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I. INTRODUCTION

Laser-induced ultrasound (LIUS), that is, the use of an external photoacoustic source for transmission and pulse-echo ultrasound imaging, is a relatively recent area of interest in the biomedical field. Such sources are readily made by the use of elastomeric composites doped with various types of optically absorbing particulate carbon. The efficiency of a material’s photoacoustic response is determined by the following equation:

\[ p_0(x, y, z) = Γη_{th}μ_a F(x, y)e^{-μ_z} \]  \hspace{1cm} (1)

Here, \( η_{th} \) and \( μ_a \) are the heat conversion efficiency percentage and optical absorption coefficient (mm\(^{-1}\)), respectively, and \( F(x, y) \) represents the light fluence on the material surface. The Grüneisen parameter \( Γ \) depends on the thermal expansion coefficient \( β \) (K\(^{-1}\)), the isothermal compressibility \( κ \) (Pa\(^{-1}\)), the density \( ρ \) (kg m\(^{-3}\)), and the isochoric specific heat capacity \( C_V \) (J kg\(^{-1}\) K\(^{-1}\)) as follows:

\[ Γ = \frac{β}{κρC_V} \]  \hspace{1cm} (2)

This means that the elastomers are usually selected to have a high thermal expansion coefficient\(^{10} \) as well as good acoustic coupling with biological samples, thus materials like polydimethylsiloxane (PDMS) and epoxy are often used.

Several implementations of LIUS imaging in conjunction with photoacoustic tomography, generally for the purpose of speed-of-sound mapping and compensation in photoacoustic tomographic reconstruction, have been shown in the previous decade. One such implementation describes 3D photoacoustic imaging of an \textit{in vivo} mouse in a cylindrical geometry, including transmission speed-of-sound maps taken with LIUS.\(^{11} \) Another earlier work\(^{12} \) again focuses on the use of LIUS for transmission speed-of-sound mapping, in this case in 2D slices of a rat kidney and a leaf skeleton. Additionally, Wurzinger \textit{et al.} demonstrated simultaneous photoacoustic and reflection mode ultrasound tomography in \textit{ex vivo} transparent zebrafish.\(^{13} \)

Currently the most common approach in clinical ultrasound imaging is to build up images sequentially by transmitting focused beams to progressively form an image line by line. Two new methods depart from this approach, for the purpose of increasing the imaging speed, by insonifying the entire image region with
either plane or diverging ultrasound waves and acquiring a full image per emission, albeit at low resolution. By combining several low-resolution images acquired by emitting the plane waves at different angles or the point-like diverging source from different positions, a high-resolution image can be obtained. The first approach is known, appropriately, as plane wave imaging and the second approach is known as synthetic transmit aperture imaging. Some work applying LIUS sources to plane wave imaging using a clinical detector array has been published, focusing on single-plane wave or multi-plane wave insonification of tissue-mimicking phantoms. Plane wave imaging is an area in which LIUS can be implemented relatively easily, as the generated acoustic fields need to only have a fairly simple geometry, and thus uniform illumination of the absorbing layer is all that is required. The LIUS analog of conventional synthetic aperture imaging has not yet been developed. Alles et al. showed synthetic aperture acquisition in both transmit and receive by scanning an elliptical spot along a LIUS transmitter and detecting with a tandem scanned fiber-optic hydrophone. This allowed 15 Hz imaging of ex vivo zebrafish and swine carotid artery.

One of the possible advantages of using LIUS for ultrasound imaging is the ability to generate clean, broadband pulses which can dramatically increase the image resolution when combined with similarly broadband detectors. Additionally, applications that rely on emission by a single ultrasound source at a time in a dense array of sensitive transducers may benefit from the use of LIUS as a means of completely eliminating inter-element crosstalk. The low cost of materials such as PDMS, polymer substrate materials and carbon black particles, as well as the relative ease of production for LIUS transmitters are also a strong point, as this allows for easy switching between absorbers with different geometrical or spectral properties using the same illumination system. This allows for a low-cost flexibility for which there is no efficient analog based on piezomaterials, as CMUTs or single-crystal piezomaterials require much more complex fabrication approaches, with the accompanying higher cost. On the illumination side, using optics or different positioning of the transmitter relative to the light source also allows one to change the emission profile of the emitted LIUS. In the context of synthetic aperture imaging specifically, for example, a diffraction-limited focus created by a lens would allow a much closer approximation of a true point source, even at high frequencies, than the elements in a clinical ultrasound probe would be able to do.

A specific example of an area in which LIUS synthetic aperture ultrasound imaging can be well integrated is hybrid imaging in conjunction with photoacoustics. This article lays the groundwork for a potential expansion of a technique introduced by Held et al., where quantitative fluence-compensated photoacoustic imaging is combined with ultrasound imaging. By using an optically narrowband absorber, it would be possible to excite laser-induced ultrasound as well as photoacoustic signals through the same fibers by changing the wavelength of the light. An optimized version of the illumination system used in the current work would allow higher imaging speeds, developing the technique of Held et al. toward in-vivo, clinical applications.

The current work aims to achieve synthetic aperture laser-induced ultrasound imaging in conjunction with a clinical detector array. The illumination of a PDMS and carbon black-based LIUS emitter by an array of optical fibers fired sequentially allows the generation of point-like sources along the imaging aperture resulting in diverging waves to insonify the image region. The use of a clinical detector, as well as the imaging not only of a large-volume tissue-mimicking breast phantom, but also in vivo human wrists and fingers, shows the possibility of applying LIUS to achieve images of a clinically acceptable level of quality. While the use of a detection bandwidth narrower than that emitted by the LIUS source diminishes the potential gain in spatial resolution, the other potential advantages of using LIUS will still become apparent. A demonstration of high-quality LIUS imaging using a conventional detector and familiar insonification geometry can be seen as a stepping stone toward new insonification schemes enabled by the use of light to shape the acoustic source, as opposed to fixed piezoelectric elements.

II. MATERIALS AND METHODS

A. Concept

To adapt synthetic aperture US imaging to incorporate a laser-induced ultrasound source, an illumination strategy and a mounting solution are devised. Figures 1(c) and 1(d) show photographs of the US detector array and mount carrying the LIUS transmitters in an imaging tank or aquarium with water for a coupling medium. The mount is 3D printed and holds the LIUS source and illumination fibers. Figures 1(a) and 1(b) show schematic representations of a side and top view of the setup. Placing the LIUS transmitters, consisting of the illumination spots from the optical fibers on a thin optically absorbing layer supported by an acoustically transparent substrate, directly in front of the detector array in the imaging plane ensures co-planar signal transmission and acquisition. An elliptical illumination spot is generated by placing the outputs of the 32 multimode optical fibers (FT600UMT, Thorlabs, USA) at a 14° angle to the transmitter surface at 3 mm above the imaging plane and wedging them in place with the detector array. The purpose of this elliptical illumination is to generate a pressure field that is confined as much as possible in the imaging plane, while maximizing the in-plane opening angle to insonify as much of the sample as possible with each individual firing. A commercial clinical ultrasound imaging array (L3-12, Alpinion Medical Systems, South Korea) is used as the source and detector to obtain conventional synthetic aperture images. It is used only for detection in the case of LIUS imaging, but in both cases the LIUS source is left in place, enabling a comparison of the techniques in conditions as similar as possible to one another. For each firing, either of a single array element for conventional SA imaging or a single optical fiber for LIUS, the echoes are picked up by most or all of the elements in the detector array.

B. Optical fiber multiplexing system

The sequential illumination of equally spaced locations on the absorbing film is achieved by pulse-to-pulse switching of the illuminated fiber with a laboratory-developed system (Fig. 2) comprising a pair of galvanometer mirrors and a telecentric scanning lens. The light source is a diode-pumped Nd:YAG laser.
(M-NANO PR147, Montfort Laser, Austria) with a 1064 nm wavelength, 4.7 ns pulse duration and a repetition rate of 100 Hz. The laser beam is first reduced in diameter from 3 mm to 0.8 mm by means of a beam reducer (BE02-1064, Thorlabs, USA), this also increases the quality of the laser spot profile. Next, the beam passes through a half-wave plate that can be used to tune the polarization of the light, allowing attenuation by means of a polarizing beam splitter. Following this, a periscope is used as a compact means to align and couple the beam into a 2-axis scanning mirror galvanometer system (GVSM002, Thorlabs, USA). The galvo system directly couples the light into a telecentric scanning lens (S4LFT3162-328, Sill Optics GmbH & Co KG, Germany), allowing near-perpendicular, selective coupling into a honeycomb array of 32 multimode optical fibers with 600 μm core diameters (FT600UMT, Thorlabs, USA). The system is controlled by an off-the-shelf DAC system (NI USB-6343, National Instruments, USA), programmed via MATLAB®. The DAC applies the desired voltages to the galvo system, as well as sending trigger pulses to signal the laser to fire, the laser in turn controls the start of acquisition by the ultrasound system. Before commencing the LIUS experiments, the fiber coupling system is characterized to ensure consistent illumination of the LIUS source per fiber. The laser pulse energy is measured before and after the fiber array, per fiber, using a pyroelectric energy meter (PE50BF-DIF-C, Ophir Photonics, Israel).

To sequentially illuminate the LIUS transmitter in 32 different locations, a specific scanning pattern of the honeycomb fiber array is required. Sequential horizontal rows of fibers are scanned left-to-right and right-to-left in an alternating pattern. Once the end of the fiber array is reached, the mirrors return the spot to the first fiber. For this resetting step the vertical mirror traverses an angle of 11.2°, the largest angle in the scanning pattern. To step horizontally between fibers and vertically between rows of fibers, the mirrors move by 2.0° and 2.5° respectively. The settling time of the galvanometer mirrors is measured for each of these angular steps, an indication of the maximum scanning rate that can be achieved with this system. Characterizing the range of power tuning enabled by the maximum pulse energies achievable by the laser, as well as the polarization-based tuning range will round out the analysis of the device performance.

C. LIUS transmitter

The LIUS transmitter is designed to insonify as much of the imaging plane as possible, while also retaining spectral characteristics well matched to the receiver array properties. It consists of a 30 μm thick film of carbon black-doped PDMS, spin coated on a polyester substrate, with a thickness of 100 μm. The shape of the illumination spot on the PDMS film determines the geometry of the generated pressure field. To ensure in-plane insonification with a sufficiently large opening angle, an elliptical illumination spot was created by placing the optical fibers at a 14° angle with respect to the transmitter surface at a distance of 3 mm. Further details on the required materials and fabrication methods can be found in previous work, using the same transmitters.17 The main difference with the previous work is in the illumination geometry, as described, and the fact that the laser wavelength is now 1064 nm rather than 532 nm. This means that the optical properties of the black PDMS film as measured by a spectrophotometer (UV1600, Shimadzu, Japan) will differ in that the absorption coefficient μa has a value of 344 mm⁻¹ at 532 nm, but 213 mm⁻¹ at 1064 nm.
This leads to the expectation that the maximum of the frequency spectrum shifts somewhat toward lower frequencies compared to the source used in our previous work on plane wave imaging.17

D. Ultrasound system

Ultrasound detection is performed with a linear array (L3-12, Alpinion Medical Systems, South Korea), with 128 elements spaced 0.3 mm apart and a 4.5 mm elevational size. The detection bandwidth is from 5 to 11 MHz (−6dB), and the elevational focus is located at 20 mm from the detector face. The data are acquired by an EC12-R research ultrasound system (Alpinion Medical Systems, South Korea), a modified version of a clinical ultrasound scanner. The same array is also used as the ultrasound source when taking conventionally generated SA images, in which case all 128 elements are excited individually, and the echoes recorded by all elements each time.

E. US and LIUS characterization

The ultrasound fields transmitted by both the linear array and the LIUS transmitter are characterized with a calibrated fiber-optic hydrophone system (Precision Acoustics, UK), the sensitivity of which is known from 1 to 30 MHz, with a maximum at 30 MHz and a −6dB cut-on at 2.5 MHz. The signals from this system are detected on a digitizer (DP105, Agilent Technologies, USA) built into a PC. Measurements are taken by raster-scanning to determine the field profile in the imaging plane and in the two planes perpendicular to it. From these scans, it is possible not only to learn the pressure distribution in the imaging area but also to determine the arrival times of the signals at all locations in the imaging plane as well as characterize individual time signals and spectra. This relatively coarse scan of arrival times can be used as a basis to fit the transmit delays to be used in the reconstruction algorithm for both techniques at a higher resolution.

F. Signal processing and image reconstruction

After applying a bandpass filter with cutoffs at 4 and 10 MHz, a basic delay-and-sum algorithm incorporating the measured transmit delays and geometrically determined receive delays is implemented per firing to generate the sub-images. The absolutes of these sub-images are then summed together to generate the final image. In the reconstruction of the conventionally excited SA image all elements are fired, but only the signals of a subset of 32...
firings spread evenly along the array are used in the reconstruction, the better to mimic the situation in the LIUS imaging case.

G. Test objects and phantoms

A wire phantom is used to characterize the point-spread function (PSF) of the imaging system for conventional and LIUS excitation. Transparent fishing wire (Extreme Nylon, JVS, The Netherlands) with a 60 \( \mu \)m diameter was strung between a pair of PMMA plates spaced 10 cm apart, in three rows. Rows 1 and 3 consist of a pair of crossed wires, while row 2, in the middle, contains three vertically aligned wires. In this manner, it is possible to check if the LIUS source and the detector array are well aligned, as a vertical misalignment would lead to easily discernible smearing and shifting of the crossed wires, but less so of the straight wires. Figure 3(a) shows a photograph of the wire phantom.

To also evaluate images of more clinically relevant samples, a commercially available breast-mimicking phantom and biopsy trainer (Model 074, CIRS, USA) with tissue-like acoustic properties is imaged. The phantom contains various hyperechoic and anechoic regions, representing tumors and cysts respectively, which present comparable images as the pathologies they are meant to mimic. Figure 3(b) shows a coronal view of the breast phantom, including the indication of the locations of the ultrasound images shown in Fig. 8. A caudocranial view and a sagittal view of the phantom are shown in Figs. 3(c) and 3(d) with the imaging planes indicated as needed.

Finally, in vivo images of the left forearm of one of the authors (D.T.), near the wrist, are also taken, to evaluate the performance on living tissue.

III. RESULTS AND DISCUSSION

A. Multiplexer characterization

Figure 4 shows the measured laser pulse energy directly before and after fiber coupling, per fiber. The coupling efficiency varies somewhat between fibers, owing to the slightly different coupling angles at different locations on the array, as well as some variability in the optimization of the energy throughput per fiber. The coupling efficiency varies between 83% and 93% which is an acceptable range.

Taking the galvo settling time based on the largest angular step of 11.2° yields a value of 1.6 ms, giving a conservative estimate of the maximum continuous scanning rate of 625 Hz. However, if one assumes the step size of 2.5° to get from fiber to fiber to be the limiting factor, this yields a maximum scanning rate of 1.67 kHz based on a settling time of 0.6 ms. This would require either a different scanning pattern to circumvent the large vertical step at the end of each 32-fiber cycle, or scanning at a variable rate, moving quickly from fiber to fiber and allowing a slightly longer pause of 1.6 ms at the end of each cycle to reset to the first fiber. Regardless, the scanning rate of the system is more than sufficient for use with the current laser at a 100 Hz repetition rate. This also opens the door to future optimization of the imaging system using more rapidly pulsed lasers.

The laser pulse energy can be tuned directly by setting the pump voltage, between 0.25 mJ and 21 mJ, while polarization tuning by the \( \lambda/2 \) plate allows further tuning in the range of 5%–95% of the laser output. This gives the system an energy tuning range of 12.5 \( \mu \)J to 19.95 mJ, giving considerable flexibility in the pressures one can generate. That said, pulse energies starting in the

![FIG. 3. (a) Photograph of the wire phantom, with two pairs of crossed wires in the front and rear, and three straight wires in-between. (b) Coronal (frontal) view of the breast-mimicking phantom, with blue and red dashed rectangles indicating the imaging planes of Figs. 8(a) and 8(b), respectively. (c) Caudocranial (bottom) view of the breast phantom, blue dashed line indicates Fig. 8(a) imaging plane. (d) Sagittal (side) view of the breast phantom, red dashed line indicates Fig. 8(b) imaging plane.](image-url)
The fluctuations in the coupling efficiency between 83% and 93% translate into similar fluctuations in the generated LIUS pressure. From this result, fluctuations in the mean intensity of the reconstructed images are to be expected in the LIUS sub-images, but not the conventional ones. Measuring the mean intensity for all sub-images of the reconstructed images presented further on actually yielded similar fluctuations for the conventional and LIUS sub-images, though it varied somewhat image per image. One possible explanation is inherent differences in the total strength of the reflected signals, due to insonification of different parts of a heterogeneous sample. In addition, it also appears that some fluctuations in the conventional sub-images were due to multiple elements firing at once, a case of intermittent crosstalk, something LIUS is not hampered by. As there are already natural fluctuations because of the nature of the imaging approach and the sub-images partially overlap, leading to some averaging in the summation of the final image, this was not deemed problematic.

B. US and LIUS transmitter characterization

Figure 5(a) shows a comparison of the hydrophone-measured time signals from the conventional (64th element) and LIUS (16th fiber) sources, as well as their frequency spectra. It is important to note they are plotted on different axes to allow a comparison of the relevant features of the two without resorting to normalization. The upper temporal axis corresponds to the conventional signal trace and is shifted by 1.2 μs relative to the lower axis which corresponds to the LIUS signal trace. The right y-axis shows the signal amplitude for the conventional source whereas the left y-axis corresponds to the LIUS pulse. Contrasting the two signals, the LIUS pulse has a much more positive nature than the conventional pulse, which is built up more or less equally of compressive and rarefactive parts. The peak-to-peak pressure of the LIUS pulses is $2.5 \pm 0.5 \text{ MPa}$, while that of the conventional pulse is $215 \text{ kPa}$ with a negligible deviation. On the temporal side, the duration of the positive part of the LIUS pulse is nearly 60 ns, while the duration including the first negative peak is 100 ns. When also taking the minor secondary wiggle after the main pulse into account, the total pulse duration comes to 180 ns. The initial compressional and rarefactive peaks in the LIUS pulse correspond to the build-up and subsequent relaxation of stress due to thermalization of the absorbed optical energy. The smaller subsequent wiggle is a reflection of the backward-propagating pulse off the interface between the substrate and the surrounding water. The duration of the entire conventional signal burst, meanwhile, is 300 ns. Given a more broadband detector, this means the use of a LIUS source has the potential to improve the PSF by virtue of the shorter pulse duration. The spectra of both signals, shown in Fig. 5(b), also highlight the more broadband nature of the LIUS source. On the whole, the frequency overlap between the LIUS source and this detector as shown in Fig. 5(b) is such that there should be no problems reconstructing an image, especially considering the much higher signal amplitudes that can be achieved when using a LIUS point source, as opposed to a conventional one.

Figures 5(c) and 5(d) show the time signals and corresponding spectra of the backscattered pulses from a fishing wire, as measured by the conventional array. The convolution of the generated LIUS pulse with the impulse response of this detector leads to a much narrower bandwidth, very close to that of the conventional source. The measured amplitude of the LIUS is still a little more than the conventional pulse, though the large difference seen in the hydrophone measurements is all but gone. The reverberations due to the presence of the LIUS transmitter in the detection path are visible but small for both signals, though they seem somewhat smaller in the LIUS case.

Figure 6 shows peak-to-peak amplitude maps of the generated acoustic fields in a top view of the imaging plane on the left. The corresponding fitted signal arrival time maps are shown on the right. In both cases, the signals and generated acoustic fields for all elements or optical fibers are similar to such a degree that they can effectively be taken as laterally shifted versions of those shown here, though the amplitudes will fluctuate a bit in the LIUS case, as described in Sec. III A. The $c^{-1}$ opening angle of the conventional source is 4° and that of the LIUS source is 29°, considerably less. However, when looking at the signal amplitude, this is actually higher throughout the imaging plane for the LIUS case. In other words, while the strength of signal coverage throughout the plane relative to the pressure generated at the source is higher in the conventional case, the signal strength is in fact higher in absolute terms in the case of the LIUS source, owing to the much stronger...
signals generated. The difference in opening angle and field geometry, in general, also manifests in differences in the time delay maps, which are used for a more accurate image reconstruction. The out-of-plane fields do differ somewhat as well, the conventional detector array being elevationally focused at a depth of 20 mm, with a post-focal opening angle of 12°, while the LIUS is an elliptical spot source with an elevational opening angle of 7.5° as seen in Figs. 6(e) and 6(f). However, for depths between 30 and 60 mm relative to the detector array, this has the fields almost completely overlapping elevationally, meaning no large differences linked to the out-of-plane opening angle should be seen at these depths in the images. When taking the filtering effect of the narrowband detection into account the conventional sources do have much broader coverage laterally, although the pressure does diminish much faster with depth, due to both the larger in-plane opening angle and the elevational profile broadening more at larger depths. Effectively this means that lateral coverage per sub-image will be larger at depths around the focal depth of 20 mm for the conventional images, while the LIUS images should have a relatively better contrast at depth.

C. SA ultrasound images

Figures 7(a) and 7(b) show a side-by-side comparison of representative images of the wire phantom taken using conventional and LIUS SA imaging. The six bright dots in both images are the
FIG. 6. (a) and (b) Field scans in the imaging plane from 11.46 mm to 90.46 mm in front of the LIUS source, for conventional (element No. 64) and LIUS (fiber No. 16) excitation, respectively. (b) and (c) show corresponding fitted time delay maps. (d) and (e) show a “side view” of the fields of element 64 and fiber 16, respectively, showing the out-of-plane behavior of the field.

FIG. 7. (a) and (b) Representative wire phantom images taken using conventional and laser-induced ultrasound transmission, for the same wire positions. (c)–(e) show lateral cross sections of the top, middle, and bottom rows of wires. (f)–(h) show axial cross sections of the left column, central wire, and right column. (i)–(k) show the lateral dependence of the lateral PSF, and (l)–(n) show the same for the axial PSF, based on the full set of wire phantom images.
wires, two at the top and bottom, three in the center of the image. All wires present a signal-to-noise ratio of 30 dB, as can also be seen in Figs. 7(c)–7(e). The lateral extents of the wires are between 0.6 and 0.7 mm at the top in both images, between 0.45 and 0.6 mm in the middle and between 1 and 2 mm at the bottom, with only small differences between conventional and LIUS. Axial PSF values in Figs. 7(a) and 7(b) are consistently around 0.3 mm in both images, though they are slightly lower for the shallowest wires, at the top in the images, again the differences between both imaging methods are minimal. In both images, a line can be seen beneath each wire, which is caused by reverberation of the signals between the LIUS absorber and the detector array. These reverberation artifacts are 2.2 mm below the wires, in the conventional image secondary reverberations at twice that distance, as well as a haziness can be seen around the three straight wires in the middle. The source of the haziness around the central wires in the conventional image is unclear, though based on its absence in the LIUS images, one could speculate it might be caused by inter-element crosstalk in the conventional array.

Lateral profiles of all wires are plotted in Figs. 7(c)–7(e) and axial profiles in Figs. 7(f)–7(h). From these profiles, it can be determined that both lateral and axial positions of the wires in both image reconstructions correspond well, and the PSF values in this particular image are identical to within about 30 μm. More details of the behavior of the PSF between wire phantom images, nine of which were taken for different elevational positions, are shown in Figs. 7(i)–7(n). For both the lateral and axial PSFs, the lateral dependence is weak in the central region of the image (5–33 mm), with stronger deviations from the mean toward the edges of the images. As is apparent in Figs. 7(i)–7(k), the lateral PSF values are slightly smaller for the conventional images throughout, although they are in the same range. This seems to be the other way around for the axial PSF, with the LIUS values being smaller throughout. A further overview of the mean values and variabilities is given in Table 1, showing the same tendencies. The most likely sources of the slightly better lateral PSF in the conventional images are the larger excitation aperture used (38 mm vs 34 mm) compared to LIUS, as well as the larger single-element opening angle. The most likely reason for the slightly better axial PSF values for LIUS throughout is the shorter ultrasound pulse duration. Although this effect is weakened by the limited detection bandwidth, it appears there is some effect still to be observed, however slight.

Figure 8 shows representative examples of conventional and LIUS images of the CIRS breast phantom. A total of seven images at different locations and orientations were taken, and contrast values were determined for ten hypoechocic structures as well as four hyperechocic structures. The locations of the imaging planes are shown in Fig. 3(b). The images are accompanied by schematics to aid in the description of the features. In Fig. 8(a), two hypoechocic (C1 and C2 in the schematic) and one hyperechocic (T) feature can be distinguished in both the conventional and LIUS images. The contrast values of the hypoechocic structures are $-2.5$ dB and $-2.3$ dB for C1 and C2, respectively, in the conventional image and $-1.4$ dB and $-2.6$ dB in the LIUS image. The lower contrast for the C1 in the LIUS image is mainly due to a decrease in the background brightness toward the edges of the image, especially at smaller depths, due to the narrower transmit aperture and smaller single-element opening angle. Feature T has a contrast of $1.77$ dB in the conventional image, 1.3 dB for LIUS. The main feature of Fig. 8(b) is a large, centrally located, hypoechocic structure (labeled C in the schematic). This feature exhibits a contrast of $-3.95$ dB in the conventional image, $-4.5$ dB in the LIUS image. All images also show some strong scatterers spread throughout the phantom volume, meant to represent microcalcifications, as well as some scattered hyperechogenicity meant to represent scattered tumorous masses or glandular tissue (marked Sc in both schematics). The prevailing tendency through all images taken of the breast phantom is that the LIUS images have better contrast for hypoechocic features, while the converse is true for hyperechocic features. Although feature visibility at depths beyond 3–4 cm appears better in the LIUS images, there were no features that were invisible for one method, yet visible for the other.

Table I. Mean lateral and axial PSF values from the nine wire phantom images, divided per row. PSF values increase with distance from the source and detector, more noticeably for the lateral cross sections. Even in row 2, which contains the straight wires, some variation in PSF is apparent.

<table>
<thead>
<tr>
<th>Row</th>
<th>Lateral PSF (μm)</th>
<th>Axial PSF (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Conventional</td>
<td>LIUS</td>
</tr>
<tr>
<td>1</td>
<td>530 ± 260</td>
<td>600 ± 120</td>
</tr>
<tr>
<td>2</td>
<td>450 ± 130</td>
<td>490 ± 100</td>
</tr>
<tr>
<td>3</td>
<td>1340 ± 400</td>
<td>1300 ± 330</td>
</tr>
</tbody>
</table>

Figure 9 shows images of the left forearm of one of the authors (D.T.) near the wrist viewed from the left [(a) and (b)] and from a palmar perspective in the carpal tunnel region [(c) and (d)]. The brightest feature in Figs. 9(a) and 9(b) is a specular reflection of a bone, the ulna, approximately 6 mm below the skin (B in the diagram). Below this reflection, several reverberations at a spacing of roughly 2 mm can be seen, corresponding to the spacing between the LIUS transmitter and the detector array. Toward the right from the brightest spot the ulnar surface can be seen to continue laterally throughout the image. The large area of reduced echogenicity above the bone is one of the muscles responsible for finger movement, likely the flexor digitorum profundus (marked M). The muscle has a contrast of $-5.3$ dB in the LIUS image, again showing better contrast for hypoechocic features in the LIUS image. In the LIUS image, a dark area can be distinguished near the apex of the dermis, with a contrast of $-3.5$ dB, which is not visible in the conventional image (marked V). This small darker area corresponds in size and location with the basilic vein, a superficial vein running more or less parallel to the ulna. The bright horizontal feature between the dermis and the large muscle likely represents the muscle sheath boundary between the large muscle and the dermis. Deeper-lying areas than the bone surface are characterized by a washed-out look, caused by various artifacts due to the acoustic impedance mismatch between soft tissue and bone. Figures 9(c) and 9(d) do not contain any strong reflections from superficial bones, contributing to a more favorable dynamic range for the visualization of soft tissue structures. From top to bottom the first clear feature is again the 2 mm thick scattering region of the dermis (D), including two blood vessels (V1 and V2),
which can be discerned both from the contour of the dermis and the decreased scattering. In the conventional image, both blood vessels exhibit a contrast of $-3.3$ dB, and in the LIUS image, it is $-4.0$ dB for V1 and $-5.5$ dB for V2. In and below a hypoechoic subdermal region, at least three tendons (T2–T4) can be discerned, with a possible fourth and fifth also possible on the left and right (T1 and T5). The most obvious tendon is T3, 7 mm below the skin just left of V2. This presents a contrast of $4.2$ dB in the

**FIG. 8.** SA images of breast phantoms. (a) and (b) Sagittal view, with side-by-side representation of conventional and LIUS images of the breast phantom. From top to bottom, the following features can be distinguished, referring to the schematic on the right: A water layer, the skin (S), a small cyst-like hypoechoic structure (C1) on the leftmost edge of the image, neighbored by a slightly larger, deeper-lying hypoechoic structure (C2). Located centrally and at a similar depth to the hypoechoic structures is a solid tumor-like hyperechoic object (T) 2 cm from the skin surface, at around 4 cm depth, a region of increased scattering (Sc) can be seen. (b) Craniocaudal view, the main feature is a large cyst-like hypoechoic object located roughly centrally 2 cm beneath the skin (C). An extended region of increased scattering (Sc) can also be seen.
conventional image, 6.3 dB in the LIUS image. About 5 mm deeper, regions of increased scattering are also visible 5 mm to the left and right of T3, presenting 4.5 and 2.9 dB contrast in the conventional image, 5.0 and 3.3 dB in the LIUS image for T2 and T4, respectively. T1 and T5 both present contrast values of 2.5 dB in the conventional image and 3.6 dB in the LIUS image.

Based on the phantom results, the enhanced visibility of small hypoechoic regions in the LIUS images was to be expected and can be clearly observed in the images in Fig. 9. The enhanced contrast of hyperechoic structures like dermis and tendons, however, does not correspond to the behavior seen in the phantom images in Fig. 8. The large variability between imaged locations and small number of in-vivo images make it difficult to identify any sort of pattern definitively, but the fact that the overall contrast is somewhat better for LIUS in both these sets of in-vivo images at least hints at some possible advantages, especially in the imaging of small vasculature and nerves, which should appear similar.

Another difficulty in comparing the conventional and LIUS images in vivo comes from slight movements between images, easily avoided in phantom images but virtually guaranteed to happen when imaging a live subject. Specifically from Figs. 9(c)–9(d), a shift in the relative positions of the three clearest tendons due to a minor finger motion can be seen.

D. Overall discussion: Outlook

While this article has shown that, in the presented configuration, conventional and LIUS synthetic aperture imaging perform with a broadly similar level of quality, it is of interest to consider a situation in which the use of LIUS insonification could be advantageous. Looking at the images taken here a possibility presents itself that smaller hypoechoic regions such as mm-size blood vessels and nerves may well be easier to spot in LIUS images, though imaging and comparison of a more diverse range of in-vivo targets would be needed to confirm or disprove this idea. The possible crosstalk-based artifact in Fig. 7(a) also shows a possible application for LIUS in applications with tightly packed arrays of sensitive ultrasound transducers, where crosstalk is likely and can be avoided by optically exciting the ultrasound instead.

Over the course of several months of experimenting, no degradation in the LIUS transmitters under normal illumination circumstances was observed, though illumination with pulse energies in excess of 1 mJ led to the detachment of the film from the substrate surface, paired with a massive degradation of the signal. A preliminary assessment of the stability of the transmitters over time, also considering the time between their use for previous work in late 2018 and early 2019, would be that the transmitters may be stable over multiple years, as long as they are not illuminated above a certain threshold, the precise value of which would depend on the optical fluence at the transmitter surface and thus the illumination geometry. Detailed work by Baac et al.21 provides more detail on the optical damage thresholds of carbon/PDMS composites.

The current setup is based on a more broadly applicable illumination apparatus. The fiber multiplexing system allows for the selective excitation of up to 42 LIUS sources, placed in any geometry that can be achieved by positioning of the optical fiber outputs.

FIG. 9. In vivo SA images. (a) and (b) Left-side view of the left wrist of one of the authors (DT), also referring to the diagram on the left, the main features from the top are a hypoechoic muscle tissue region (M), and the bone surface of the ulna (B). (b) also has an additional hypoechoic region within the dermal layer (V), likely corresponding to the basilic vein, which cannot be seen in (a). (c) and (d) Palmar view of the wrist, showing the dermis (D), including a pair of superficial blood vessels (V1 and V2). Three tendons (T2–T4 in the diagram) can be clearly distinguished, with a further two (T1 and T5) less clearly visible to either side. At larger depth a tissue interface, possibly bone (marked “B?”) can be distinguished.
This opens the door to many imaging geometries besides linear-array synthetic aperture imaging. For example, a sample could be placed between a detector and the LIUS array for transmission imaging. Another interesting possibility would be to spread the transmitters three-dimensionally on a rotating mount, to allow for tomographic imaging using similarly positioned detectors. This would allow the detectors to be fully optimized for detection and also facilitate crosstalk-free ultrasound emission. Further still, in any setup based upon the current fiber multiplexing unit, changing the emission bandwidth would be as simple as replacing the absorbing material with another, having different optical absorption characteristics or indeed physical geometry. This would form a solid basis for highly adaptable ultrasound imaging equipment, at the cost of some PDMS and any optically absorbing material that can be mixed with it. Aside from this, the option to add optics or change the positioning of fibers relative to the absorbing material would also allow for adaptations to the illumination spot shape, and thus the ultrasound field geometry.

A drawback of the setup as it is now is that it would be quite challenging to use in a clinical setting, the need for a stably positioned fiber multiplexer and the need for water for coupling between the LIUS transmitter and the detector preclude handheld usage of the system. The need for the setup to be in an aquarium also makes most parts of the body difficult to reach, meaning the earlier suggestion to measure a wide range of targets would also meet with difficulties. A miniaturized version of the illumination solution, possibly based on an array of diode lasers, might help us to make the setup more portable. A solution to achieve acoustic matching between the front side of the LIUS transmitter and the target in handheld mode would also need to be devised. Additionally, the current frame rate for LIUS imaging, at 3 Hz with 32 emissions is on the low side, especially for in-vivo imaging this could lead to major motion artifacts. As discussed in Sec. III A, the scanning rate is limited by the repetition rate of the laser. While the 100 Hz rep rate laser is part of the setup to also allow imaging in future experiments where higher pulse energies will be required, a more specialized illumination setup for SA imaging with LIUS could incorporate a more rapidly pulsed diode laser. Such diode lasers can reach multiple kHz rep rates, meaning the frame rate would then be limited by the scanning mirrors, to 52 Hz when using 32 emissions.

One of the main challenges in obtaining the images as presented here was to find a good distance to place the LIUS source from the detector array. Ideally, the distance would be as small as possible, to prevent any reverberations between the source and the detector at all. However, this would leave no room for the light to reach the absorber as it would be blocked by the detector array itself. As could be seen in Figs. 7(a)–7(b) and 9(a)–9(b), the presence of strong specular reflectors like fishing wires or superficial bone produces reverberation artifacts at multiples of the LIUS-detector separation, which is 2.2 mm in this instance. A way to lessen the impact of these reverberations could be to have a larger distance between the source and the detector. The problem with this solution is that now the reverberations of the initial pulse between source and detector arrive at the same time as the scattered signals from the sample itself. This manifests as a series of lines cutting straight across the image, obscuring many interesting features. In fact, an earlier iteration of the setup was constructed in just such a manner, leading to great limitations in the image quality. While it should be possible to diminish or get rid of this sort of artifact in post-processing, early attempts indicated that physically removing them by repositioning the setup would be less time-consuming and allow for a complete removal of the large artifacts. Currently, the limited number of channels used (32) is down to the diameter of the multimode fibers. Their size does not allow much more than 32 fibers to be positioned within the detector aperture, which puts some limits on the image SNR. Using smaller multimode fibers, as the required pulse energy is much less than the maximum that can be safely transmitted through the fibers, would increase the number of transmit channels.

In the future, the use of a less broadband optical absorber such as Au nanoparticles and multiple wavelengths of light could enable the combination of laser-induced SA imaging and photoacoustic imaging. In this setup, one wavelength of light, for example, 532 nm, would be absorbed by a PDMS/Au film to generate LIUS as in this work, and another, for example, the fundamental Nd:YAG wavelength at 1064 nm would be transmitted through the film to be absorbed by the tissue. Combining all this in the illumination system presented in this work would be a large step toward clinical application of hybrid laser-induced ultrasound and quantitative photoacoustic imaging as presented by Held et al.

IV. CONCLUSION

We have demonstrated the use of laser-induced ultrasound with a serial fiber-optically illuminated light-absorbing film, resulting in images of very similar quality to conventional synthetic aperture imaging with a medical ultrasound array. In this particular instance, the in-plane opening angle of the conventional ultrasound elements (44°) is larger than that of the LIUS elements (29°), as determined by the geometry of the illumination spot. However, the application of optics to shape the illumination for a more similar ultrasound emission pattern could serve to remove this difference, should it be desired. Another feature of this approach to LIUS imaging is the use of a flexible source, which itself may also be shaped to further influence any focusing behavior that might be needed. Based on the comparable PSF and contrast values reported here as well as the demonstration of in vivo imaging on a human subject, the use of a LIUS source in ultrasound imaging has the potential to add a degree of flexibility to the emission that cannot be achieved by more conventional means.

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DATA AVAILABILITY

The raw data that support the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES