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<th>GPU-accelerated two dimensional synthetic aperture focusing for photoacoustic microscopy</th>
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<td><strong>Author(s)</strong></td>
<td>Liu, Siyu; Feng, Xiaohua; Gao, Fei; Jin, Haoran; Zhang, Ruochong; Luo, Yunqi; Zheng, Yuanjin</td>
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Acoustic resolution photoacoustic microscopy (AR-PAM) generally suffers from limited depth of focus, which had been extended by synthetic aperture focusing techniques (SAFTs). However, for three dimensional AR-PAM, current one dimensional (1D) SAFT and its improved version like cross-shaped SAFT do not provide isotropic resolution in the lateral direction. The full potential of the SAFT remains to be tapped. To this end, two dimensional (2D) SAFT with fast computing architecture is proposed in this work. Explained by geometric modeling and Fourier acoustics theories, 2D-SAFT provide the narrowest post-focusing capability, thus to achieve best lateral resolution. Compared with previous 1D-SAFT techniques, the proposed 2D-SAFT improved the lateral resolution by at least 1.7 times and the signal-to-noise ratio (SNR) by about 10 dB in both simulation and experiments. Moreover, the improved 2D-SAFT algorithm is accelerated by a graphical processing unit that reduces the long period of reconstruction to only a few seconds. The proposed 2D-SAFT is demonstrated to outperform previous reported 1D SAFT in the aspects of improving the depth of focus, imaging resolution, and SNR with fast computational efficiency. This work facilitates future studies on in vivo deeper and high-resolution photoacoustic microscopy beyond several centimeters. © 2018 Author(s). All article content, except where otherwise noted, is licensed under a Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/). https://doi.org/10.1063/1.5005145

I. INTRODUCTION

Photoacoustic microscopy (PAM) is a hybrid imaging modality that combines strong optical-absorption contrast and deep ultrasonic penetration. It has been proved to be a promising tool for wide range of structural and functional imaging including melanoma detection, sentinel lymph node mapping, body temperature monitoring, and oxygen saturation imaging in blood vessel. Taking advantage of low scattering and deep focusing capability of high-frequency ultrasonic wave, acoustic resolution photoacoustic microscopy (AR-PAM) with tight acoustic focusing has been developed for deep tissue imaging with the maximum imaging depth of several centimeters.

In AR-PAM, in order to achieve high resolution in both the lateral and axial directions, a focused ultrasonic transducer with a high center-frequency (generally larger than 10 MHz) and large numerical aperture (NA) is normally employed to detect the photoacoustic wave. After the imaging system (including laser source and receiving transducer) scans in a horizontal plane above the region of interest (ROI), one-dimensional (1D) depth-encoded signals recorded from each location could be gathered and then reconstructed to a three-dimensional (3D) image. However, owing to the large NA of the ultrasonic transducer, lateral resolution would be significantly deteriorated when the imaging plane is out of focus, which greatly limits the depth of focus of the microscopy system. To overcome this limitation, Li et al. advocated applying synthetic aperture focusing technique (SAFT) into AR-PAM for the first time, which was widely used in ultrasound imaging and radar sensing.
Combined with virtual-detector and coherent weighting techniques, an improvement of lateral-resolution of up to 600% was obtained along the SAFT direction. Afterwards, to improve the lateral resolution in the two scanning directions simultaneously, Deng et al. suggested employing a cross-shaped synthetic aperture with a coherent weighting factor (CF). Nevertheless, compared to the original 1D aperture method, an obvious resolution degradation of up to 200% was observed in this method along the direction of the line-shaped aperture. On the other hand, owing to the anisotropic reconstruction process in cross SAFT, lateral resolution is not identical from the different directions in the imaging plane, inducing significant artifacts and deterioration of imaging quality. Though some other efforts such as adaptive SAFT with active selection of the 1D SAFT direction were adopted to minimize the side effect brought by the cross SAFT, complex distribution of the vascular network and off-line extraction of blood vessel lead to increased computational costs and high signal-to-noise ratio (SNR)-sensitive imaging quality.

Recently, some other studies about three-dimensional spatial impulse response synthetic aperture focusing techniques for photoacoustic microscopy have mentioned to use two-dimensional synthetic aperture technique (2D-SAFT) in the process of image reconstruction. However, taking account of the dramatically increased parallel computation from 1D to 2D-SAFT, the 2D-SAFT operation over three-dimensional volumetric data would become time-consuming (up to several hours). Therefore, the extremely prolonged computational cost becomes the bottleneck for 2D-SAFT to be applied into practical photoacoustic microscopic imaging. And in addition, since Refs. 12 and 13 are mainly focused on spatial impulse response SAFTs and deconvolution techniques, the improvement of imaging performance of the 2D-SAFT in the aspect of imaging resolution, SNR, depth of focus, and its underlying mechanism were not fully exploited in either of these two references.

In this paper, we propose improved two dimensional synthetic aperture focusing technique (2D-SAFT) for 3D AR-PAM with fast computational architecture, which is also accelerated by graphical processing unit (GPU) programming. Explained by geometric modeling and Fourier acoustics analysis, this technique can provide significant resolution improvement and improved depth of focus in both. In addition, due to coherent addition mechanism of SAFT operation, the increased aperture area and number of virtual detectors help 2D-SAFT to own the better SNR improvement, compared to previously reported 1D-SAFT. Good performances including resolution and SNR improvement are demonstrated in both simulation and AR-PAM setup. Utilizing improved computational architecture and also powerful GPU programming, previous time-consuming 2D-SAFT algorithm is accelerated with highly improved computational efficiency.

II. THEORIES

A. Synthetic-aperture focusing technique in AR-PAM

In AR-PAM, to simplify the optical implementation, a weakly focused light beam from large-core multimode fiber is normally utilized, which enables optical focus to be much more flexible and wider than ultrasonic focus. In addition, the focal point of a spherically focused transducer can be considered as a virtual point detector to receive both upward-propagating and imaginary downward-propagating acoustic signals from the region below and above the virtual detector, as illustrated in Fig. 1. Hence, attributed to sufficient coverage of light illumination and wide receiving angle of the virtual detector, all photoacoustic waves generated within a certain solid angle would be superimposed and then received by the virtual detector. Such wide-range receiving introduces an averaging effect, leading to resolution degradation especially at the position that is far away from the virtual detector.

When a linear mechanical scanning is performed in a horizontal (x-y) plane, the photoacoustic wave from a point source could be received by the virtual detector at several adjacent positions in a certain area, which facilitates SAFT, to enhance both imaging resolution and SNR. By properly delaying and summing the received photoacoustic signals from several different positions, a large aperture with dynamic focus could be synthesized. In the 1D-SAFT, the equivalent photoacoustic signal received by a synthesized line-shaped aperture can be expressed as
FIG. 1. Schematic of the virtual-detector concept and SAFT realization.

\[ P_{SAFT}(t) = \sum_{m=1}^{N} P(m, t - \Delta t), \] (1)

where \( P(m, t) \) is the raw signal received at scan line \( m \), \( P_{SAFT}(t) \) denotes the processed A-line signal after SAFT operation, \( \Delta t \) is the acoustic time of flight from the synthetic focus to the virtual detector, and \( N \) is the maximum number of scan lines.

B. Two dimensional synthetic-aperture focusing technique (2D-SAFT) with improved computational architecture

The idea underlying resolution enhancement by the 2D-SAFT is based on the geometrical modeling and Fourier acoustics theories, to extend the SAFT technique to 3D space with spherical aperture construction. As shown in Fig. 2(a), except the data points located at the edge of the ROI, photoacoustic signals are actually received by a virtual spherical-square aperture,

\[ P_{2D-SAFT}(n_x, n_y, t) = \sum_{i=1}^{N_x(n_x, n_y, t)} \sum_{j=1}^{N_y(n_x, n_y, t)} P(i, j, t - c\Delta t_{ij}), \] (2)

where \( P(i, j, t) \) is the raw signal received at the \( i,j \)th scan line, \( P_{2D-SAFT}(n_x, n_y, t) \) is the post-focused signal at \( (n_x, n_y) \) after 2D-SAFT processing, and \( N_x(n_x, n_y, t) \) and \( N_y(n_x, n_y, t) \) describe the number of virtual detectors included on one side of the 2D square-shaped synthetic aperture in the \( x \) and \( y \) directions, which can be calculated by

\[ N_i(n_x, n_y, t) = \begin{cases} n_i + \text{ceil} \left( \frac{|ct - z_{VD}|}{2\Delta l \cdot F_N} \right), & \text{if } n_i \leq \text{ceil} \left( \frac{|ct - z_{VD}|}{2\Delta l \cdot F_N} \right) \\ 2 \cdot \text{ceil} \left( \frac{|ct - z_{VD}|}{2\Delta l \cdot F_N} \right) + 1, & \text{if } \text{ceil} \left( \frac{|ct - z_{VD}|}{2\Delta l \cdot F_N} \right) \leq n_i < N - \text{ceil} \left( \frac{|ct - z_{VD}|}{2\Delta l \cdot F_N} \right) \\ N - n_i + \text{ceil} \left( \frac{|ct - z_{VD}|}{2\Delta l \cdot F_N} \right) + 1, & \text{if } n_i \geq N - \text{ceil} \left( \frac{|ct - z_{VD}|}{2\Delta l \cdot F_N} \right) \end{cases}, \] (3)

where \( i \) is \( x \) or \( y \) to indicate the aperture size in the different directions, \( \Delta l \) is the scanning step size, \( N \) is the maximum number of scan lines, and \( F_N \) is the F-number which can be roughly expressed as the ratio of the focal distance to transducer diameter and is determined by the directivity of the focused transducer.\(^{16}\) A round-down function \( \text{ceil()} \) is used, as \( N_i(n_x, n_y, t) \) must be an integer. It is important to notice that instead of the full synthetic aperture size (signals from all virtual detectors are utilized to construct the synthetic aperture at each positions) employed in the previously reported 1D-SAFT\(^{7,11}\) and 2D-SAFT,\(^{12,13}\) different numbers of virtual detectors \([N_x(n_x, n_y, t) \cdot N_y(n_x, n_y, t)]\) would be employed to construct the synthetic aperture at different depths in this improved
2D-SAFT method. Such optimization of aperture construction architecture is based on the consideration of enhancing the computational efficiency of 2D-SAFT algorithm. Due to limited view and directivity of the focused transducer, only parts of the virtual detectors contribute to the construction of the synthetic aperture efficiently. Using out-of-view virtual detectors to construct the synthetic aperture does not only help us to improve imaging performance, thus increasing the computational cost, but also may introduce unwanted artifact. For example, for a computational voxel located at the focal plane of the focused transducer ($t = \frac{Z_{VD}}{c}$), one single virtual detector $[N_x(n_x, n_y, t) = N_y(n_x, n_y, t) = 1]$ constitutes the synthetic aperture itself. That is to say, there is no valid SAFT performed in the virtual-detector plane for the proposed improved 2D-SAFT. However, $N^2$ virtual detectors at different positions are still employed to construct the synthetic aperture in the previously reported 2D-SAFT algorithm. Such uniform choice of aperture size at different depths can be considered as employing the virtual point detectors with infinite F-number, however, which is unpractical for the normal ultrasound transducer. Considering most of the energy would be received within a cone-shaped region, a finite F-number determined by $-6$ dB directivity of focused transducer is employed to avoid the redundant computation while keeping the effect of SAFT operation. Therefore, such improved choice of synthetic aperture size in the improved 2D-SAFT not only greatly improves the computational efficiency but also avoids unwanted artifacts.

In Eq. (3), $\Delta t_{ij}$ is the time delay applied to the received signal at the $ij$'th scan, which is given by

$$\Delta t_{ij} = \frac{\text{sign}(ct - z_{VD}) \sqrt{(ct - z_{VD})^2 + (n_x - i)^2 \Delta l^2 + (n_y - j)^2 \Delta l^2}}{c}.$$  

(4)

Taking into account the normal cylindrical wavefront of the photoacoustic wave from blood vessel and computational efficiency, a 1D line-shaped SAFT was widely reported in the previous literature. In this sense, the SAFT technique, in fact, is a method of geometric modeling of line-shaped virtual ultrasonic apertures at each data position. If we properly delay the received signals to be in-phase and then add them together, it is equivalent to adjust the spatial position of the virtual detector to reshape the line aperture, thus to manipulate focusing to an arbitrary position.

For a focused transducer, the pressure pattern at the focal plane (in Fresnel region) shares the same form with that in the Fraunhofer region for a planar transducer. Therefore, the field pattern in the focal plane can be calculated by

$$P(z) = \frac{e^{ikz}}{z} \int \sigma(x_a, y_a)e^{ik\left(\frac{(x_a-x)^2+(y_a-y)^2}{2z}\right)} dx_a dy_a$$

$$= \frac{e^{ikz} e^{i\left(\frac{x^2+y^2}{2z}\right)}}{z} \cdot \int \sigma(x_a, y_a)e^{-i\left(\frac{z_{VD}x_a}{c}\right)} dx_a dy_a,$$

(5)
where $\sigma(x_n, y_n)$ is the aperture function that indicates the 2D-projected geometrical shape of the acoustic aperture. After simple variable substitution, (5) can be expressed as

$$P(z) = \frac{e^{ikz}e^{ik(x_n^2+y_n^2)}\Im\{\sigma(x,y)\}}{z}.$$

(6)

Noted that amplitude distribution of the received acoustic signal in the focal plane is proportional to Fourier transform of the aperture function. That is to say, the size of focal point is diffraction limited by the distribution of $\Im\{\sigma(x,y)\}$ in the k space. When a point $(x, y)$ is located inside this acoustic aperture, $\sigma(x, y) = 1$; otherwise, $\sigma(x, y) = 0$. Thus, in SAFT realization, the aperture function of the synthesized focused transducer would determine its focusing property.

Figure 2(b) illustrates the post-focusing patterns of SAFTs with different synthetic apertures. Specially, for the raw data without any SAFT operation, an equivalent point-like aperture is first synthesized to neutralize the phase distortion induced by acoustic inhomogeneity. This factor can be deduced as the ratio of the coherent energy to the total energy of photoacoustic signals,

$$CF_{2D-SAFT} = \frac{\sum_{i=1}^{N_x} \sum_{j=1}^{N_y} P(i,j,z-c\Delta t_{ij})}{\sum_{i=1}^{N_x} \sum_{j=1}^{N_y} N_x(n_x,n_y,t) N_y(n_x,n_y,t) \left( \sum_{i=1}^{N_x} \sum_{j=1}^{N_y} P(i,j,z-c\Delta t_{ij}) \right)^2}.$$

(7)

Note a value of CF ranging from 0 to 1 can be obtained to indicate the level of coherence, in which a maximal value of “1” corresponds to the perfectly coherent signal from each channel without any amplitude and phase distortion. Combined this CF to the SAFT process, one can finally express which a maximal value of “1” corresponds to the perfectly coherent signal from each channel without any amplitude and phase distortion. Combined this CF to the SAFT process, one can finally express the CF weighted 2D-SAFT signal as

$$P_{2D-SAFT-CF} = P_{2D-SAFT} \cdot CF_{2D-SAFT}.$$

(8)

For simplicity, the “SAFT” used in the rest of article all refers to the CF weighted SAFT.

**C. Fast 2D-SAFT realization in GPU**

In the proposed improved 2D-SAFT method, the reconstructed photoacoustic signal at a voxel grid $(n_x, n_y, t)$ is effectively the sum of all acoustic pressure contributions weighted in a spherical aperture area. Since calculation of aperture size $N(n_x, n_y, t)$, temporal delay $\Delta t_{ij}$, construction of synthetic aperture $P_{2D-SAFT}$, CF weighting $CF_{2D-SAFT}$ at different data positions can be calculated independently from Eqs. (3), (4), and (8) without any output conflict, the 2D-SAFT method is inherently data-parallel when decomposed into volumetric grid points.

Large-scale single-instruction multiple-data (SIMD) processes such as ultrasonic beamforming have been reported to enjoy tremendous speedup when parallelized on a GPU platform. To facilitate fast processing of 2D-SAFT algorithm, besides the improved computational architecture, GPU programming can be further utilized, by which a middle-end GPU (GeForce GTX 980 M, NVIDIA, USA) is programmed by the OpenCL framework to run intensive parallel operation in this work. The open-source package Pyopencl, as the OpenCL wrapper for python, enables us to access the entire OpenCL parallel computation application programming interface (API). The compilation of the python code is automatically executed in the internal CPython interpreter. Figure 3(a) shows a serial diagram of data transfer between central processing unit (CPU) and GPU. During 2D-SAFT
FIG. 3. (a) Data flow between the GPU and CPU. (b) Simplified code for 2D SAFT OpenCL kernel.

computation, the reshaped raw data are first transferred from the host (CPU) to GPU device memory and then streamed into each processor cores, in the form of work items, to facilitate kernel execution point by point in parallel. As shown in Fig. 3(b), the OpenCL kernel is simply the inner loop for aperture size calculation, delay time calculation, CF weighting, and 2D-SAFT beamforming; while the OpenCL dispatcher becomes the outer loop over grid points. Finally, the post-SAFT data are copied back to the CPU for reshaping, storage, post-processing, and imaging display. To summarize, the reconstruction procedure consists of the following steps, as illustrated in Fig. 3(b).

To fully take advantage of the locality of concurrent accesses to the pre-beamformed data, data are partially staged in the on-chip local memory to avoid frequent global memory transition. For additional optimization of the kernel, other optimization involving vector types is also applied, which reduces the global work dimensions by increasing the usage of GPU register. All optimizations are all contributed to amplify the effective memory bandwidth available to the algorithm without any sacrifice of computational accuracy.

III. METHODS
A. Numerical simulation

Photoacoustic simulations in 3D space are executed using k-wave simulation. Based on the k-space pseudospectral method applied in coupled first-order acoustic equations, the acoustic field of a 3D homogeneous or heterogeneous medium can be constructed accurately.

Figure 4(a) shows the simulation geometry. A 3D computational grid with a simulation volume of $10 \times 10 \times 4.5 \text{ mm}^3$ is utilized to simulate the photoacoustic propagation. A perfectly matched boundary layer is created to satisfy the boundary condition. For simplicity, we employ $200 \times 200$ ideal point sensors (50 $\mu\text{m}$ interval) as virtual detectors to acquire the photoacoustic wave simultaneously, instead of scanning one sensor element in the horizontal plane step by step. Therefore, it is under the assumption that the pulsed light beam is homogeneous and wide enough to cover the whole ROI, corresponding to the computational grid shown in Fig. 4(a). The directivity of each point sensor is designed to coincide with the radiation pattern of a 0.25 NA focused transducer, which shares the same parameters with the real ultrasonic transducer used in the following phantom experiment.

To study the performance of the SAFT at different imaging depths, three ideal point absorbers [5 $\mu\text{m} \times 5$ $\mu\text{m} \times 5$ $\mu\text{m}$, red solid dots in Fig. 4(a)] located, respectively, 0.5 mm, 1 mm, and 1.5 mm away from the virtual detector plane are utilized to generate photoacoustic waves. A total of 1000 time steps, separated by 10 ns, are used in the simulation. The maximal supported frequency is 150 MHz, which is limited by the size of unit voxel grid (5 $\mu\text{m}$). The overall time for such simulation costs about 127 min. After simulation, $-12 \text{ dB}$ random noise is added into the simulated volumetric data to investigate the SNR improvement of SAFT operation.
B. Phantom experiments

For 3D volumetric imaging, a backward-mode AR-PAM for SAFT implementation is constructed, as in Ref. 6. A 532 nm Q-switched pulsed laser (1.2 ns pulse width and 1 mJ energy) is employed to deliver the pulsed light excitation with a repetition rate of 100 Hz. After passing through the conical lens and reflected by mirror, dark-field light is weakly focused with a beam size of 6 mm and the fluence of about 1 mJ/cm² per pulse, well below the American National Standards Institute (ANSI) safety standards (20 mJ/cm²).

As indicated in Fig. 4(b), a focused ultrasonic transducer (V317, Olympus, USA) with a center frequency of 20 MHz, an aperture diameter of 6.35 mm, and a focus length of 12.70 mm (0.25 NA) is utilized to acquire the photoacoustic wave from underwater phantom. Milk is added into water tank with a solution of 2% to mimic the optical scattering medium as biological tissue.

A homemade plastic-encapsulated phantom printed with the “2D SAFT” is positioned 2-2.5 mm away from the ultrasonic focus, and then a 2D mechanical scanning is carried out on an area of 10.0 × 10.0 mm² with a step of 50 µm. To increase temporal and spatial accuracy during SAFT operation, linear interpolation in all the directions is performed on the raw volumetric data.

IV. RESULTS AND DISCUSSION

A. Simulation results

Simulated imaging results before and after various SAFT operations are illustrated in Fig. 5. Conventionally, a maximum amplitude projection (MAP) of volumetric photoacoustic signals is preferred for explicit visualization of microscopy image. A time gain compensation (TGC) is adopted here to manually balance the imaging nonuniformity in the depth direction. Figure 5(a) displays the MAP of the original microscopy image. As expected, though 3 ideal point absorbers can be roughly observed, the image suffers from low SNR and significant degradation of lateral resolution. To quantitatively characterize the imaging resolution, the normalized signal amplitude of each pixel along the white dashed lines (y = -2.5 mm, 0 mm, 2.5 mm) are plotted as scatter diagrams in Fig. 5(b). Then iterative Gaussian fitting is performed on these data to generate point spread function (PSF) at three different depths. Lateral resolutions, defined as full-width-half-maximum (FWHM) of the interpolated PSF, are 290 µm, 498 µm, and 740 µm, at the imaging depths of 0.5 mm, 1 mm, and 1.5 mm, respectively. In line with the beam pattern of the spherically focused transducer, increasing the distance from the photoacoustic source to virtual detector gives rise to the broadening of the acoustic beam width and deterioration of lateral resolution.

After that, similar images processed by the 1D line x-direction SAFT, cross-SAFT, and 2D-SAFT are shown in Figs. 5(c), 5(e), and 5(g), respectively. The corresponding amplitude scatters, and the PSF at the same positions are plotted in the right column [Figs. 5(d), 5(f), and 5(h)].
FIG. 5. Simulation results for various SAFT methods: The left column shows the MAP of (a) original image, (c) 1D SAFT image, (e) cross SAFT image, and (g) 2D SAFT image, respectively; the right column [(b), (d), (f), and (h)] shows corresponding PSF for three ideal point absorbers at different depths. Specifically, the black dashed line and red solid line are amplitude line and its corresponding Gaussian fitted PSF in the 1D SAFT direction; the blue dashed line and green solid line are amplitude line and its corresponding Gaussian fitted PSF along the direction that is perpendicular to the SAFT operation.

Slightly different from other SAFT methods, for 1D SAFT, due to its inhomogeneous resolution along the different directions in the 1D SAFT, amplitude lines in all the directions should be given to indicate the complete lateral resolution. Here, for simplicity, only the amplitude lines in the direction of highest resolution (x-direction and red lines) and the lowest resolution (y-direction and green lines) are given in Fig. 5(d).

Obviously, all the SAFT operations exhibit various degree of resolution improvement and contrast enhancement, compared to the original MAP. In order to have a quantitative comparison of the imaging performance between these SAFT methods, −6 dB lateral resolution and SNR at imaging depths of 0.5 mm, 1.0 mm, 1.5 mm are benchmarked in Table I. In which, lateral resolution for the 1D SAFT is expressed in the form of “x-direction resolution/y-direction resolution.” For lateral resolution, the 1D SAFT only improves the x-direction resolution, leaving y-direction resolution unchanged, or even worse (e.g., 517 µm in 1.0 mm depth and 897 µm in 1.5 mm depth); in the cross-shaped SAFT, though consideration is given to resolution improvement in both the x and y directions, whereas, an approximately 1.6 times resolution degradation in the x direction compared to the 1D SAFT can be clearly observed at various depths; when it comes to the 2D-SAFT, as expected, owing to the narrowest Fourier spectrum of the synthetic aperture, we get the best lateral resolution of about 180 µm, which is close to the −6 dB focal diameter at focal plane for the given ultrasonic transducer (183 µm).

For imaging contrast and SNR, the 2D-SAFT also outperforms all other SAFT methods. The SNR analysis on the maximal amplitude projected (MAP) image is employed as \( \text{SNR} = 20 \log\left(\frac{S}{\sqrt{\sigma_o^2}}\right) \).

TABLE I. Comparison of lateral resolution and SNR.

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<th>Methods</th>
<th>Lateral resolution (µm) at different depths</th>
<th>SNR improvement (dB)</th>
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<tr>
<td></td>
<td>0.5 mm</td>
<td>1.0 mm</td>
</tr>
<tr>
<td>Original</td>
<td>290</td>
<td>498</td>
</tr>
<tr>
<td>1D-SAFT</td>
<td>178/272</td>
<td>181/517</td>
</tr>
<tr>
<td>Cross-SAFT</td>
<td>284</td>
<td>281</td>
</tr>
<tr>
<td>2D-SAFT</td>
<td>171</td>
<td>188</td>
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where $S_i$ is the averaged brightness value (signal amplitude) of three point absorbers and $\sigma_0^2$ is the variance of the background noise in the image. Delaying and in-phase adding mechanism of SAFT operation provide an averaging effect on the received photoacoustic signal. From the original microscopy image to 1D line-shaped SAFT and cross-shaped SAFT, and finally to the 2D-SAFT, the increase in aperture size leads to an increased number of signal average, leading to better suppression of noise. Therefore, for imaging of ideal point sources in this simulation, the 2D-SAFT shows better lateral resolution and imaging SNR compared to all reported 1D SAFTs.

**B. Experimental results**

To further investigate the performance of the 2D-SAFT on arbitrary-shape sources instead of only ideal point absorbers, phantom imaging experiments are carried out (Fig. 6). The TGC weighted MAP image of original PAM, 1D-SAFT PAM, cross-SAFT PAM, and 2D-SAFT PAM is plotted in Figs. 6(a)–6(d), respectively. Owing to low SNR and lateral resolution at the out-of-focus region, the character “2D SAFT” is obviously blurred. Notably, after various SAFT operations, both lateral resolution and imaging contrast are substantially improved. It is worthy to note that some edges in Fig. 6(b) seem to be sharper than the same edges in Fig. 6(c), especially for the edges that are perpendicular to the x-direction (direction of 1D-SAFT), which is consistent with the former analysis in Sec. II. However, the image is to some extent distorted due to inhomogeneous resolution at different locations and directions, which makes it difficult to match this MAP to the original pattern of the phantom. The cross-SAFT in Fig. 6(c) performs much better in aspects of resolution homogeneity, yet resolution improvement is not so impressive compared to the results of 1D-SAFT. On the other hand, intensive artifacts around the real optical absorber in phantom cannot be effectively removed. The 2D-SAFT provides best visualization among all these methods. For example, the intact letter “S” can be clearly identified only in Fig. 6(d); however, only part of it can be obtained in Figs. 6(a)–6(c).

**FIG. 6.** Phantom imaging result: (a)–(d) are MAP visualization of “2D SAFT” phantom in the (a) original image, (b) 1D SAFT image, (c) cross SAFT image, and (d) 2D SAFT image; (e) ESF in the MAP image using various methods; (f)–(i) are statistical analysis of phantom imaging results in the (f) original image, (g) 1D SAFT image, (h) cross SAFT image, and (i) 2D SAFT image; (j) 3D rendering of the phantom image after 2D SAFT operation.
Figure 6(j) also gives the 3D rendering of the microscopy image after 2D-SAFT operation to illustrate the distribution of phantom.

The lateral resolutions are quantified by imaging the sharp edge of letter “T” within the white dashed boxes. The edge spread function [ESF, Fig. 6(e)] is calculated by averaging the perpendicular amplitude lines along the sharp edge (shown in the inset). Taking the derivative of the interpolated ESF and then Gaussian curve fitting yields the line spread function [LSF, Figs. 6(f)–6(i)]. In both ESF and LSF, curves for 2D-SAFT show the narrowest width and lowest standard deviation, which indicate the best lateral resolution and imaging SNR. Consistent with the simulated results shown in Table I, the 2D-SAFT exhibits the best SNR improvement of 18.6 dB and lateral resolution of 190 µm. Such results demonstrate the superiority of the 2D-SAFT over other SAFT techniques, in the aspects of not only SNR enhancement but also resolution improvement. Because ESF analysis is carried out not in the x and y directions, local resolution is comparable to that of cross SAFT while realistic resolution is ranging from 630 µm to 202 µm. Based on the narrowest Fourier spectrum in both the x and y directions, the 2D-SAFT provides homogenous and greatest spatial resolution among all SAFT operation. In addition, an increased number of virtual detectors and thus increased aperture area facilitate great SNR improvement.

C. GPU acceleration of 2D-SAFT

Both simulated and experimental results demonstrate that the 2D-SAFT in AR-PAM could provide a dramatically improved lateral resolution and imaging SNR. However, taking account of the dramatically increased parallel computation from the 1D to 2D SAFT, computational speed is highly limited under normal CPU processing, even for improved computational architecture in this work. For microscopy imaging over a range of 10 mm × 10 mm with (400 × 400 × 1000 × 4.0 bytes = 610.3 MB) volumetric data, the 1D-SAFT costs about 10 min using normal CPU processing. Being equivalent to 2 perpendicular 1D-SAFT operation, the cross-shaped SAFT costs about 17 min, which is approximately twofold consuming time of 1D-SAFT. Compared to normal mechanical scanning time of about several minutes, sacrificing such comparable time for SAFT operations to improve spatial resolution and SNR is definitely worthwhile. However, when it comes to the 2D-SAFT, extremely prolonged computational costs of more than 2 h becomes the bottleneck.

By employing the 2D-SAFT with improved computational architecture, the operation time of 2D-SAFT reduces more than three times to be about 4013.6 s. Further using parallel GPU processing, the computation time is spectacularly shortened to be only 3.13 s. As Fig. 7 shows, initialization progress including obtaining device, creating context, creating command queue, and allocating memories only occupies 323 ms. Data transfer time from the CPU to GPU and from the GPU to CPU is approximately 103 and 101 ms, respectively, corresponding to a data transfer speed about 5.9 GB/s between the CPU and GPU memory. The processing duration of OpenCL kernel is 2602 ms, which is the longest process in the overall process, during which SAFT and CF calculations dominate the time consumption due to the large number of multiplication operation. Therefore, accelerated by GPU programming, time duration for the 2D-SAFT process can be shortened to be about several seconds, which is negligible even compared to the imaging time of the fastest voice-coil mechanical scanning microscopy system.24

![Graph showing time consumption of the 2D SAFT method in the CPU and GPU.](image_url)
V. CONCLUSION

This paper suggests to post-focus the photoacoustic microscopy imaging by using the GPU-accelerated 2D-SAFT. By implementing dynamic focus among each position in the whole volume, a large range of depth of focus can be realized with relative homogeneous lateral resolution. Based on Fourier acoustic analysis, the 2D-SAFT provides the narrowest Fourier spectrum of aperture function, which enables homogeneous and narrower focusing capability. Good agreement is found between the simulation and experimental studies; both indicate that the GPU-based improved 2D-SAFT exhibits high computational efficiency and superior imaging performance including lateral resolution and imaging SNR.

In this work, a 20 MHz 0.25 NA focused transducer is used in the AR-PAM system to record the raw data. The higher-frequency ultrasonic transducer (up to hundreds of megahertz) can be employed to further improve focusing performance. However, accompanied by higher center frequency, the penetration depth in biological is restricted within 5 mm for a 50 MHz focused transducer. Moreover, the short focal length of the transducer induced significant near field unstable and turbid radiation pattern of the transducer, to some extent, avoids clear near surface imaging. In addition, a smaller F-number beyond the directivity of the focused transducer can be employed to construct the synthetic aperture to further improve the imaging performance since ultrasound can still detect the signal outside the directivity region, though with relatively low intensities. However, such choice of $F_N$ may slightly increase the computational cost. Some other methods such as deconvolution and delay-multiply and sum can be additional leveraged in this 2D-SAFT to further improve imaging performance. On the other hand, SAFTs also have their internal limitations. Techniques employing the focused ultrasound detector always suffer limited-view artifacts, which cannot be well eliminated by using general SAFT methods. Recently, to facilitate clear visualization of the descending microvasculature propagating at steep angles, Deán-Ben et al. have proposed to employ a hemispherical array with broad 180° tomographic coverage to avert image artifacts associated with limited-view acquisition geometries. This inspires us to change the scanning method and adopt full-angle synthetic aperture focusing to further improve the imaging performance in the future.
