stands for transpose conjugate and \circ for the Hadamard prod-
 509 uct. The same process is then applied to the input correlation matrix \mathbf{C}_{in} for the
 510 estimation of the input transmission matrix, $\mathbf{T}_{\text{in}}(z) = \mathbf{G}_{\rho\mathbf{c}}^{\top}(z) \times \mathbf{H}_{\text{in}}(z)$.

511 **Multi-scale analysis of wave distortions.** To ensure the convergence of the
 512 IPR algorithm, several iterations of the aberration correction process are performed
 513 while reducing the size of the patches \mathcal{W} with an overlap of 50% between them.
 514 Three correction steps are performed in the pork tissue experiment, whereas six
 515 are performed in the head phantom experiment [as described in Table III]. At each

516 step, the correction is performed both at input and output and reciprocity between
517 input and output aberration laws is checked. The correction process is stopped if
518 the normalized scalar product $P_{\text{in/out}}$ does not reach 0.9.

	Pork tissue			Head phantom					
Correction step	1°	2°	3°	1°	2°	3°	4°	5°	6°
Number of transverse patches	1 × 1	2 × 2	4 × 4	1 × 1	2 × 2	3 × 3	4 × 4	5 × 5	6 × 6
$w_{\rho} = (w_x, w_y)$ [mm]	16	12	8	20	15	13.3	10	8	6.6
w_z [mm]	3	3	3	5.5	5.5	5.5	5.5	5.5	5.5

519 **TABLE III. Parameters of UMI in both experiments.**

520
521 **Synthesise a 1D linear array.** To estimate the benefits of 3D imaging compared
522 to 2D UMI, a simulation of a 1D array is performed on experimental ultrasound
523 data acquired with our 2D matrix array. To that aim, cylindrical time delays are
524 applied at input and output:

$$\tau'(\theta^{(s)}, s, z) = \frac{s \sin \theta^{(s)} + z \cos \theta^{(s)}}{c_0} \quad (22)$$

525

$$\tau'(u^{(s)}, s, z) = \frac{\sqrt{(s - u^{(s)})^2 + z^2}}{c_0}. \quad (23)$$

526 with $s = x$ or y , depending on our focus plane choice.

The focused \mathbf{R} -matrix is still built in the time domain but using this time the following delay-and-sum beamforming:

$$R^{(2D)}(y_{\text{in}}, y_{\text{out}}, z) = \sum_{\theta_{\text{in}}} \sum_{\mathbf{u}_{\text{out}}} R \left(\theta_{\text{in}}, \mathbf{u}_{\text{out}}, \overbrace{\tau'(\theta_{\text{in}}^{(y)}, y_{\text{in}}, z) + \tau'(u_{\text{out}}^{(y)}, y_{\text{out}}, z)}^{\text{2D beamforming along } (y,z)\text{-plane}} \right. \\ \left. + \underbrace{\tau'(\theta_{\text{in}}^{(x)}, x_{\text{f}}, z_{\text{f}}) + \tau'(u_{\text{out}}^{(x)}, x_{\text{f}}, z_{\text{f}}) - 2z_{\text{f}}/c_0}_{\text{Cylindrical law to focus at } (x_{\text{f}}, z_{\text{f}})} \right). \quad (24)$$

527 The images displayed in Fig. 6b,c are obtained by synthesizing input and output

528 beams collimated in the (y, z) -plane by focusing on a line located at $(x_f = 0$ mm,
 529 $z_f = 37.25$ mm), thereby mimicking the beamforming process by a conventional
 530 linear array of transducers.

531 **Estimation of contrast and resolution.** Contrast and resolution are evaluated
 532 by means of the RPSF. Equivalent to the full width at half maximum commonly
 533 used in 2D UMI, the transverse resolution $\delta\rho$ is assessed in 3D based on the area
 534 $\mathcal{A}_{(-3dB)}$ at half maximum of the RPSF amplitude:

$$\delta\rho_{(-3dB)} = \sqrt{\mathcal{A}_{(-3dB)}/\pi} \quad (25)$$

535 The contrast, \mathcal{F} , is computed locally by decomposing the normalised RPSF as the
 536 sum of three components²⁸:

$$\overline{RPSF}(\mathbf{r}_p, \Delta\rho) = \frac{RPSF(\mathbf{r}_p, \Delta\rho)}{RPSF(\mathbf{r}_p, \Delta\rho = \mathbf{0})} = \alpha_S(\mathbf{r}_p) + \alpha_M(\mathbf{r}_p) + \alpha_N(\mathbf{r}_p). \quad (26)$$

537 α_S is the single scattering rate that corresponds to the confocal peak. α_M is a
 538 multiple scattering rate that gives rise to a diffuse halo; α_N corresponds to the
 539 electronic noise rate which results in a flat plateau. A local contrast can then be
 540 deduced from the ratio between α_S and the incoherent background $\alpha_B = \alpha_M + \alpha_N$,

$$\mathcal{F}(\mathbf{r}_p) = \frac{\alpha_S(\mathbf{r}_p)}{\alpha_B(\mathbf{r}_p)} = \frac{1 - \alpha_B(\mathbf{r}_p)}{\alpha_B(\mathbf{r}_p)} \quad (27)$$

541 **Single and multiple scattering rates.** The single scattering, multiple scatter-
 542 ing and noise rates can be directly computed from the decomposition of the RPSF
 543 (Eq. 26). However, at large depths, multiple scattering and noise are difficult to
 544 discriminate since they both give rise to a flat plateau in the RPSF. In that case,
 545 the spatial reciprocity symmetry can be invoked to differentiate their contribution.
 546 The multiple scattering component actually gives rise to a symmetric \mathbf{R} -matrix

547 while electronic noise is associated with a fully random matrix. The relative part
 548 of the two components can thus be estimated by computing the degree of anti-
 549 symmetry β in the \mathbf{R} -matrix. To that aim, the \mathbf{R} -matrix is first projected onto
 550 its anti-symmetric subspace at each depth :

$$\mathbf{R}_{\rho\rho}^{(A)}(z) = \frac{\mathbf{R}_{\rho\rho}(z) - \mathbf{R}_{\rho\rho}^\top(z)}{2} \quad (28)$$

551 where the superscript \top stands for matrix transpose. In a common midpoint
 552 representation, (Eq. 28) re-writes:

$$R_{\mathcal{M}}^{(A)}(\mathbf{r}_m, \Delta\rho) = \frac{R_{\mathcal{M}}(\mathbf{r}_m, \Delta\rho) - R_{\mathcal{M}}(\mathbf{r}_m, -\Delta\rho)}{2}. \quad (29)$$

553 A local degree of anti-symmetry β is then computed as follows:

$$\beta(\mathbf{r}_p) = \frac{\left\langle \left| R_{\mathcal{M}}^{(A)}(\mathbf{r}_m, \Delta\rho) \right|^2 \mathcal{W}(\mathbf{r}_m - \mathbf{r}_p) \mathcal{D}(\Delta\rho) \right\rangle_{[\mathbf{r}_m, \Delta\rho]}}{\left\langle \left| R_{\mathcal{M}}(\mathbf{r}_m, \Delta\rho) \right|^2 \mathcal{W}(\mathbf{r}_m - \mathbf{r}_p) \mathcal{D}(\Delta\rho) \right\rangle_{[\mathbf{r}_m, \Delta\rho]}} \quad (30)$$

where $\mathcal{D}(\Delta\rho)$ is a de-scanned window function that eliminates the confocal peak such that the computation of β is only made by considering the incoherent background. Typically, we chose $\mathcal{D}(\Delta\rho) = 1$ for $\Delta\rho > 6\delta\rho_0(z)$, and zero otherwise. Assuming equi-partition of the electronic noise between its symmetric and anti-symmetric subspace, the multiple scattering rate α_M and noise ratio α_N can then be deduced (see Supplementary Section 11):

$$\alpha_M(\mathbf{r}_p) = (1 - 2\beta(\mathbf{r}_p)) \alpha_B(\mathbf{r}_p) \quad (31)$$

$$\alpha_N(\mathbf{r}_p) = 2\beta(\mathbf{r}_p) \alpha_B(\mathbf{r}_p) \quad (32)$$

554 In the head phantom experiment [Fig. 5b], these rates are estimated at each depth
 555 by averaging over a window of size $\mathbf{w} = (w_\rho, w_z) = (20, 5.5)$ mm.

556 **Computational insights.** While the UMI process is close to real-time for 2D
557 imaging (*i.e.* for linear, curve or phased array probes), 3D UMI (using a fully
558 populated matrix array of transducers) is still far from it (see Tab. IV) as it in-
559 volves the processing of much more ultrasound data. Even if computing a confocal
560 3D image only requires a few minutes, building the focused \mathbf{R} -matrix from the
561 raw data takes a few hours (on GPU with CUDA language) while one step of
562 aberration correction only lasts for a few minutes. All the post-processing was
563 realized with Matlab (R2021a) on a working station with 2 processors @2.20GHz,
564 128Go of RAM, and a GPU with 48 Go of dedicated memory.

565

		2D imaging		3D imaging	
Number of channels [Input \times Output]		$32 \times 32 \approx 10^3$		$1024 \times 1024 \approx 10^6$	
Field-of-view $(\Delta x, \Delta y, \Delta z)$		(20, 0, 80) mm		(20, 20, 80) mm	
		Data	Time	Data	Time
Reflection matrix acquisition: $\mathbf{R}_{\mathbf{uu}}(t)$		6 Mo	8 ms	6 Go	260 ms
Confocal image $\mathcal{I}(\mathbf{r})$		53 ko	5.1 ms	2.2 Mo	1.3 min
Matrix Imaging	Focused \mathbf{R} -matrix: $\mathbf{R}_{\rho\rho}(z)$	2.2 Mo	15 ms	3.6 Go	2.3 h
	Estimation of \mathbf{T} & correction		0.15 s		4.5 min

TABLE IV. **Computational insights.** Here, we compare the typical amount of data and computational time at each post-processing step of UMI. The comparison between 2D and 3D imaging is made using a single line of transducers *versus* all the transducers of our matrix array. In both cases, the pixel/voxel resolution is fixed at 0.5 mm, which corresponds approximately to one wavelength. The maximum distance between the input and output focusing points is set to 10 mm. The estimation of \mathbf{T} is here investigated without a multi-scale analysis on a single iteration at input and output.

566 **Data availability.** The ultrasound data generated in this study is available at
567 Zenodo⁶⁰ (<https://zenodo.org/record/8159177>).

568

569 **Code availability.** Codes used to post-process the ultrasound data within this
570 paper are available from the corresponding author upon request.

571

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577

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579 the project. F.B. and A.L.B. coded the ultrasound acquisition sequences. F.B.
580 and J.R. performed the experiments. F.B., A.L.B., and W.L. developed the post-
581 processing tools. F.B., J.R. and A.A. analyzed the experimental results. A.A.
582 performed the theoretical study. F.B. prepared the figures. F.B., J.R. and A.A.
583 prepared the manuscript. F.B., J.R., A.L.B., W.L., M.F., and A.A. discussed the
584 results and contributed to finalizing the manuscript.

585

586 **Competing interests.** A.A., M.F., and W.L. are inventors of a patent related
587 to this work held by CNRS (no. US11346819B2, published May 2022). W.L. had
588 his PhD funded by the SuperSonic Imagine company and is now an employee of
589 this company. All authors declare that they have no other competing interests.

590

Supplementary Information

591 This document provides further information on: (i) the UMI workflow; (ii) the
 592 RPSF and the common midpoint basis; (iii) the comparison between iterative
 593 time reversal and phase reversal; (iv) the bias of the \mathbf{T} -matrix estimator; (v) the
 594 comparison between a multi-scale and local analysis of wave distortions; (vi) the
 595 impact of the confocal filter; (vii) the effect of an incompleteness of the illumination
 596 basis.

597 S1. WORKFLOW

598 Supplementary Figure S1 shows a workflow that sums up the different steps of
 599 the UMI procedure performed in the accompanying paper.

601 S2. RPSF AND COMMON MIDPOINT

602 To probe the local focusing quality, the reflection point spread function (RPSF)
 603 can be investigated. Its extraction from the focused reflection matrix, $\mathbf{R}_{\rho\rho}(z) =$
 604 $[R(\boldsymbol{\rho}_{\text{in}}, \boldsymbol{\rho}_{\text{out}}, z)]$, consists in the following change of variable to project the data into
 605 a common midpoint basis:

$$\underbrace{\begin{bmatrix} \boldsymbol{\rho}_{\text{in}} \\ \boldsymbol{\rho}_{\text{out}} \\ z \end{bmatrix}}_{\text{Focused}} \rightarrow \underbrace{\begin{bmatrix} \Delta\boldsymbol{\rho} \\ \boldsymbol{\rho}_m \\ z \end{bmatrix}}_{\text{Common midpoint}} = \begin{bmatrix} \boldsymbol{\rho}_{\text{out}} - \boldsymbol{\rho}_{\text{in}} \\ \frac{\boldsymbol{\rho}_{\text{in}} + \boldsymbol{\rho}_{\text{out}}}{2} \\ z \end{bmatrix}. \quad (\text{S1})$$

606 This operation is described schematically in Supplementary Figure S2 for the sim-
 607 ple case of 2D imaging with a linear array of transducers. It consists in extracting
 608 each antidiagonal of the focused reflection matrix $\mathbf{R}_{xx}(z)$ (red boxes in Supplemen-
 609 tary Figure S2a), corresponding to a matrix rotation by 45° . In this representation,

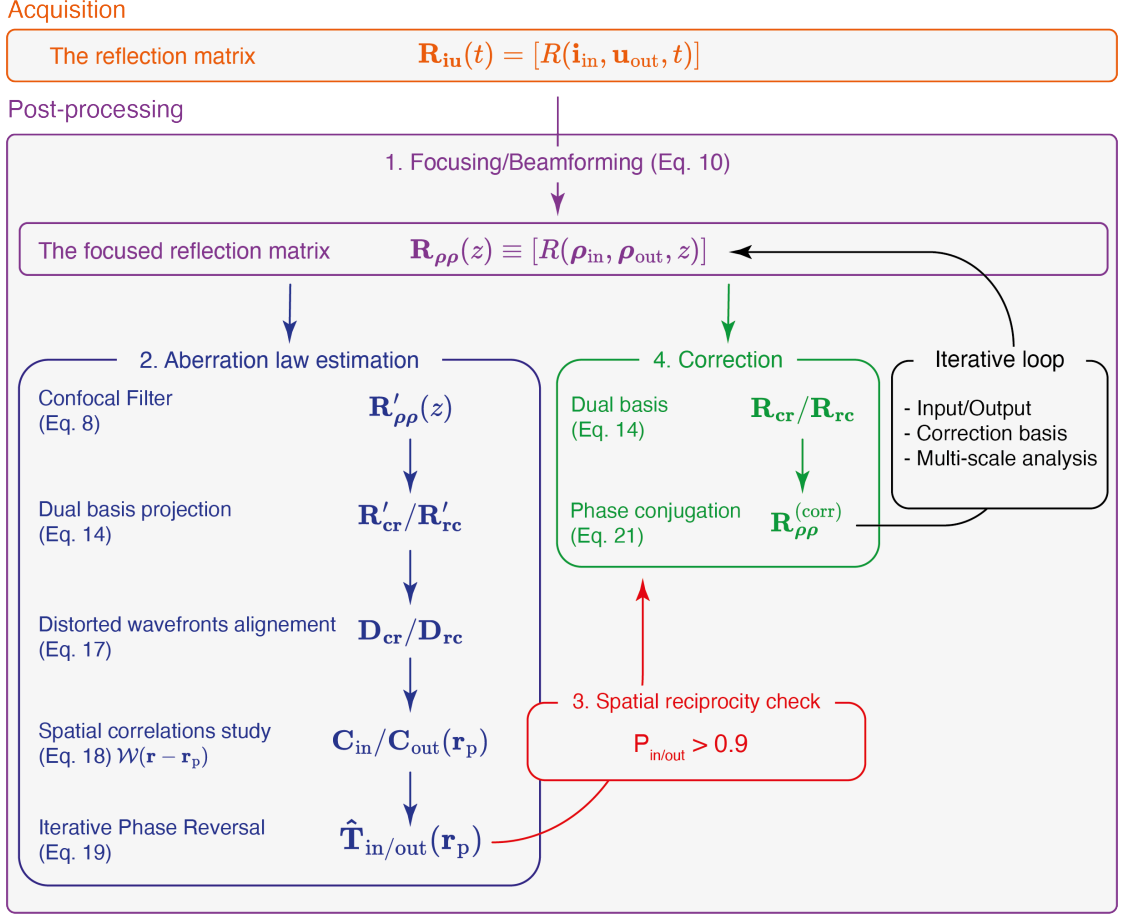


FIG. S1. Flowchart of the UMI process.

610 $x_m = (x_{\text{in}} + x_{\text{out}})/2$ is the common midpoint between the input and output focal
 611 spot, with the two separated by a distance $\Delta x = x_{\text{out}} - x_{\text{in}}$. These considerations
 612 can be extended to 3D imaging, so that the transverse coordinate, previously x ,
 613 now becomes $\boldsymbol{\rho} = (x, y)$.

614 S3. CORRELATION MATRIX OF WAVE DISTORTIONS

615 In the accompanying paper, an iterative phase reversal (IPR) process and a
 616 multi-scale analysis of \mathbf{D} have been implemented to retrieve the \mathbf{T} -matrix. In

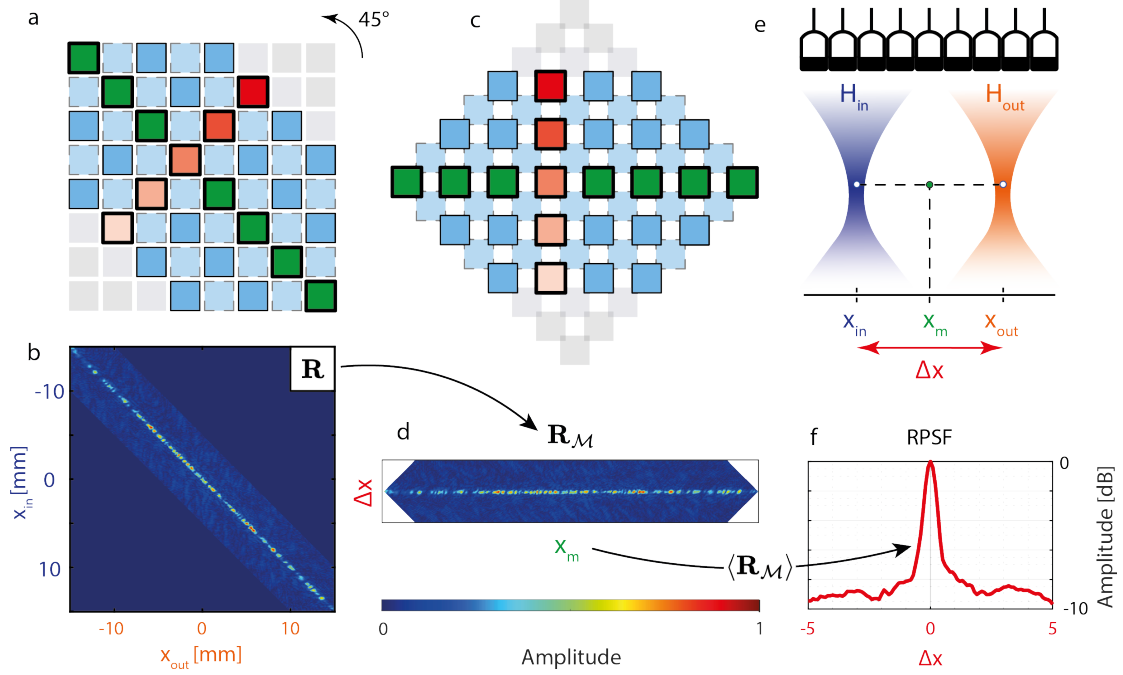


FIG. S2. **Common midpoint representation.** In 2D ultrasound imaging with linear or convex probes, the change from a (a,b) conventional to a (c,d) common midpoint representation corresponds to a 45° rotation of the focused reflection matrix. Panels a and c show a schematic representation of such a transformation, while panels b and d show experimental ultrasound data in speckle of an ultrasound phantom with a linear probe. Note that the change from the focused to the common midpoint representation implies two new sampling grids, represented by solid and dashed lines. (e) Schematic representation of the position of the input (x_{in}) and output (x_{out}) focal spots, spaced by Δx and their common midpoint x_m . (f) Extracted RPSF by spatial averaging over all midpoints x_m at depth $z = 30$ mm.

617 the following, we provide a theoretical framework to justify this process, outline
 618 its limits and conditions of success. For sake of lighter notation, the dependence
 619 over \mathbf{r}_p will be omitted in the following.

620 At each step of the aberration correction process, a local correlation matrix
 621 of \mathbf{D} is computed. The UMI process assumes the convergence of the correlation
 622 matrix \mathbf{C} towards its ensemble average $\langle \mathbf{C} \rangle$, the so-called covariance matrix^{17,19}.
 623 In fact, this convergence is never fully realized and \mathbf{C} should be decomposed as

624 the sum of this covariance matrix $\langle \mathbf{C} \rangle$ and a perturbation term $\delta \mathbf{C}$:

$$\mathbf{C} = \langle \mathbf{C} \rangle + \delta \mathbf{C}. \quad (\text{S2})$$

625 The intensity of the perturbation term scales as the inverse of the number $N_{\mathcal{W}} =$
 626 $(w_\rho^2 w_z)/(\delta \rho_0^2 \delta z_0)$ of resolution cells in each sub-region^{16,17,19}:

$$\langle |\delta C(\mathbf{c}, \mathbf{c}', \mathbf{r}_p)|^2 \rangle = \frac{\langle |C(\mathbf{c}, \mathbf{c}', \mathbf{r}_p)|^2 \rangle}{N_{\mathcal{W}}} \quad (\text{S3})$$

627 This perturbation term can thus be reduced by increasing the size of the spatial
 628 window \mathcal{W} , but at the cost of a resolution loss. In the following, we express
 629 theoretically the bias induced by this perturbation term on the estimation of \mathbf{T} -
 630 matrices. In particular, we will show how it scales with $N_{\mathcal{W}}$ in each spatial window
 631 \mathcal{W} and the focusing quality. To that aim, we will consider the output correlation
 632 matrix \mathbf{C}_{out} but a similar demonstration can be performed at input.

633 **S4. COVARIANCE MATRIX: SYNTHESIS OF A VIRTUAL GUIDE** 634 **STAR**

635 Under assumptions of local isoplanicity in each spatial window and random
 636 reflectivity, the covariance matrix can be expressed as follows¹⁷:

$$\langle \mathbf{C}_{\text{out}} \rangle = \mathbf{T}_{\text{out}} \times \mathbf{C}_H \times \mathbf{T}_{\text{out}}^\dagger, \quad (\text{S4})$$

637 or in terms of matrix coefficients,

$$\langle \mathbf{C}(\mathbf{c}, \mathbf{c}') \rangle = T_{\text{out}}(\mathbf{c}) T_{\text{out}}^*(\mathbf{c}') \underbrace{\int d\rho |H_{\text{in}}(\rho)|^2 e^{-i2\pi \frac{(\mathbf{c}-\mathbf{c}') \cdot \rho}{\lambda z_p}}}_{=C_H(\mathbf{c}, \mathbf{c}')}. \quad (\text{S5})$$

638 \mathbf{C}_H is a reference correlation matrix associated with a virtual reflector whose
639 scattering distribution corresponds to the input focal spot intensity $|H_{\text{in}}(\boldsymbol{\rho})|^2$. This
640 scatterer plays the role of virtual guide star in the UMI process (Fig. 1k of the
641 accompanying paper).

642 **S5. COMPARISON BETWEEN ITERATIVE TIME REVERSAL AND** 643 **PHASE REVERSAL**

644 In previous works on 2D UMI^{17,19}, the \mathbf{T} -matrix was estimated by performing
645 a singular value decomposition of \mathbf{D}_{rc} :

$$\mathbf{D}_{\text{rc}} = \mathbf{V}_{\text{in}}^\dagger \times \boldsymbol{\Sigma} \times \mathbf{U}_{\text{out}}, \quad (\text{S6})$$

646 or, equivalently, the eigenvalue decomposition of \mathbf{C}_{out} :

$$\mathbf{C}_{\text{out}} = \mathbf{U}_{\text{out}}^\dagger \times \boldsymbol{\Sigma}^2 \times \mathbf{U}_{\text{out}}. \quad (\text{S7})$$

647 $\boldsymbol{\Sigma}$ is a diagonal matrix containing the singular values σ_i in descending order: $\sigma_1 >$
648 $\sigma_2 > \dots > \sigma_N$. \mathbf{U}_{out} and \mathbf{V}_{in} are unitary matrices that contain the orthonormal set
649 of output and input eigenvectors, $\mathbf{U}_{\text{out}}^{(i)} = [U_{\text{out}}^{(i)}(\mathbf{c})]$ and $\mathbf{V}_{\text{in}}^{(i)} = [V_{\text{in}}^{(i)}(\mathbf{r})]$.

650 The reason of this eigenvalue decomposition can be intuitively understood by
651 considering the asymptotic case of a point-like input focusing beam. In this ideal
652 case, Eq. S7 becomes $C_{\text{out}}(\mathbf{c}, \mathbf{c}') = T_{\text{out}}(\mathbf{c})T_{\text{out}}^*(\mathbf{c}')$. \mathbf{D}_{rc} is then of rank 1 – the first
653 output singular vector $\mathbf{U}_{\text{out}}^{(1)}$ yields the aberration transmittance \mathbf{T}_{out} .

654 However, in reality, the input PSF H_{in} is of course far from being point-like.
655 The spectrum of \mathbf{D}_{rc} displays a continuum of singular values [Supplementary Fig-
656 ure S3d]. The effective rank of \mathbf{C}_{out} is shown to scale as the number of resolution

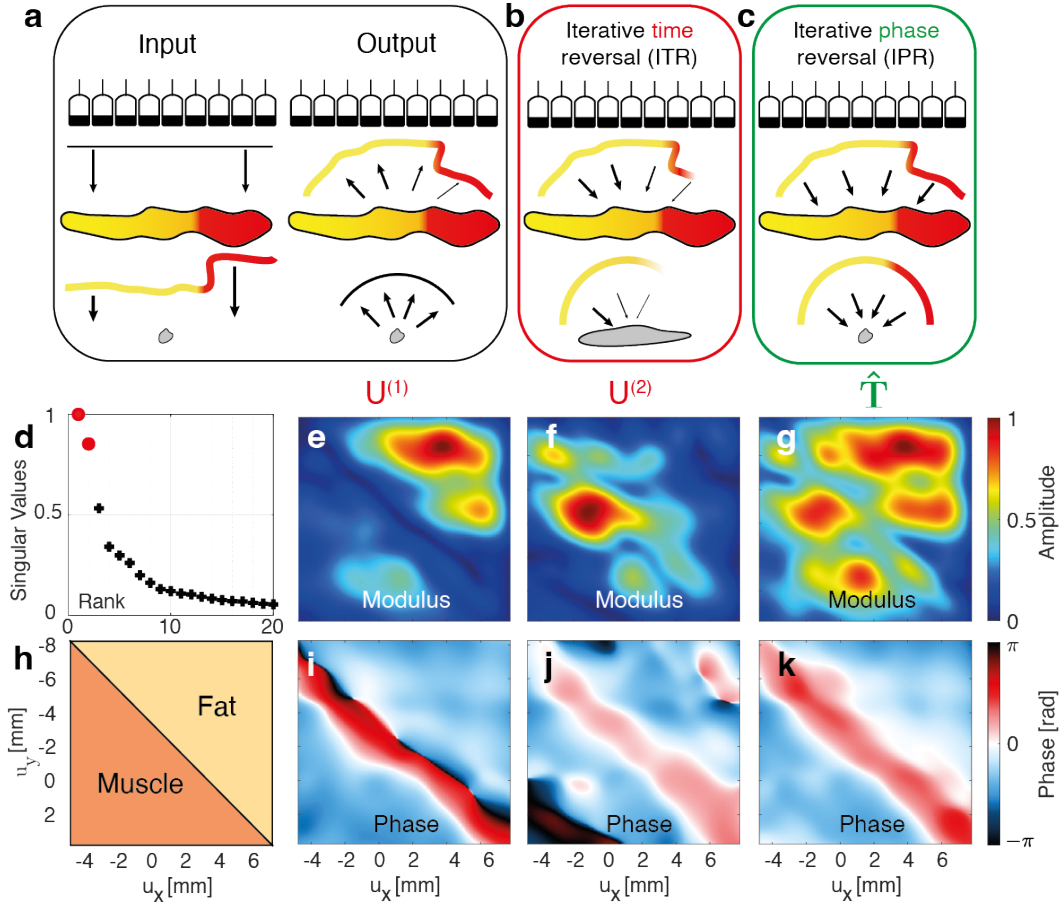


FIG. S3. **Iterative Time Reversal vs. Iterative Phase Reversal.** (a) The first step of ITR and IPR corresponds to the following fictitious experiment: Insonifying the medium by an arbitrary wave-front (here a plane wave) using an array of transducers and recording the reflected wave-front with the same probe. (b) The ITR process consists in time-reversing this wave-front in post-processing and sending it back into the medium, recording again the reflected wave-front, and so on. (c) The IPR process is similar but normalizes the amplitude of the time-reversed wavefront at every iteration. (d) Singular value distribution of \mathbf{D}_{rc} for a box \mathcal{W} of dimension $\mathbf{w} = (w_x, w_y, w_z) = (2, -5, 2)$ mm centered around point $\mathbf{r}_p = (3, -5.5, 23)$ mm. (e,f) Modulus of the two first eigenvectors $\mathbf{U}_{out}^{(i)}$. (g) Modulus of the vector $\mathbf{C}_{out} \times \hat{\mathbf{T}}_{out}$. (h) Delimitation of muscle and fat over the probe surface. (i,j,k) Phase of $\mathbf{U}_{out}^{(1)}$, $\mathbf{U}_{out}^{(2)}$ and $\hat{\mathbf{T}}_{out}$.

657 cells covered by the input PSF H_{in} ¹⁹:

$$M_{\delta} \sim (\delta\rho_{\text{in}}/\delta\rho_0)^2. \quad (\text{S8})$$

658 with $\delta\rho_{\text{in}}$ the spatial extension of H_{in} . The amplitude of the corresponding eigen-
 659 vectors $\mathbf{U}_{\text{out}}^{(i)}$ depends on the exact shape of the virtual guide star, that is to say,
 660 on aberrations induced by the incident wave-front.

661 Supplementary Figures S3e and f show the modulus of two first eigenvectors,
 662 $\mathbf{U}_{\text{out}}^{(1)}$ and $\mathbf{U}_{\text{out}}^{(2)}$. They clearly show a complementary feature. While $\mathbf{U}_{\text{out}}^{(1)}$ is associ-
 663 ated with the fat layer, $\mathbf{U}_{\text{out}}^{(2)}$ maps onto the muscle part of the pork chop [Supple-
 664 mentary Figure S3h]. This result can be understood by the discontinuity of the
 665 speed-of-sound between the muscle and fat parts of the pork chop that breaks the
 666 spatial invariance and isoplanicity. As a consequence, the SVD process tends to
 667 converge onto eigenstates associated with the most isoplanatic components of \mathbf{D}_{rc} .

668 This property is not satisfactory in the present case since each eigenvector only
 669 covers a part of the probe aperture. In other words, the phases of $\mathbf{U}^{(1)}$ [Supplemen-
 670 tary Figure S3i] and $\mathbf{U}^{(2)}$ [Supplementary Figure S3j] are only satisfying estimators
 671 of \mathbf{T} over some parts of the probe. Therefore, they cannot independently lead to
 672 an aberration compensation over the full numerical aperture.

673 To circumvent that problem, one can take advantage of the analogy with itera-
 674 tive time reversal (ITR). The eigenvector $\mathbf{U}_{\text{out}}^{(1)}$ can actually be seen as the result of
 675 the following fictitious experiment that consists in illuminating the virtual scatterer
 676 by an arbitrary wave-front and recording the reflected wave-field [Supplementary
 677 Figure S3a]. This wave-field is time-reversed and back-emitted towards the virtual
 678 scatterer [Supplementary Figure S3b]. This process can then be iterated many
 679 times and each step can be mathematically written as:

$$\sigma\mathbf{W}^{(n+1)} = \mathbf{C}_{\text{out}} \times \mathbf{W}^{(n)} \quad (\text{S9})$$

680 with $\mathbf{W}^{(n)}$, the wave-front at iteration n of the ITR process and σ , the scatterer
681 reflectivity. ITR is shown to converge towards a time-reversal invariant that is
682 nothing other than the first eigenvector, $\mathbf{U}_{\text{out}}^{(1)} = \lim_{n \rightarrow +\infty} \mathbf{W}^{(n)}$.

683 To optimize the estimation of aberrations over the full probe aperture, our idea
684 is to modify the ITR process by still re-emitting a phase-reversed wave-field but
685 with a constant amplitude on each probe element [Supplementary Figure S3c]. In
686 practice, this operation is performed using the following IPR algorithm:

$$\hat{\mathbf{T}}_{\text{out}}^{(n+1)} = \exp \left[i \arg \left\{ \mathbf{C}_{\text{out}} \times \hat{\mathbf{T}}_{\text{out}}^{(n)} \right\} \right] \quad (\text{S10})$$

687 where $\hat{\mathbf{T}}_{\text{out}}^{(n)}$ is the estimator of \mathbf{T}_{out} at the n^{th} iteration of IPR. $\hat{\mathbf{T}}_{\text{out}}^{(0)}$ is an arbi-
688 trary wave-front that initiates IPR (typically a plane wave). $\hat{\mathbf{T}}_{\text{out}} = \lim_{n \rightarrow \infty} \hat{\mathbf{T}}_{\text{out}}^{(n)}$
689 is the result of this IPR process. Unlike ITR, IPR equally addresses each angular
690 component of the imaging process to reach a diffraction-limited resolution. Sup-
691 plementary Figure S3g illustrates this fact by showing the modulus of $\mathbf{C}_{\text{out}} \times \hat{\mathbf{T}}_{\text{out}}$.
692 Compared with $\mathbf{U}_{\text{out}}^{(1)}$ [Supplementary Figure S3e] and $\mathbf{U}_{\text{out}}^{(2)}$ [Supplementary Fig-
693 ure S3f], it clearly shows that the phase-reversed invariant $\hat{\mathbf{T}}_{\text{out}}$ simultaneously
694 addresses each angular component of the aberrated wave-field. $\hat{\mathbf{T}}_{\text{out}}$ is thus a much
695 better estimator of the \mathbf{T} -matrix [Supplementary Figure S3k] than the aberration
696 phase laws extracted by the SVD process [Supplementary Figures S3i and j].

697 When applied to the whole field-of-view, the IPR algorithm is mathematically
698 equivalent to the CLASS algorithm developed in optical microscopy²⁰. However,
699 the IPR algorithm is much more efficient for a local compensation of aberrations.
700 For IPR, the angular resolution $\delta\theta$ of the aberration phase law is only limited by the
701 angular pitch of the plane wave illumination basis or the pitch p of the transducer
702 array in the canonical basis: $\delta\theta_I \sim \lambda/p$. With CLASS, the resolution $\delta\theta_C$ of the
703 aberration law is governed by the size of the spatial window \mathcal{W} on which the focused
704 reflection matrix is truncated: $\delta\theta_C \sim z/w_\rho$. It can be particularly detrimental

705 when high-order aberrations and small isoplanatic patches are targeted.

706 **S6. BIAS ON THE \mathbf{T} -MATRIX ESTIMATION**

707 In practice, however, the \mathbf{T} -matrix estimator is still impacted by the blurring
 708 of the synthesized guide star and the presence of diffusive background and/or
 709 noise. Therefore, the whole process shall be iterated at input and output in order
 710 to gradually refine the guide star and reduce the bias on our \mathbf{T} -matrix estimator.
 711 Moreover, the spatial window \mathcal{W} over which the \mathbf{C} -matrix is computed shall be
 712 gradually decreased in order to address the high-order aberration components, the
 713 latter one being associated with smaller isoplanatic patches.

714 To understand the parameters controlling the bias $\delta\mathbf{T}_{\text{out}}$ between $\hat{\mathbf{T}}_{\text{out}}$ and \mathbf{T}_{out} ,
 715 one can express $\hat{\mathbf{T}}_{\text{out}}$ as follows:

$$\hat{\mathbf{T}}_{\text{out}} = \exp\left(j\arg\left\{\mathbf{C}_{\text{out}} \times \hat{\mathbf{T}}_{\text{out}}\right\}\right) = \frac{\mathbf{C}_{\text{out}} \times \hat{\mathbf{T}}_{\text{out}}}{\|\mathbf{C}_{\text{out}} \times \hat{\mathbf{T}}_{\text{out}}\|} \quad (\text{S11})$$

716 By injecting Eq. S2 into the last expression, $\hat{\mathbf{T}}_{\text{out}}$ can be expressed, at first order,
 717 as the sum of its expected value \mathbf{T}_{out} and a perturbation term $\delta\hat{\mathbf{T}}_{\text{out}}$:

$$\hat{\mathbf{T}}_{\text{out}} = \underbrace{\frac{\langle\mathbf{C}_{\text{out}}\rangle \times \mathbf{T}_{\text{out}}}{\|\langle\mathbf{C}_{\text{out}}\rangle \times \mathbf{T}_{\text{out}}\|}}_{=\mathbf{T}_{\text{out}}} + \underbrace{\frac{\delta\mathbf{C}_{\text{out}} \times \mathbf{T}_{\text{out}}}{\|\langle\mathbf{C}_{\text{out}}\rangle \times \mathbf{T}_{\text{out}}\|}}_{\simeq\delta\mathbf{T}_{\text{out}}}. \quad (\text{S12})$$

718 The bias intensity can be expressed as follows:

$$|\delta\mathbf{T}_{\text{out}}|^2 = \frac{\mathbf{T}_{\text{out}}^\dagger \times \delta\mathbf{C}_{\text{out}}^\dagger \times \delta\mathbf{C}_{\text{out}} \times \mathbf{T}_{\text{out}}}{\mathbf{T}_{\text{out}}^\dagger \times \langle\mathbf{C}_{\text{out}}\rangle^\dagger \times \langle\mathbf{C}_{\text{out}}\rangle \times \mathbf{T}_{\text{out}}} \quad (\text{S13})$$

719 Using Eq. S3, the numerator of the last equation can be expressed as follows:

$$\mathbf{T}_{\text{out}}^\dagger \times \delta\mathbf{C}_{\text{out}}^\dagger \times \delta\mathbf{C}_{\text{out}} \times \mathbf{T}_{\text{out}} = N_u^2 \langle |\delta C(\mathbf{c}, \mathbf{c}')|^2 \rangle = N_u^2 |C(\mathbf{c}, \mathbf{c})|^2 / N_{\mathcal{W}}. \quad (\text{S14})$$

720 with N_u the number of transducers.

721 The denominator of Eq. S13 can be expressed as follows:

$$\mathbf{T}_{\text{out}}^\dagger \times \langle \mathbf{C}_{\text{out}} \rangle^\dagger \times \langle \mathbf{C}_{\text{out}} \rangle \times \mathbf{T}_{\text{out}} = M^2 \left| \sum_{\mathbf{c}} T_{\text{in}} \overset{\mathbf{c}}{\otimes} T_{\text{in}}(\mathbf{c}) \right|^2 \quad (\text{S15})$$

722 The bias intensity is thus given by:

$$|\delta T_{\text{out}}(\mathbf{c})|^2 = \frac{\left| T_{\text{in}} \overset{\mathbf{c}}{\otimes} T_{\text{in}}(\mathbf{0}) \right|^2}{N_{\mathcal{W}} \left| \sum_{\mathbf{c}} T_{\text{in}} \overset{\mathbf{c}}{\otimes} T_{\text{in}}(\mathbf{c}) \right|^2} \quad (\text{S16})$$

723 In the last expression, we recognize the ratio between the coherent intensity (energy
724 deposited exactly at focus) and the mean incoherent input intensity. This quantity
725 is known as the coherence factor in ultrasound imaging^{8,16}:

$$\mathcal{C}_{\text{in}} = \frac{\sum_{\mathbf{c}} T_{\text{in}} \overset{\mathbf{c}}{\otimes} T_{\text{in}}(\mathbf{c})}{T_{\text{in}} \overset{\mathbf{c}}{\otimes} T_{\text{in}}(\mathbf{0})} = \frac{|H_{\text{in}}(\boldsymbol{\rho} = \mathbf{0})|^2}{\Delta \rho_{\text{max}}^{-2} \int d\boldsymbol{\rho} |H_{\text{in}}(\boldsymbol{\rho})|^2} \quad (\text{S17})$$

726 In the speckle regime and for a 2D probe, the coherence factor \mathcal{C} ranges from 0,
727 for strong aberrations and/or multiple scattering background, to 4/9 in the ideal
728 case⁶¹. The bias intensity can thus be rewritten as:

$$|\delta T_{\text{out}}(\mathbf{c})|^2 = \frac{1}{\mathcal{C}_{\text{in}}^2 N_{\mathcal{W}}} \quad (\text{S18})$$

729 This last expression justifies the multi-scale analysis proposed in the accompanying
730 paper. A gradual increase of the focusing quality, quantified by \mathcal{C} , is required to
731 address smaller spatial windows that scale as $N_{\mathcal{W}}$. Following this scheme, the bias
732 made of our \mathbf{T} -matrix estimator can be minimized.

733 **S7. PROBING THE BIAS INTENSITY WITH SPATIAL RECIPROcity**

734 In the accompanying paper, we use the scalar product $P_{\text{in/out}}$ between input and
 735 output aberration phase laws to monitor the bias $|\delta T|^2$ of our \mathbf{T} -matrix estimator.
 736 Here we demonstrate the link between both quantities. To do so, the estimator
 737 can be written as:

$$\hat{T}(\mathbf{c}, \mathbf{r}_p) = \exp [j \{ \phi(\mathbf{c}, \mathbf{r}_p) + \delta\phi(\mathbf{c}, \mathbf{r}_p) \}] \quad (\text{S19})$$

738 with $T(\mathbf{c}, \mathbf{r}_p) = \exp [j\phi(\mathbf{c}, \mathbf{r}_p)]$ and $\delta\phi(\mathbf{c}, \mathbf{r}_p)$ the phase error of the estimator.

739 On the one hand, the bias intensity can be rewritten using Eq. 6 as follows:

$$|\delta T(\mathbf{c}, \mathbf{r}_p)|^2 = |1 - \exp[j\delta\phi(\mathbf{c}, \mathbf{r}_p)]|^2 = 4 \sin^2 \left[\frac{\delta\phi(\mathbf{c}, \mathbf{r}_p)}{2} \right] \stackrel{\delta\phi \ll 1}{\approx} [\delta\phi(\mathbf{c}, \mathbf{r}_p)]^2 \quad (\text{S20})$$

740 On the other hand, the scalar product $P_{\text{in/out}}$ is given by

$$P_{\text{in/out}} = N_c^{-1} \sum_{\mathbf{c}} \exp [j \{ \delta\phi_{\text{in}}(\mathbf{c}, \mathbf{r}_p) - \delta\phi_{\text{out}}(\mathbf{c}, \mathbf{r}_p) \}] \quad (\text{S21})$$

741 In the previous equation, the sum over \mathbf{c} can be replaced by an ensemble average
 742 since $N_c = N_u \gg 1$:

$$P_{\text{in/out}} = \langle \exp [j \{ \delta\phi_{\text{in}}(\mathbf{c}, \mathbf{r}_p) - \delta\phi_{\text{out}}(\mathbf{c}, \mathbf{r}_p) \}] \rangle. \quad (\text{S22})$$

743 Assuming a small phase error ($\delta\phi_{\text{in/out}} \ll 1$), the last equation can be rewritten
 744 as follows

$$P_{\text{in/out}} \simeq 1 + j \langle \delta\phi_{\text{in}}(\mathbf{c}, \mathbf{r}_p) - \delta\phi_{\text{out}}(\mathbf{c}, \mathbf{r}_p) \rangle - \frac{\langle [\delta\phi_{\text{in}}(\mathbf{c}, \mathbf{r}_p) - \delta\phi_{\text{out}}(\mathbf{c}, \mathbf{r}_p)]^2 \rangle}{2}. \quad (\text{S23})$$

745 Since $\langle \delta\phi_{\text{in/out}} \rangle = 0$ and $\langle \delta\phi_{\text{in}}\delta\phi_{\text{out}} \rangle = 0$, the last expression simplifies into

$$P_{\text{in/out}} \simeq 1 - \frac{\langle |\delta\phi_{\text{in}}(\mathbf{c}, \mathbf{r}_p)|^2 \rangle}{2} - \frac{\langle |\delta\phi_{\text{out}}(\mathbf{c}, \mathbf{r}_p)|^2 \rangle}{2}. \quad (\text{S24})$$

746 Assuming an equivalent phase error at input and output ($\langle |\delta\phi_{\text{in}}(\mathbf{c}, \mathbf{r}_p)|^2 \rangle =$
747 $\langle |\delta\phi_{\text{out}}(\mathbf{c}, \mathbf{r}_p)|^2 \rangle$) finally leads to:

$$P_{\text{in/out}} \simeq 1 - \langle |\delta\phi(\mathbf{c}, \mathbf{r}_p)|^2 \rangle. \quad (\text{S25})$$

748 Combining the latter expression with Eq. S20 leads to the final result:

$$P_{\text{in/out}} \simeq 1 - \langle |\delta T(\mathbf{c}, \mathbf{r}_p)|^2 \rangle. \quad (\text{S26})$$

749 $P_{\text{in/out}}$ is thus a relevant quantity to estimate the bias intensity (see Fig. 3b of the
750 accompanying paper).

751 **S8. MULTI-SCALE ANALYSIS OF WAVE DISTORTIONS**

752 Supplementary Figure S4 demonstrates the benefit of a multi-scale analysis of
753 wave distortions with a gradual decrease of spatial windows \mathcal{W} at each step of
754 the UMI process [Supplementary Figure S4a]. To that aim, this aberration cor-
755 rection scheme is compared with a direct estimation of the \mathbf{T} -matrix over the
756 smallest patches \mathcal{W} [Supplementary Figure S4d]. The estimated transmission ma-
757 trices $\hat{\mathbf{T}}$ differ in both cases (see comparison between Supplementary Figures S4b
758 and e) especially in the fat layer. The RPSFs obtained after phase conjugation of
759 $\hat{\mathbf{T}}$ demonstrate the benefit of the multi-scale analysis [Supplementary Figure S4c]
760 compared with a direct local investigation of wave distortions [Supplementary Fig-
761 ure S4f]. The fat area is actually the most aberrated in the field-of-view (see initial
762 RPSFs displayed by Fig. 2b of the accompanying paper). The initial coherence



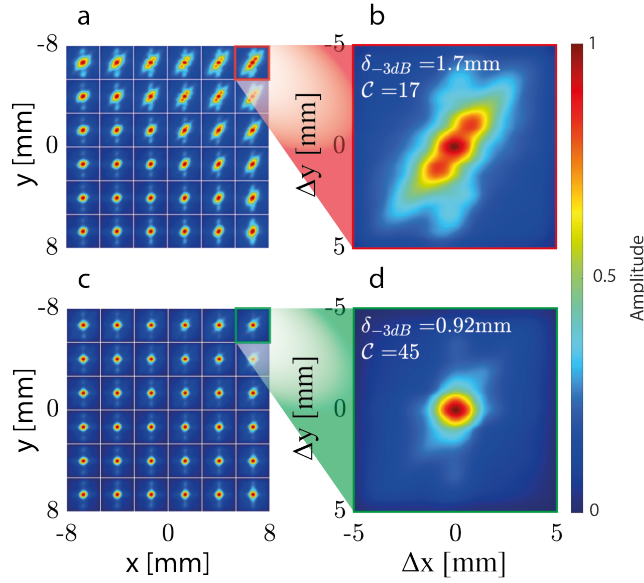
LittlebyLittlevsDirectALex.png

FIG. S4. **Multi-scale *versus* direct local analysis of wave distortions** (pork chop experiment, $z = 29$ mm). **(a)** Representation of the spatial windows used at each step of UMI (see Tab. III of the accompanying paper). **(b)** Aberration phase laws ($\hat{\mathbf{T}}$) extracted by a multi-scale analysis. **(c)** RPSFs after multi-scale aberration compensation. **(d)** Representation of the spatial windows used for a direct local compensation of wave distortions. **(e)** Aberration phase laws ($\hat{\mathbf{T}}$) extracted by a local analysis of **D**. **(f)** RPSFs after local aberration compensation.

⁷⁶³ factor \mathcal{C} is thus much smaller in this area, which induces a strong bias on \mathbf{T} when
⁷⁶⁴ wave distortions are investigated over a reduced isoplanatic patch. On the con-

765 trary, a multi-scale analysis enables a gradual enhancement of this coherence factor
 766 in this area and finally leads to an unbiased estimation of \mathbf{T} .

767 Supplementary Figure S5 shows the performance of UMI by comparing the
 768 RPSFs before and after aberration compensation. In the most aberrated area (top
 769 right of the field-of-view), the resolution is improved by almost a factor two, while
 770 the contrast is increased by 4.2 dB.



771 **FIG. S5. Contrast & resolution enhancement in the pork chop experiment.** (a) Maps of local RPSF ($z = 29$ mm). (b) Local RPSF on the top right of the field-of-view. (c) Map of RPSF after the UMI process. (d) Corrected RPSF on the top right of the field-of-view. The resolution is evaluated at -3dB (see Methods in the accompanying paper). The contrast \mathcal{F} is the ratio between the confocal peak and the multiple scattering/noise background (see also Methods).

772

773 Supplementary Figure S6 shows the evolution of the RPSF during the UMI
 774 process applied to the head phantom experiment. A gradual enhancement of the
 775 focusing process is observed at each step of UMI, which enables an estimation of
 776 the \mathbf{T} -matrix at a higher resolution.

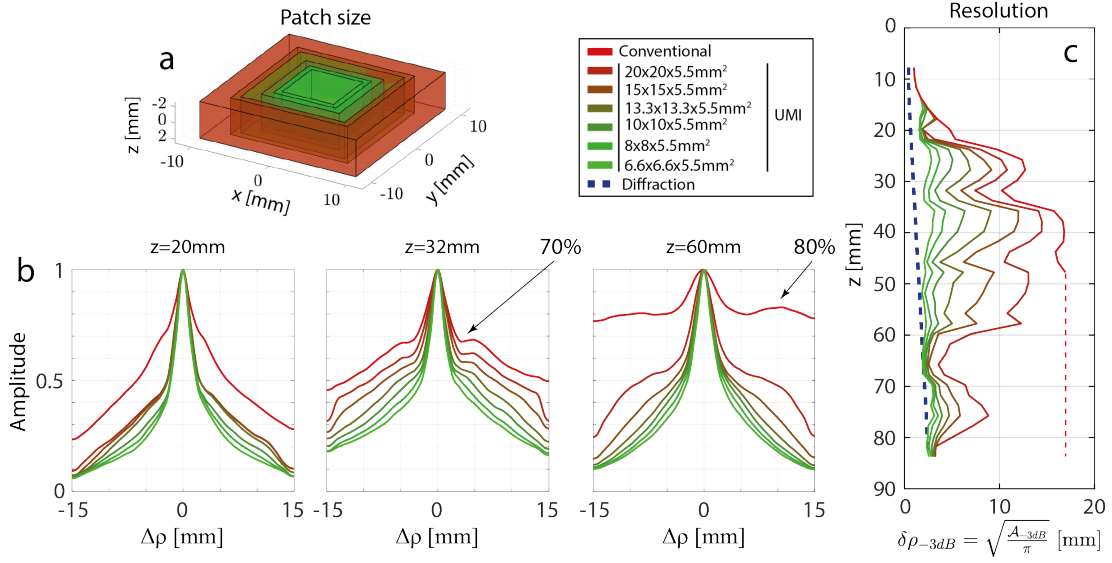


FIG. S6. **Multi-scale compensation of wave distortions in the head phantom.** (a) Successive patches used to perform a multi-scale analysis of wave distortions. (b) Radial profile of the RPSF amplitude at each step for three different depths (From left to right: $z = 20$, $z = 32$ and $z = 60$ mm). (c) Resolution as a function of depth at each step of correction (from red to green). At large depth (red dashed line), initial resolution can not be extracted as the incoherent background is larger than $1/2$ as shown in panel (b) for $z = 60$ mm.

778 S9. CONFOCAL FILTER

779 Supplementary Figure S7 shows the effect of the confocal filter on the \mathbf{T} -matrix
780 estimation. The output aberration phase laws contained in $\hat{\mathbf{T}}_{\text{out}}$ look much more
781 noisy in absence of an adaptive confocal filter (see the comparison between Supple-
782 mentary Figures S7a and b). As shown by the scalar product between input and
783 output aberration phase laws [Supplementary Figure S7c], this “noise” comes from
784 the imperfect convergence of $\hat{\mathbf{T}}$ towards \mathbf{T} . Without any confocal filter, multiple
785 scattering drastically reduces the coherence factor and induces a strong bias on
786 estimation of \mathbf{T} (see Supplementary Section S5). On the contrary, the adaptive
787 confocal filter enables an enhancement of this coherence factor \mathcal{C} to ensure a sat-
788 isfactory estimation of \mathbf{T} . The high degree of correlation between $\hat{\mathbf{T}}_{\text{in}}$ and $\hat{\mathbf{T}}_{\text{out}}$

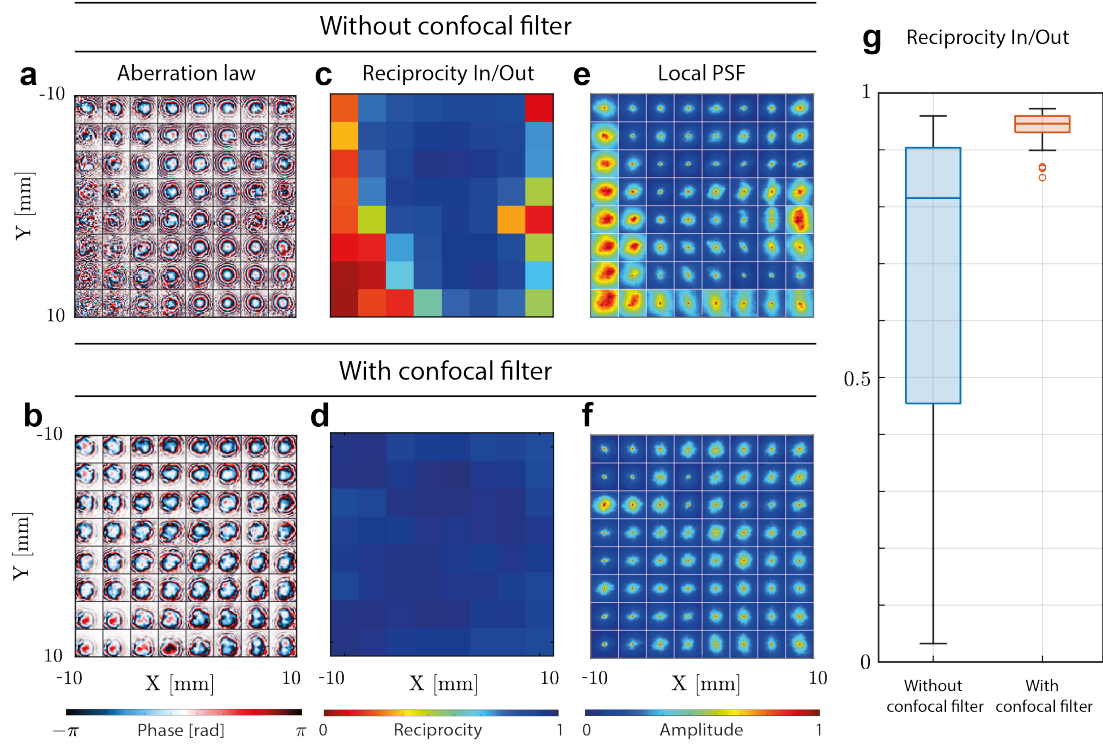


FIG. S7. **Confocal filter in transcranial imaging.** (a,b) Output aberration phase laws ($\hat{\mathbf{T}}_{\text{out}}$) extracted without and with a confocal filter. (c,d) Normalised scalar products $P_{\text{in/out}}$ without and with a confocal filter, respectively. (e,f) RPSFs obtained with UMI without and with a confocal filter. (g) Box plot corresponding to the panels (c,d). Experimental data shown in this figure correspond to the head phantom experiment described in the accompanying paper ($z = 50\text{mm}$).

789 proves this last assertion [Supplementary Figure S7d]. The effect of the confocal
790 filter is also particularly obvious when looking at the RPSF obtained at the end
791 of the UMI process. While a strong incoherent background subsists on the lat-
792 eral parts of the field-of-view when no confocal filter is applied [Supplementary
793 Figure S7e], a homogeneous focusing quality is obtained with the confocal filter
794 [Supplementary Figure S7f].

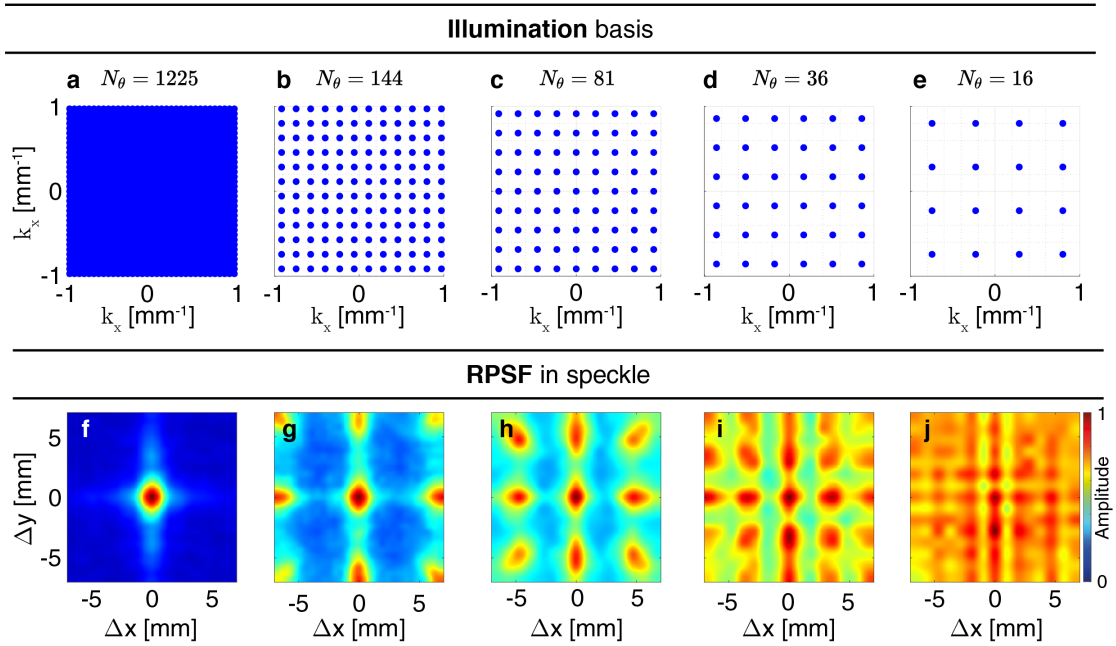


FIG. S8. **Illumination sequence.** (a-e) Representation of different plane wave illumination sequence in the \mathbf{k} -space. (f-j) Aliasing effect exhibited by the RPSFs due to incompleteness of illumination sequence displayed in panels a-e, respectively. These RPSFs have been measured in a speckle area of a tissue-mimicking phantom.

795 S10. ILLUMINATION BASIS

796 Supplementary Figure S8 shows the impact of the illumination sequence on
797 UMI. If the input illumination basis is complete [Supplementary Figure S8a], the
798 RPSF exhibits the expected diffraction-limited resolution [Supplementary Fig-
799 ure S8f]. The side lobes along the y -axis are due to the probe geometry made
800 of four blocks of transducers separated by a distance of 0.5 mm (three inactive
801 rows of transducers along the y -axis).

802 When the number of illuminating plane waves is reduced [Supplementary Fig-
803 ures S8b-e], spatial aliasing occurs on corresponding RPSFs [Supplementary Fig-
804 ures S8g-j]. The maximal extension $\Delta\rho_{\max}$ of the RPSF has to be fixed to avoid
805 the spatial aliasing induced by the incompleteness of the plane wave illumina-
806 tion basis; $\Delta\rho_{\max}$ is inversely proportional to the angular step $\delta\theta$ of the plane wave

807 illumination basis:

$$\Delta\rho_{\max} \sim \lambda_c/(2\delta\theta) \quad (\text{S27})$$

808 with λ_c the central wavelength and $\delta\theta$ the angular pitch used for the illumination
 809 sequence. Thus, to avoid spatial aliasing, the coefficients $R(\boldsymbol{\rho}_{\text{in}}, \boldsymbol{\rho}_{\text{out}}, z)$ associated
 810 with a transverse distance $|\boldsymbol{\rho}_{\text{out}} - \boldsymbol{\rho}_{\text{in}}|$ larger than the superior bound $\Delta\rho_{\max}$ should
 811 be filtered via a confocal filter.

812 Equation S27 implies the necessity of recording a high-dimension \mathbf{R} -matrix for
 813 transcranial imaging, as aberrations are particularly important in that configura-
 814 tion (see Fig. 5 of the accompanying paper). The number of independent incident
 815 waves should scale as the number of resolution cells over which the RPSF spreads.

816 **S11. DISCRIMINATE MULTIPLE SCATTERING FROM ELECTRONIC**
 817 **NOISE**

818 We consider here the background of the focused reflection matrix for a given
 819 point \mathbf{r}_p :

$$B(\Delta\boldsymbol{\rho}, \mathbf{r}_p) = \langle R_{\mathcal{M}}(\Delta\boldsymbol{\rho}, \mathbf{r}_m) \mathcal{D}(\Delta\boldsymbol{\rho}) \mathcal{W}(\mathbf{r}_m - \mathbf{r}_p) \rangle_{\mathbf{r}_m} \quad (\text{S28})$$

820 where $\mathcal{D}(\Delta\boldsymbol{\rho})$ is a de-scanned window function that eliminates the confocal peak
 821 and \mathcal{W} is a spatial average window function around the targeted focal point \mathbf{r}_p .

822 The background can be decomposed as the sum of a fully symmetric matrix
 823 associated to multiple scattering (due to spatial reciprocity) and a fully random
 824 matrix associated to the electronic noise as follows:

$$\underbrace{\mathbf{B}}_{\text{Background}} = \underbrace{\mathbf{M}}_{\text{Multiple scattering}} + \underbrace{\mathbf{N}}_{\text{Noise}} \quad (\text{S29})$$

825 Projecting the \mathbf{B} -matrix onto its anti-symmetric subspace directly holds the anti-

826 symmetric part of the electronic noise such that:

$$\mathbf{B}^{(A)} = \frac{\mathbf{B} - \mathbf{B}^\top}{2} = \mathbf{N}^{(A)} \quad (\text{S30})$$

Assuming equi-repartition of the electronic noise onto its symmetric and anti-symmetric subspace leads to:

$$\|\mathbf{B}^{(A)}\|^2 = \|\mathbf{N}^{(A)}\|^2 = \frac{1}{2}\|\mathbf{N}\|^2 \quad (\text{S31})$$

827 The norm of the background can be expressed as follows:

$$\|\mathbf{B}\|^2 = \|\mathbf{M}\|^2 + \|\mathbf{N}\|^2 + 2 \underbrace{\langle \mathbf{M} | \mathbf{N} \rangle}_{\sim 0} \quad (\text{S32})$$

Assuming that the scalar product between the electronic noise and the multiple scattering is zero on average, the multiple scattering rate α_M can be derived by combining equations (S31) & (S32):

$$\alpha_M = \frac{\|\mathbf{M}\|^2}{\|\mathbf{B}\|^2} = 1 - 2 \underbrace{\frac{\|\mathbf{B}^{(A)}\|^2}{\|\mathbf{B}\|^2}}_{\beta} \quad (\text{S33})$$

828 with β the anti-symmetric rate of the \mathbf{B} -matrix.

829 **S12. NOTATION AND SYMBOLS**

830 **References.**

- 831 [1] W. Lambert, L. A. Cobus, M. Couade, M. Fink, and A. Aubry, Reflection Matrix
 832 Approach for Quantitative Imaging of Scattering Media, Phys. Rev. X **10**, 021048
 833 (2020).

Symbol	Meaning
\mathbf{R}	Reflection matrix
\mathbf{H}	Point spread function matrix
$RPSF$	Reflection point spread function
\mathbf{G}	Propagation matrix
\mathbf{D}	Distortion matrix
\mathbf{C}	Correlation matrix
$\delta\mathbf{C}$	Perturbation term of \mathbf{C}
\mathbf{T} and $\hat{\mathbf{T}}$	Transmission matrix and its estimator
$ \delta T ^2$	Bias intensity of \mathbf{T} -matrix estimator
$P_{\text{in/out}}$	Scalar product between $\hat{\mathbf{T}}_{\text{in}}$ and $\hat{\mathbf{T}}_{\text{out}}$
\mathbf{i}	Illumination basis
\mathbf{c}	Correction basis
\mathbf{u}	Transducer basis
\mathbf{k}	Fourier basis
$\boldsymbol{\theta}$	Plane wave basis
l_c	Confocal filter size
ITR	Iterative Time Reversal
IPR	Iterative Phase Reversal
$\mathbf{W}^{(n)}$	Wave-front of the ITR process at iteration n
\mathbf{r}_m	Common midpoint
\mathbf{r}_p	Central point of a patch
$\Delta\boldsymbol{\rho} = \boldsymbol{\rho}_{\text{out}} - \boldsymbol{\rho}_{\text{in}}$	Distance input/output focusing points
$\mathcal{D}(\Delta\boldsymbol{\rho})$	De-scanned window function

TABLE S5. List of symbols for matrix imaging.

- 834 [2] V. Ntziachristos, Going deeper than microscopy: The optical imaging frontier in
835 biology, *Nat. Methods* **7**, 603 (2010).
- 836 [3] 'Oz Yilmaz, *Seismic Data Analysis* (Society of Exploration Geophysicists, 2001).
- 837 [4] H. W. Babcock, The possibility of compensating astronomical seeing, *Publ. As-*
838 *tron. Soc. Pac.* **65**, 229 (1953).
- 839 [5] F. Roddier, ed., *Adaptive Optics in Astronomy* (Cambridge University Press, Cam-
- 840 bridge, 1999).
- 841 [6] M. O'Donnell and S. Flax, Phase-aberration correction using signals from point
842 reflectors and diffuse scatterers: measurements, *IEEE Trans. Ultrason. Ferroelectr.*

Basis	Symbol	Adapted for
Acquisition basis	$\mathbf{R}_{\mathbf{i}\mathbf{u}}(t) = [R(\mathbf{i}_{\text{in}}, \mathbf{u}_{\text{out}}, t)]$	Data recording
Focused basis Common midpoint	$\mathbf{R}_{\rho\rho}(z) = [R(\boldsymbol{\rho}_{\text{in}}, \boldsymbol{\rho}_{\text{out}}, z)]$ $\mathbf{R}_{\mathcal{M}}(z) = [R(\Delta\rho, \boldsymbol{\rho}_{\text{m}}, z)]$	Focusing quality and multiple scattering quantification ¹⁹
Dual basis (input)	$\mathbf{R}_{\mathbf{c}\mathbf{r}} = [R(\mathbf{c}_{\text{in}}, \mathbf{r}_{\text{out}})]$ $\mathbf{D}_{\mathbf{c}\mathbf{r}} = [D(\mathbf{c}_{\text{in}}, \mathbf{r}_{\text{out}})]$ $\mathbf{C}_{\text{in}} = [C(\mathbf{c}_{\text{in}}, \mathbf{c}'_{\text{in}})]$ $\hat{\mathbf{T}}_{\text{in}} = [\hat{T}(\mathbf{c}_{\text{in}}, \mathbf{r}_{\text{p}})]$	Local aberration compensation ²⁸
Dual basis (output)	$\mathbf{R}_{\mathbf{r}\mathbf{c}} = [R(\mathbf{r}_{\text{in}}, \mathbf{c}_{\text{out}})]$ $\mathbf{D}_{\mathbf{r}\mathbf{c}} = [D(\mathbf{r}_{\text{in}}, \mathbf{c}_{\text{out}})]$ $\mathbf{C}_{\text{out}} = [C(\mathbf{c}_{\text{out}}, \mathbf{c}'_{\text{out}})]$ $\hat{\mathbf{T}}_{\text{out}} = [\hat{T}(\mathbf{r}_{\text{p}}, \mathbf{c}_{\text{out}})]$	

TABLE S6. Matrix notations.

Symbol	Meaning
\times	Matrix product
\circ	Hadamard product
\otimes	Convolution product
\dagger	Transpose conjugate of a matrix
\top	Matrix transpose
$\hat{}$	Estimator of a physical quantity
SVD	Singular Value Decomposition
$\mathbf{U}^{(i)}$	i^{th} right singular vector of a matrix
$\mathbf{V}^{(i)}$	i^{th} left singular vector of a matrix
σ_i	i^{th} singular value of a matrix
$\langle \dots \rangle$	Ensemble average

TABLE S7. Mathematical symbols.

843 Freq. Control **35**, 768 (1988).

844 [7] L. Nock, G. E. Trahey, and S. W. Smith, Phase aberration correction in medical
845 ultrasound using speckle brightness as a quality factor, J. Acoust. Soc. Am. **85**,
846 1819 (1989).

847 [8] R. Mallart and M. Fink, Adaptive focusing in scattering media through sound?speed
848 inhomogeneities: The van Cittert Zernike approach and focusing criterion, J.

Symbol	Meaning
\mathcal{I}	Image \Leftrightarrow Estimation of the reflectivity
$\mathbf{r} = (x, y, z)$	Focal point
$\boldsymbol{\rho} = (x, y)$	Transverse coordinate
λ_c	Wavelength at the central frequency
f_s	Sampling frequency
f_c	Central frequency
c_0	Speed-of-sound hypothesis
$\mathbf{u} = (u_x, u_y, 0)$	Transducer position
$\delta\rho_0$	Transverse ideal resolution
t	Time
τ	Time-of-flight
$\Delta\tau$	Time-delay
γ	Medium reflectivity
$\boldsymbol{\theta} = [\theta_x, \theta_y]$	Plane wave
$\mathbf{k} = [k_x, k_y]$	Fourier basis
β	Anti-symmetric rate of a matrix
θ_{max}	Directivity of transducers
$\delta\theta$	Plane wave sampling
$\Delta\mathbf{u} = (\Delta u_x, \Delta u_y)$	Probe dimension
\mathcal{C}	Coherence factor
$\mathcal{A}_{(-3\text{dB})}$	Area above 1/2 on RPSF amplitude
$\delta\rho_{(-3\text{dB})}$	Experimental RPSF resolution
$\delta\rho_0$	Diffraction-limited resolution
\mathcal{F}	RPSF contrast
α_S	RPSF single scattering rate
α_M	RPSF multiple scattering rate
α_N	RPSF electronic noise rate
α_B	RPSF background rate
\mathcal{W}	Spatial average window function
$N_{\mathcal{W}}$	Number of resolution cells in \mathcal{W}
$\mathbf{w} = (w_\rho, w_z) = (\{w_x, w_y\}, w_z)$	Dimension of \mathcal{W}
A	Apodization term of synthetic aperture

TABLE S8. List of general symbols.

- 850 [9] R. Ali, T. Brevett, L. Zhuang, H. Bendjador, A. S. Podkowa, S. S. Hsieh, W. Simson,
851 S. J. Sanabria, C. D. Herickhoff, and J. J. Dahl, Aberration correction in diagnostic
852 ultrasound: A review of the prior field and current directions, *Z. Med. Phys.* (in
853 press) 10.1016/j.zemedi.2023.01.003 (2023).
- 854 [10] S.-E. Måsøy, T. Varslot, and B. Angelsen, Iteration of transmit-beam aberration
855 correction in medical ultrasound imaging, *J. Acoust. Soc. Am.* **117**, 450 (2005).
- 856 [11] G. Montaldo, M. Tanter, and M. Fink, Time Reversal of Speckle Noise, *Phys. Rev.*
857 *Lett.* **106**, 054301 (2011).
- 858 [12] M. Pernot, M. Tanter, and M. Fink, 3-D real-time motion correction in high-
859 intensity focused ultrasound therapy, *Ultrasound Med. Biol.* **30**, 1239 (2004).
- 860 [13] M. Jaeger, E. Robinson, H. G. Akarçay, and M. Frenz, Full correction for spatially
861 distributed speed-of-sound in echo ultrasound based on measuring aberration delays
862 via transmit beam steering, *Phys. Med. Biol.* **60**, 4497 (2015).
- 863 [14] G. Chau, M. Jakovljevic, R. Lavarello, and J. Dahl, A Locally Adaptive Phase
864 Aberration Correction (LAPAC) Method for Synthetic Aperture Sequences, *Ultra-*
865 *son. Imaging* **41**, 3 (2019).
- 866 [15] T. Varslot, H. Krogstad, E. Mo, and B. A. Angelsen, Eigenfunction analysis of
867 stochastic backscatter for characterization of acoustic aberration in medical ultra-
868 sound imaging, *J. Acoust. Soc. Am.* **115**, 3068 (2004).
- 869 [16] J.-L. Robert and M. Fink, Green's function estimation in speckle using the de-
870 composition of the time reversal operator: Application to aberration correction in
871 medical imaging, *J. Acoust. Soc. Am.* **123**, 866 (2008).
- 872 [17] W. Lambert, L. A. Cobus, T. Frappart, M. Fink, and A. Aubry, Distortion matrix
873 approach for ultrasound imaging of random scattering media, *Proc. Nat. Acad. Sci.*
874 *USA* **117**, 14645 (2020).
- 875 [18] H. Bendjador, T. Deffieux, and M. Tanter, The SVD Beamformer: Physical Prin-
876 ciples and Application to Ultrafast Adaptive Ultrasound, *IEEE Trans. Med. Imag.*

- 877 **39**, 3100 (2020).
- 878 [19] W. Lambert, J. Robin, L. A. Cobus, M. Fink, and A. Aubry, Ultrasound matrix
879 imaging – Part I: The focused reflection matrix, the F-factor and the role of multiple
880 scattering, *IEEE Trans. Med. Imag.* **41**, 3907 (2022).
- 881 [20] S. Kang, P. Kang, S. Jeong, Y. Kwon, T. D. Yang, J. H. Hong, M. Kim, K. Song,
882 J. H. Park, J. H. Lee, M. J. Kim, K. H. Kim, and W. Choi, High-resolution adaptive
883 optical imaging within thick scattering media using closed-loop accumulation of
884 single scattering, *Nat. Commun.* **8**, 2157 (2017).
- 885 [21] A. Badon, V. Barolle, K. Irsch, A. C. Boccara, M. Fink, and A. Aubry, Distortion
886 matrix concept for deep optical imaging in scattering media, *Sci. Adv.* **6**, eaay7170
887 (2020).
- 888 [22] S. Yoon, H. Lee, J. H. Hong, Y.-S. Lim, and W. Choi, Laser scanning reflection-
889 matrix microscopy for aberration-free imaging through intact mouse skull, *Nat.*
890 *Commun.* **11**, 5721 (2020).
- 891 [23] Y. Kwon, J. H. Hong, S. Kang, H. Lee, Y. Jo, K. H. Kim, S. Yoon, and W. Choi,
892 Computational conjugate adaptive optics microscopy for longitudinal through-skull
893 imaging of cortical myelin, *Nat. Commun.* **14**, 105 (2023).
- 894 [24] U. Najar, V. Barolle, P. Balondrade, M. Fink, A. C. Boccara, M. Fink, and
895 A. Aubry, Non-invasive retrieval of the transmission matrix for optical imaging
896 deep inside a multiple scattering medium, *arXiv: 2303.06119* (2023).
- 897 [25] T. Blondel, J. Chaput, A. Derode, M. Campillo, and A. Aubry, Matrix Approach of
898 Seismic Imaging: Application to the Erebus Volcano, Antarctica, *J. Geophys. Res.*
899 *: Solid Earth* **123**, 10936 (2018).
- 900 [26] R. Touma, T. Blondel, A. Derode, M. Campillo, and A. Aubry, A distortion matrix
901 framework for high-resolution passive seismic 3-D imaging: Application to the San
902 Jacinto fault zone, California, *Geophys. J. Int.* **226**, 780 (2021).

- 903 [27] T. I. Sommer and O. Katz, Pixel-reassignment in ultrasound imaging, *Appl. Phys.*
904 *Lett.* **119**, 123701 (2021).
- 905 [28] W. Lambert, L. A. Cobus, J. Robin, M. Fink, and A. Aubry, Ultrasound matrix
906 imaging – Part II: The distortion matrix for aberration correction over multiple
907 isoplanatic patches, *IEEE Trans. Med. Imag.* **41**, 3921 (2022).
- 908 [29] N. M. Ivancevich, J. J. Dahl, G. E. Trahey, and S. W. Smith, Phase-aberration
909 correction with a 3-D ultrasound scanner: Feasibility study, *IEEE Trans. Ultrason.*
910 *Ferroelectr. Freq. Control* **53**, 1432 (2006).
- 911 [30] J. Lacefield and R. Waag, Time-shift estimation and focusing through distributed
912 aberration using multirow arrays, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*
913 **48**, 1606 (2001).
- 914 [31] B. D. Lindsey and S. W. Smith, Pitch-catch phase aberration correction of multiple
915 isoplanatic patches for 3-D transcranial ultrasound imaging, *IEEE Trans. Ultrason.*
916 *Ferroelectr. Freq. Control* **60**, 463 (2013).
- 917 [32] D.-L. Liu and R. Waag, Estimation and correction of ultrasonic wavefront distortion
918 using pulse-echo data received in a two-dimensional aperture, *IEEE Trans. Ultrason.*
919 *Ferroelectr. Freq. Control* **45**, 473 (1998).
- 920 [33] L. Ratsimandresy, P. Mauchamp, D. Dinet, N. Felix, and R. Dufait, A 3 MHz
921 two dimensional array based on piezocomposite for medical imaging, in *2002 IEEE*
922 *Ultrasonics Symposium, 2002. Proceedings.*, Vol. 2 (IEEE, Munich, Germany, 2002)
923 pp. 1265–1268.
- 924 [34] J. Provost, C. Papadacci, J. E. Arango, M. Imbault, M. Fink, J.-L. Gennisson,
925 M. Tanter, and M. Pernot, 3D ultrafast ultrasound imaging in vivo, *Phys. Med.*
926 *Biol.* **59**, L1 (2014).
- 927 [35] J. Provost, C. Papadacci, C. Demene, J.-L. Gennisson, M. Tanter, and M. Pernot,
928 3-D ultrafast Doppler imaging applied to the noninvasive mapping of blood vessels
929 in Vivo, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* **62**, 1467 (2015).

- 930 [36] S. A. Goss, R. L. Johnston, and F. Dunn, Compilation of empirical ultrasonic
931 properties of mammalian tissues. II, *J. Acoust. Soc. Am.* **68**, 93 (1980).
- 932 [37] L. M. Hinkelman, D. Liu, L. A. Metlay, and R. C. Waag, Measurements of ultrasonic
933 pulse arrival time and energy level variations produced by propagation through
934 abdominal wall, *J. Acoust. Soc. Am.* **95**, 530 (1994).
- 935 [38] J. Lacefield and R. Waag, Examples of design curves for multirow arrays used with
936 time-shift compensation, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* **49**, 1340
937 (2002).
- 938 [39] N. M. Ivancevich, G. F. Pinton, H. A. Nicoletto, E. Bennett, D. T. Laskowitz,
939 and S. W. Smith, Real-time 3-D contrast-enhanced transcranial ultrasound and
940 aberration correction, *Ultrasound Med. Biol.* **34**, 1387 (2008).
- 941 [40] A. Bertolo, M. Nouhoum, S. Cazzanelli, J. Ferrier, J.-C. Mariani, A. Kliewer, B. Bel-
942 liard, B.-F. Osmanski, T. Deffieux, S. Pezet, Z. Lenkei, and M. Tanter, Whole-Brain
943 3D Activation and Functional Connectivity Mapping in Mice using Transcranial
944 Functional Ultrasound Imaging, *J. Vis. Exp.* **168**, e62267 (2021).
- 945 [41] A. Chavignon, B. Heiles, V. Hingot, C. Orset, D. Vivien, and O. Couture, 3D Tran-
946 scranial Ultrasound Localization Microscopy in the Rat Brain With a Multiplexed
947 Matrix Probe, *IEEE Trans. Biomed. Eng.* **69**, 2132 (2022).
- 948 [42] C. Demené, J. Robin, A. Dizeux, B. Heiles, M. Pernot, M. Tanter, and F. Perren,
949 Transcranial ultrafast ultrasound localization microscopy of brain vasculature in
950 patients, *Nat. Biomed. Imag.* **5**, 219 (2021).
- 951 [43] D. E. Soulioti, D. Espindola, P. A. Dayton, and G. F. Pinton, Super-Resolution
952 Imaging Through the Human Skull, *IEEE Trans. Ultrason. Ferroelectr. Freq. Con-
953 trol* **67**, 25 (2020).
- 954 [44] J. Robin, C. Demené, B. Heiles, V. Blanvillain, L. Puke, F. Perren-Landis, and
955 M. Tanter, In vivo Adaptive Focusing for Clinical Contrast- Enhanced Transcranial
956 Ultrasound Imaging in Human, *Phys. Med. Biol* **68**, 025019 (2023).

- 957 [45] M. Tanter and M. Fink, Ultrafast imaging in biomedical ultrasound, *IEEE Trans.*
958 *Ultrason. Ferroelectr. Freq. Control* **61**, 102 (2014).
- 959 [46] M. Jaeger, G. Held, S. Peeters, S. Preisser, M. Gr'unic, and M. Frenz, Computed
960 ultrasound tomography in echo mode for imaging speed of sound using pulse-echo
961 sonography: proof of principle, *Ultrasound Med. Biol* **41**, 235 (2015).
- 962 [47] M. Imbault, A. Faccineto, B.-F. Osmanski, A. Tissier, T. Deffieux, J.-L. Gennisson,
963 V. Vilgrain, and M. Tanter, Robust sound speed estimation for ultrasound-based
964 hepatic steatosis assessment, *Phys. Med. Biol* **62**, 3582 (2017).
- 965 [48] M. Jakovljevic, S. Hsieh, R. Ali, G. Chau Loo Kung, D. Hyun, and J. J. Dahl,
966 Local speed of sound estimation in tissue using pulse-echo ultrasound: Model-based
967 approach, *J. Acoust. Soc. Am.* **144**, 254 (2018).
- 968 [49] A. Aubry and A. Derode, Multiple scattering of ultrasound in weakly inhomoge-
969 neous media: Application to human soft tissues, *J. Acoust. Soc. Am.* **129**, 225
970 (2011).
- 971 [50] C. Brütt, A. Aubry, B. Gérardin, A. Derode, and C. Prada, Weight of single and
972 recurrent scattering in the reflection matrix of complex media, *Phys. Rev. E* **106**,
973 025001 (2022).
- 974 [51] C. Papadacci, M. Tanter, M. Pernot, and M. Fink, Ultrasound backscatter tensor
975 imaging (BTI): analysis of the spatial coherence of ultrasonic speckle in anisotropic
976 soft tissues, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* **61**, 986 (2014).
- 977 [52] A. Rodriguez-Molares, A. Fatemi, L. Lovstakken, and H. Torp, Specular Beam-
978 forming, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* **64**, 1285 (2017).
- 979 [53] D. Zhao, L. N. Bohs, and G. E. Trahey, Phase aberration correction using echo
980 signals from moving targets i: Description and theory, *Ultrason. Imaging* **14**, 97
981 (1992).
- 982 [54] B.-F. Osmanski, G. Montaldo, M. Tanter, and M. Fink, Aberration correction by
983 time reversal of moving speckle noise, *IEEE Trans. Ultrason. Ferroelectr. Freq.*

- 984 Control **59**, 1575 (2012).
- 985 [55] F. Berland, T. Fromenteze, D. Boudescoque, P. Di Bin, H. H. Elwan, C. Aupetit-
986 Berthelemot, and C. Decroze, Microwave photonic mimo radar for short-range 3d
987 imaging, *IEEE Access* **8**, 107326 (2020).
- 988 [56] G. Montaldo, M. Tanter, J. Bercoff, N. Benech, and M. Fink, Coherent plane-wave
989 compounding for very high frame rate ultrasonography and transient elastography,
990 *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* **56**, 489 (2009).
- 991 [57] V. Perrot, M. Polichetti, F. Varray, and D. Garcia, So you think you can DAS? A
992 viewpoint on delay-and-sum beamforming, *Ultrasonics* **111**, 106309 (2021).
- 993 [58] M. Fink and C. Dorme, Aberration correction in ultrasonic medical imaging with
994 time-reversal techniques, *Int. J. Imaging Syst. Technol.* **8**, 110 (1997).
- 995 [59] J. Mertz, H. Paudel, and T. G. Bifano, Field of view advantage of conjugate adaptive
996 optics in microscopy applications, *Appl. Opt.* **54**, 3498 (2015).
- 997 [60] F. Bureau, J. Robin, A. Le Ber, W. Lambert, M. Fink, and A. Aubry, Ultrasound
998 matrix imaging [data]. Zenodo (2023).
- 999 [61] S. Silverstein, Ultrasound scattering model: 2-d cross-correlation and focusing
1000 criteria-theory, simulations, and experiments, *IEEE Trans. Ultrason. Ferroelectr.*
1001 *Freq. Control* **48**, 1023 (2001).