Validation of delay-multiply-and-standard-deviation weighting factor for improved photoacoustic imaging of sentinel lymph node

Paridar, Roya; Pramanik, Manojit; Orooji, Mahdi; Periyasamy, Vijitha; Mehrmohammadi, Mohammad; Mozaffarzadeh, Moein; Basij, Maryam

2018

Paridar, R., Mozaffarzadeh, M., Periyasamy, V., Basij, M., Mehrmohammadi, M., Pramanik, M., & Orooji, M. (2019). Validation of delay-multiply-and-standard-deviation weighting factor for improved photoacoustic imaging of sentinel lymph node. *Journal of Biophotonics*, 12(6), e201800292-. doi:10.1002/jbio.201800292

<https://hdl.handle.net/10356/93621>

<https://doi.org/10.1002/jbio.201800292>

This is the peer reviewed version of the following article: Paridar, R., Mozaffarzadeh, M., Periyasamy, V., Basij, M., Mehrmohammadi, M., Pramanik, M., & Orooji, M. (2019). Validation of delay-multiply-and-standard-deviation weighting factor for improved photoacoustic imaging of sentinel lymph node. *Journal of Biophotonics*, 12(6), e201800292-. doi:10.1002/jbio.201800292, which has been published in final form at <http://dx.doi.org/10.1002/jbio.201800292>. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Use of Self-Archived Versions.

ARTICLE TYPE

Validation of Delay-Multiply-and-Standard-Deviation Weighting Factor for Improved Photoacoustic Imaging of Sentinel Lymph Node

Roya Paridar¹ | Moein Mozaffarzadeh¹ | Vijitha Periyasamy² | Maryam Basij³ | Mohammad Mehrmodammadi³ | Manojit Pramanik² | Mahdi Orooji*¹

¹Department of Biomedical Engineering, Tarbiat Modares University, Tehran, Iran.

²School of Chemical and Biomedical Engineering, Nanyang Technological University, 62 Nanyang Drive, Singapore

³Department of Biomedical Engineering, Wayne State University, Detroit, MI, United States.

Correspondence

*Mahdi Orooji, morooji@modares.ac.ir

Delay-and-sum (DAS) is one of the most common algorithms used to construct the photoacoustic images due to its low complexity. However, it results in images with high sidelobes and low resolution. Delay-and-standard-deviation (DASD) weighting factor can improve the contrast of the images compared to DAS. However, it still suffers from high sidelobes. In this work, a new weighting factor, named delay-multiply-and-standard-deviation (DMASD) is introduced to enhance the contrast of the reconstructed images compared to other mentioned methods. In the proposed method, the standard deviation of the mutual multiplied delayed signals are calculated, normalized and multiplied to DAS beamformed data. The results show that DMASD improves the signal-to-noise-ratio about 19.29 dB and 7.3 dB compared to DAS and DASD, respectively, for *in vivo* imaging of the sentinel lymph node. Moreover, the contrast-ratio is improve by the DMASD about 23.61 dB and 10.81 dB compared to DAS and DASD, respectively.

KEYWORDS:

Photoacoustic imaging, photoacoustic linear-array tomography, weighting factor, noise suppression, image reconstruction.

1 | INTRODUCTION

Photoacoustic imaging (PAI) is a promising non-invasive medical imaging modality^[1,2]. It is based on the photoacoustic (PA) effect^[3,4], where the energy of the irradiated laser pulse is absorbed by the tissue chromophores and results in local temperature rise. Consequently, pressure waves (in the form of ultrasound) are generated and propagated to the surface of the tissue^[5–7]. This hybrid imaging modality provides the high contrast of the pure optical imaging while maintaining larger penetration depth of ultrasound imaging^[8,9].

PAI has demonstrated its great potential for a wide range of applications, such as structural and functional imaging^[10], tumor detection^[11,12], ocular imaging^[13], imaging the whole

body of small animals^[14] etc. In this work, we focus on the clinical application of PA in sentinel lymph node (SLN) imaging^[15–17]. SLN is defined as the first node in the lymphatic system which drains a tumor site^[18]. The detection of SLN has an important role in cancer staging and its treatment procedure. Sentinel lymph node biopsy (SLNB) is a less-invasive standard clinical technique done in breast cancer staging. Firstly, the status of the SLN is determined using the injection of dyes. Then, it is surgically resected for further examination. From the SLNB result, it can be determined that the cancer is present in the SLN, near nodes and also other organs, or not. Due to the strong optical absorption of the injected dye, it has been proposed to use PAI, as a pre-surgical assessment, to accurately identify the status of the SLNs^[19].

We use a linear-array ultrasound probe for PAI to reduce

the data acquisition time compared to single element transducer^[15]. After the photoacoustic waves are acquired, a reconstruction algorithm is used to construct the absorption distribution map of the tissue. One of the reconstruction algorithms commonly used in ultrasound (US) and PA, is the non-adaptive delay-and-sum (DAS) due to its low complexity and simple implementation. However, this algorithm results in a reconstructed image with a low resolution and high sidelobes. Several modifications have been applied to DAS in order to enhance the reconstructed images^[20–22]. The non-linear delay-multiply-and-sum (DMAS) beamformer was introduced, where the signals are mutually coupled and multiplied before the summation procedure in order to reject the off-axis signal contribution more efficiently, compared to DAS^[23]. A modified version of DMAS, named Double-stage DMAS, was also introduced which results in image improvement compared to DMAS at the expense of higher computational complexity^[21,24]. Another beamforming method, named Delay-and-Standard-Deviation (DASD), was used as supplementary information to enhance the image contrast for some special cases of US imaging such as needle biopsy or cardiac catheterization^[25]. It has been concluded that DASD is not suitable to replace DAS. However, it can be fused with DAS by applying the normalized DASD to the conventional DAS beamformer as a weighting factor (weighted-DAS) and leads to contrast improvement. In contrast to non-adaptive beamformers, adaptive beamformers are also used to construct the US and PA images by weighting the received signals adapted to the characteristics of the received signals. Minimum variance (MV) is one of the adaptive beamformers where the weights are calculated in the way that the variance of the output is minimized^[26,27]. Some other modifications of MV are introduced to improve the image quality compared to MV^[28–31]. These adaptive beamformers improve the quality of the reconstructed images compared to non-adaptive ones at the expense of higher computational complexity.

In this work, it is proposed to use a novel weighting factor, named Delay-Multiply-and-Standard-Deviation (DMASD), to enhance the SLN imaging and improve the contrast of the reconstructed images compare to DAS and DASD weighting factor. In this new weighting factor, which can be interpreted as the modified version of the existing DASD method, the delayed signals are first mutually coupled and multiplied with the aim of off-axis signal contribution cancellation and more sidelobe suppression. Then, the standard deviation of the multiplied signals are calculated to further contrast improvement. Finally, the output is fused with DAS beamformer. The results show that DMASD significantly improves the reconstructed images compared to the conventional DAS and DASD weighting factor in terms of noise reduction and sidelobe suppression.

The rest of the paper is organized as follows. A brief explanation about DAS, DMAS and DASD methods along with the proposed method are presented in section 2. The results from the experimental study are presented in section 3. Finally, the discussion and the conclusion are reported in section 4 and 5, respectively.

2 | MATERIALS AND METHODS

2.1 | Delay-and-Sum beamformer

In DAS beamformer, the received signals are delayed proportional to the distance between the array sensor and the tissue. Then, the delayed signals are summed to construct PA images. Considering a linear-array sensor consisting of N elements, the output ($y_{DAS}(t)$) is obtained as below^[29]:

$$y_{DAS}(t) = \sum_{i=1}^N v_i(t - \Delta_i), \quad (1)$$

where t is time index, v_i is the received signal from i^{th} element, and Δ is the time delay.

2.2 | Delay-Multiply-and-Sum beamformer

DMAS, as a non-linear algorithm, is introduced to improve the reconstructed images in terms of mainlobe width and sidelobe levels compared to DAS. This algorithm is formulated as below:

$$y_{DMAS}(t) = \sum_{i=1}^{N-1} \sum_{j=i+1}^N s_i(t)s_j(t), \quad (2)$$

where:

$$s_i(t) = \text{sign}(v_i(t - \Delta_i)) \cdot \sqrt{|v_i(t - \Delta_i)|}. \quad (3)$$

It can be seen from Eq. (2) that the delayed signals are mutually coupled and multiplied to reject the off-axis signal contribution more efficiently compared to DAS. Then, the multiplied signals are summed to construct the image. Note that the output would be dimensionality squared due to the multiplication step. In order to address this problem, the sign and the square root of the absolute value of the delayed signals are multiplied and taken into consideration for the mutual multiplication step, as shown in Eq. (3)^[32].

2.3 | Delay-and-Standard-Deviation beamformer

DASD proposes to calculate the standard deviation of the delayed signals:

$$y_{DASD}(t) = \sqrt{\sum_{i=1}^N [\text{abs}(v_i(t - \Delta_i)) - m(t)]^2}, \quad (4)$$

where $m(t)$ is the mean amplitude of the delayed signals:

$$m(t) = \frac{1}{N} \sum_{i=1}^N \text{abs} (v_i(t - \Delta_i)) . \quad (5)$$

It has been concluded that the contrast of US images would be improved by calculating the standard deviation of the delayed signals; the standard deviation of the amplitude of the delayed signal across the aperture is larger for the specular reflections than for the diffuse echo^[25]. Therefore, the contrast would be enhanced. It should be noted that DASD improves the contrast in some special cases of imaging procedure, such as imaging the needle biopsy. Moreover, it was shown that DASD could be used as supplementary information, and DAS algorithm cannot be replaced by DASD, as mentioned before^[25]. DASD could be combined with DAS beamformer to enhance the visibility of the specular reflectors as below:

$$y_{DAS+DASD}(t) = \sum_{i=1}^N v_i(t - \Delta_i) \times w(t), \quad (6)$$

where $w(t)$ is the normalized DASD:

$$w(t) = \frac{y_{DASD}(t)}{\max(y_{DASD}(t))}. \quad (7)$$

It can be seen from Eq. (6) that $w(t)$ is multiplied to the conventional DAS beamformer, as a weighting factor.

2.4 | Proposed Method

In this work, a new weighting factor is introduced and proposed to use in PA image formation in order to suppress the sidelobes and improve the contrast compared to DAS and the existing DASD weighting factor. In the proposed DMASD method, a multiplication step is added to the existing DASD method in the way that the delayed signals are mutually coupled and multiplied before calculating the standard deviation. Therefore, the contribution of the off-axis signals would be rejected more efficiently compared to the case that no multiplication is applied^[32]. The output of the proposed weighting factor is formulated as follows:

$$y_{DMASD}(t) = \sqrt{\sum_{i=1}^{N-1} \sum_{j=i+1}^N (s_i(t).s_j(t) - m_M(t))^2}. \quad (8)$$

M stands for “multiply”, and $m_M(t)$ is the mean amplitude of the mutual multiplied delayed signals:

$$m_M(t) = \frac{1}{N/2(N-1)} \sum_{i=1}^{N-1} \sum_{j=i+1}^N s_i(t).s_j(t). \quad (9)$$

$N/2(N-1)$ in the denominator of Eq. (9), is the number of mutual multiplied delayed signals. Finally, the output of the DMASD beamformed signals is normalized and multiplied to

the conventional DAS beamformer as below:

$$y_{DAS+DMASD}(t) = \sum_{i=1}^N v_i(t - \Delta_i) \times w_{DMASD}(t). \quad (10)$$

where:

$$w_{DMASD}(t) = \frac{y_{DMASD}(t)}{\max(y_{DMASD}(t))}. \quad (11)$$

In other words, it can be said that the proposed DMASD method suppresses the noise level in two steps; the first step where the signals are mutually multiplied and result in off-axis signal contribution rejection, and the second step where the standard deviation of the multiplied signals are calculated which leads to contrast enhancement. The results in the next section show that the proposed DMASD weighting factor improves the images in terms of noise reduction and sidelobe suppression. Also, it has been shown that this weighting factor can be applied to other beamformers and improve the reconstructed images compared to the case that no weighting factor is applied.

2.5 | Ex vivo Imaging

The designed phantom and the imaging procedure are shown in Fig. 1 (a) and Fig. 1 (b), respectively. A Nd:YAG laser pulse was used to illuminate the phantom. The pulse repetition rate and the wavelength of the laser pulse is 30 *Hz* and 532 *nm*, respectively. A linear-array transducer (128 elements), operating between 4 to 11 *MHz*, is used to receive the propagated acoustic waves. Also, a high speed FPGA was used in imaging system with the aim of synchronizing the light excitation and the acoustic signal acquisition. The imaging procedure was performed on an *ex vivo* phantom. The *ex vivo* phantom is designed in the way that two pencil leads, having a diameter of 0.5 *mm*, are positioned inside a chicken breast tissue with the axial and the lateral distance of 5 *mm* and 12 *mm*, respectively, starting from 23 *mm* of the surface of the chicken breast tissue. The dimensions of the chicken breast tissue is about 4 *cm* ×

FIGURE 1 (a) The photograph of the *ex vivo* phantom used for imaging where arrows show the targets. (b) The imaging setup.

4 cm × 5 cm. Note that the pencil leads are the strong optical absorbers.

2.6 | In Vivo Imaging of the Sentinel Lymph Node

An *in vivo* imaging of the SLN was performed using the system described in^[33]. Its experimental setup is presented in Fig. 2. Nd:YAG pump laser (Continuum, Surelite Ex, San Jose, California, USA) was used to generate nanosecond pulses of wavelength 1064 nm at a pulse repetition rate of 10 Hz with an energy of 10 mJ/cm² to illuminate the tissue. Plano-concave lens (Thor labs, LC1439-C) of focal length -50 mm was used to illuminate the input end of the fiber bundle which was separated into two bundles at the output with 400 fiber-tips each. A small percentage of the beam from the laser was reflected to the photodiode using a beam-splitter in order to trigger the US system. Clinical US system (E-CUBE 12R, Alpinion, South Korea) has a 128 element transducer (3.85 cm × 1 cm) which was operated at a frequency of 8.5 MHz. Note that the axial resolution of the system used in this work is 207 ± 45 μm, and the lateral resolution which depends on the size of the array element is 300 μm^[17]. Chicken breast tissue of 5 mm thickness was placed on the anesthetized rat of weight 250 gms to mimic the human SLN imaging. Black ink was injected in the fore-paw of the rat after depleting the fur on the animal. After the imaging procedure was performed, the animal was euthanized and the SLN is exposed, as shown in Fig. 2 (c) and Fig. 2 (d). All animal experiments were performed in accordance with the approved guidelines and regulations, and were approved by the institutional Animal Care

and Use committee of Nanyang Technological University, Singapore (Animal Protocol Number ARF-SBS/NIE-A0263)

3 | RESULTS

3.1 | Ex vivo Images

For the phantom experiment, the reconstructed images are presented in Fig 3, with a dynamic range of 50 dB. DAS results in a reconstructed image with high level of noise as shown in Fig. 3 (a). The noise level is reduced and therefore, the contrast is improved by applying the DASD weighting factor. However the reconstructed image still suffers from high sidelobes across the point targets, shown with white arrows in Fig. 3 (b). Comparing Fig. 3 (b) and Fig. 3 (c), it can be seen that the proposed weighting factor, DMASD, suppresses the noise level more efficiently compared to DASD weighting factor. It is due to the multiplication step added to the existing DASD procedure. The lateral variations are presented in Fig. 4 to evaluate the beamformers in detail. The white dashed lines in Fig. 3 (c) show the planes which are used to create the lateral variations. It can be seen that the DASD weighting factor couldn't suppress the sidelobes efficiently across the reconstructed wire targets in both depths in comparison with DAS, and it only reduces the background noise, as shown in Fig. 3 (b). The proposed DMASD weighting factor leads to more sidelobe suppression, and the reconstructed point targets are more clearly seen compared to other mentioned beamformers, as shown with green circles and arrows in Fig. 4. The statistical evaluation shows that the proposed DAMSD weighting factor improves the sidelobes about 45.11 ± 1.89 dB and 30.04 ± 1.3 dB compared to DAS and the existing DASD

FIGURE 2 (a) The experimental setup of the *in vivo* imaging, (b) the animal used for imaging, (c) exposing the SLN from the animal after the imaging procedure and (d) the excised SLN.

FIGURE 3 The reconstructed images of the *ex vivo* phantom (shown in Fig 1) using (a) DAS, (b) DAS+DASD and (c) DAS+DMASD. The noise across the reconstructed point targets are shown with white arrows in Fig. 3 (b).

TABLE 1 The calculated SNR (dB) for the *ex vivo* phantom.

Beamformer \ Depth (mm)	DAS	DAS+DASD	DAS+DMASD
23	38.59	47.00	72.44
25	38.30	44.89	71.51

weighting factor, respectively.

Two evaluation metrics, Signal-to-Noise-Ratio (SNR) and Contrast-Ratio (CR), are used to evaluate the performance of the beamformers in terms of contrast improvement quantitatively. SNR is defined as the ratio of the difference between the maximum and the minimum intensity to the standard deviation of the reconstructed image^[21], and CR is defined as the ratio of the mean intensity of the background to the mean intensity inside the target^[24]. The higher values of SNR and CR indicate the better performance of the beamformer in term of contrast improvement. Note that CR is used to evaluate the reconstructed images of the cyst phantoms. However, the diameter of the wire targets are big enough, and therefore, CR could be used to evaluate the performance of the reconstructed

images. The calculated SNR and CR of the reconstructed images are presented in Table 1 and Table 2, respectively. It can be concluded that the proposed DMASD method leads to 33.53 dB and 26.03 dB SNR improvement compared to DAS and DASD weighting factor, respectively. Also, the DMASD weighting factor improves the CR for about 39.3 dB and 33.37 dB , in average, compared to DAS and DASD weighting factor, respectively, indicating the good performance of DMASD in noise reduction and contrast improvement compared to other mentioned methods.

3.2 | In vivo Images

The reconstructed images of the SLN experiment are presented in Fig 5. It can be seen that the quality of the reconstructed image is improved using the DASD weighting factor; The calculated SNR and CR are improved about 11.99 dB and 12.8 dB , respectively, compared to DAS beamformer. Comparing DASD and DMASD weighing factors, it can be seen that the proposed DMASD weighting factor leads to more noise reduction. Moreover, the quantitative evaluation metrics are performed and it is concluded that the DMASD method improves the SNR about 19.29 dB and 7.3 dB compared to

FIGURE 4 The lateral variations of the *ex vivo* imaging at the depth of (a) 23 mm and (b) 25 mm. The green arrows and circles show the contrast improvement using DMASD weighting factor.

FIGURE 5 The reconstructed images of the *in vivo* experiment shown in Fig 2 using (a) DAS, (b) DAS+DASD and (c) DAS+DMASD. The reconstructed SLN is shown with the red arrow in Fig. 5 (c).

TABLE 2 The calculated CR (dB) for the *ex vivo* phantom.

Beamformer	DAS	DAS+DASD	DAS+DMASD
Depth (mm)			
23	30.03	36.32	69.74
25	29.45	35.03	68.35

DAS and DASD weighting factor, respectively. Also, 23.61 dB and 10.81 dB CR improvement occurred in comparison with DAS and DASD weighting factor, respectively, indicating the high performance of the proposed DMASD method in terms of contrast improvement.

It is worth to note that the good performance of the proposed DMASD is not limited only to the DAS output beamformer; this weighting factor can be applied to other beamformers and it has been shown that the reconstructed images would be improved compared to the conventional existing beamformers. Figure 6 shows the reconstructed images of the mentioned phantoms using DMAS and MV beamformers, with and without applying the existing DASD and the proposed DMASD weighting factors. It is obvious from the figures that the reconstructed images are significantly improved in terms of noise reduction and sidelobe suppression by applying DMASD weighting factor to DMAS and MV outputs, compared to the cases that DMASD isn't applied. Quantitative evaluation shows that the CR would be improved about 22.43 dB compared to the conventional DMAS (comparing Fig 6 (a) and (c)), and 23.6 dB compared to the conventional MV (comparing Fig 6 (d) and (f)), by applying the proposed DMASD weighting factor to the output of each beamformers in *in vivo* experiment. Also, 29.25 dB and 34.26 dB CR improvement is obtained in average, for the *ex vivo* experiment by applying DMASD to the output of the DMAS (comparing Fig 6 (g) and (i)) and MV (comparing Fig 6 (j) and (l)) beamformers, respectively. The performance of the existing DASD and the proposed DMASD weighting factors are evaluated and compared in more details in the next section.

4 | DISCUSSION

The major benefit of the proposed DMASD method is sidelobe suppression and contrast improvement. The non-adaptive DAS beamformer results in the reconstructed images with a low resolution and high sidelobes. DASD improves the contrast of the US images by calculating the standard deviation of the delayed signals; the standard deviation of the specular reflection is larger compared to the standard deviation of the diffuse echo, and therefore, the contrast would be improved. However, this algorithm is not suitable to replace DAS in order to improve the contrast^[25]. Also, DASD can be used only in some special cases of imaging, such as imaging the needle during the biopsy procedure, and it cannot be employed to improve the point-like phantoms. The reconstructed images would be improved by applying a proportional weighting factor to the output of the DAS beamformed signals. It has been shown that DAS and DASD could be fused, in the way that the normalized version of DASD acts as a weighting factor and multiplied to DAS. The results show that the DASD weighting factor improves the contrast, as shown in Fig. 3, for instance, where the SNR is improved about 8.41 dB and 6.59 dB at the depth of 23 mm and 25 mm , respectively. However, the DASD weighting factor only leads to background noise reduction, and the point targets still suffer from high sidelobes. It can be more clearly seen from Fig. 4, where the lateral variations of the phantom shown in Fig. 3 are almost matched across the reconstructed wire targets with and without applying the weighting factor. It is proposed to modify the DASD weighting factor to address this limitation and improve the images. The proposed DMASD weighting factor is calculated in three steps; In the first step, the delayed signals are mutually coupled and multiplied. This leads to the off-axis signal contribution to be more rejected by calculating the auto-correlation of the delayed signals. In the second step, the standard deviation of the multiplied signals are calculated and results in specular reflection enhancement. Finally, the output is normalized and multiplied to the conventional DAS beamformer. The results show that the DMASD weighting factor reduces the

FIGURE 6 The reconstructed images of the *in vivo* experiment (first row) and the *ex vivo* experiment (second row) using DMAS and MV beamformers, with and without applying the existing DASD and the proposed DMASD weighting factors.

noise level and suppresses the sidelobes more efficiently compared to DASD weighting factor due to the multiplication step added to the existing DASD procedure, as shown in Fig. 3 and Fig. 5, where the SNR is improved about 26.03 dB and 7.3 dB compared to DASD weighting factor, for the *ex vivo* and *in vivo* phantom, respectively. Also, the calculated CR is improved about 33.37 dB for the *ex vivo* phantom, and 10.81 dB for the *in vivo* phantom, compared to the DASD weighting factor by using the proposed DMASD weighting factor. Moreover, from the lateral variations shown in Fig. 4, it can be seen that DMASD suppresses the sidelobes efficiently across the point targets compared to other mentioned beamformers, and the point targets would be more clearly seen. As mentioned before, DMASD can be applied to other beamformers and its performance is not limited to only DAS beamformer. Moreover, the performance of the proposed DMASD weighting factor would be improved compared to DASD when it is applied to other beamformers, as shown in Fig. 6 where the two mentioned weighting factors are applied to DMAS and MV algorithms. It is obvious that both weighting factors lead to more noise reduction and sidelobe suppression compared to the conventional cases. Comparing DASD and DMASD, it can be seen that DMASD leads to more contrast improvement compared to DASD. Quantitative results show that DMASD leads to SNR improvement about 20.78 dB when it is applied to DMAS beamformer (comparing Fig. 6 (a) and (c)), and 20.14 dB when it is applied to MV beamformer (comparing Fig. 6 (d) and (f)) for the reconstructed images of the *in vivo* phantom. Also, the SNR is improved about 5.74 dB and 6.65 dB when DMASD is applied to DMAS and MV beamformers, respectively, compared to the case that DASD is applied to the mentioned beamformers (comparing Fig. 6 (b) and (c) for DMAS beamformer, and Fig. 6 (e) and (f) for MV beamformer). For the *ex vivo* phantom, the calculated SNR is

improved about 34.91 dB and 35.05 dB in average by applying the DMASD weighting factor to the DMAS (comparing Fig. 6 (g) and (i)) and MV (comparing Fig. 6 (j) and (l)) beamformers, respectively. Furthermore, comparing Fig. 6 (h) and (i), 26.24 dB SNR improvement occurred when DMASD is applied to DMAS, and comparing Fig. 6 (k) and (l), 28.5 dB SNR improvement occurred when it is applied to MV, compared to the case that the DASD weighting factor is applied.

It is worth comparing the results obtained from the fusion of the proposed DMASD weighting factor and DAS method (DAS+DMASD) with the existing DMAS beamformer. Comparing Fig. 5 (c) and Fig. 6 (a), it can be seen that the noise level is reduced more efficiently compared to DMAS using DAS+DMASD method. Also, the calculated SNR and CR are improved about 14.73 dB and 16.87 dB , respectively, compared to DMAS method. Therefore, it can be concluded that DAS+DMASD outperforms DMAS in terms of sidelobe suppression and contrast improvement. Note that the off-axis signal contribution is reduced in DMAS and the proposed DMASD methods following the multiplication step which is similar in both two methods. Therefore the reconstructed images are improved compared to DAS. However, due to the calculation of the standard deviation of the multiplied signals in DMASD (instead of the summation procedure which exists in DMAS method), the sidelobes would be suppressed more efficiently and results in contrast improvement compared to DMAS.

5 | CONCLUSION

In this work, a novel weighting factor was introduced to enhance the SLN imaging. The DMASD method was directly multiplied to DAS beamformed data as a weighting factor to improve the image contrast compared to DAS beamformer.

The results obtained from the *ex vivo* imaging showed that DMASD improves the *SNR* for about 33.53 *dB* and 26.03 *dB*, in average, compared to DAS and the DASD weighting factor, respectively. Also, for the *in vivo* experiment, the calculated *CR* was improved about 23.61 *dB* and 10.81 *dB* compared to DAS and DASD, respectively. The results indicated the high performance of the DMASD weighting factor in terms of noise reduction and sidelobe suppression.

References

- [1] Li Lin, Peng Hu, Junhui Shi, Catherine M Appleton, Konstantin Maslov, Lei Li, Ruiying Zhang, Lihong V Wang, *Nature communications* **2018**, 9 (1), 2352.
- [2] Lei Li, Liren Zhu, Cheng Ma, Li Lin, Junjie Yao, Lidai Wang, Konstantin Maslov, Ruiying Zhang, Wanyi Chen, Junhui Shi, et al., *Nature biomedical engineering* **2017**, 1 (5), 0071.
- [3] Lihong V Wang, Song Hu, *science* **2012**, 335 (6075), 1458–1462.
- [4] Mohammad Mehrmohammadi, Soon Joon Yoon, Douglas Yeager, Stanislav Y Emelianov, *Current molecular imaging* **2013**, 2 (1), 89–105.
- [5] Paul K Upputuri, Manojit Pramanik, *Journal of Biomedical Optics* **2016**, 22 (4), 041006.
- [6] Yi Tan, Kaiye Xia, Qiushi Ren, Changhui Li, *Optics express* **2017**, 25 (7), 8022–8028.
- [7] Santiago J Arconada-Alvarez, Jeanne E Lemaster, Junxin Wang, Jesse V Jokerst, *Photoacoustics* **2017**, 5, 17–24.
- [8] Lihong V Wang, Junjie Yao, *Nature methods* **2016**, 13 (8), 627.
- [9] Yong Zhou, Junjie Yao, Lihong V Wang, *Journal of biomedical optics* **2016**, 21 (6), 061007.
- [10] Mohammadreza Nasiriavanaki, Jun Xia, Hanlin Wan, Adam Quentin Bauer, Joseph P Culver, Lihong V Wang, *Proceedings of the National Academy of Sciences* **2014**, 111 (1), 21–26.
- [11] Bin Guo, Jian Li, Henry Zmuda, Mark Sheplak, *IEEE Transactions on Biomedical Engineering* **2007**, 54 (11), 2000–2010.
- [12] Sarah E Bohndiek, Laura S Sasportas, Steven Machtaler, Jesse V Jokerst, Sharon Hori, Sanjiv S Gambhir, *Journal of nuclear medicine: official publication, Society of Nuclear Medicine* **2015**, 56 (12), 1942.
- [13] Seung Yun Nam, Stanislav Y Emelianov, *Journal of the Optical Society of Korea* **2014**, 18 (2), 151–155.
- [14] Jun Xia, Lihong V Wang, *IEEE Trans. Biomed. Engineering* **2014**, 61 (5), 1380–1389.
- [15] Chulhong Kim, Kwang Hyun Song, Feng Gao, Lihong V Wang, *Radiology* **2010**, 255 (2), 442–450.
- [16] Moein Mozaffarzadeh, Vijitha Periyasamy, Manojit Pramanik, Bahador Makkiabadi, *Journal of Biomedical Optics* **2018**, 23 (12), 121604.
- [17] Kathyayini Sivasubramanian, Vijitha Periyasamy, Manojit Pramanik, *Journal of biophotonics* **2018**, 11 (1), e201700061.
- [18] Alejandro Garcia-Urbe, Todd N Erpelding, Arie Krumholz, Haixin Ke, Konstantin Maslov, Catherine Appleton, Julie A Margenthaler, Lihong V Wang, *Scientific reports* **2015**, 5, 15748.
- [19] Yu Wang, Zijian Guo, Lihong V Wang, Todd N Erpelding, Ladislav Jankovic, Jean-Luc Robert, Guillaume David, *Journal of Biomedical Optics* **2012**, 17 (6), 061208.
- [20] S-L Wang, P-C Li, *IEEE transactions on ultrasonics, ferroelectrics, and frequency control* **2009**, 56 (10).
- [21] Moein Mozaffarzadeh, Ali Mahloojifar, Mahdi Orooji, Saba Adabi, Mohammadreza Nasiriavanaki, *IEEE Transactions on Biomedical Engineering* **2018**, 65 (1), 31–42.
- [22] Moein Mozaffarzadeh, Yan Yan, Mohammad Mehrmohammadi, Bahador Makkiabadi, *Journal of biomedical optics* **2018**, 23 (2), 026005.
- [23] Jongin Park, Seungwan Jeon, Jing Meng, Liang Song, Jin S Lee, Chulhong Kim, *Journal of biomedical optics* **2016**, 21 (3), 036010.
- [24] Moein Mozaffarzadeh, Masume Sadeghi, Ali Mahloojifar, Mahdi Orooji, *Ultrasound in medicine & biology* **2018**, 44 (3), 677–686.
- [25] Raja Sekhar Bandaru, Anders Rasmus Sornes, Jeroen Hermans, Eigil Samset, Jan DâŽžhooge, *IEEE transactions on ultrasonics, ferroelectrics, and frequency control* **2016**, 63 (12), 2057–2068.
- [26] Jack Capon, *Proceedings of the IEEE* **1969**, 57 (8), 1408–1418.
- [27] Johan-Fredrik Synnevag, Andreas Austeng, Sverre Holm, *IEEE transactions on ultrasonics, ferroelectrics, and frequency control* **2009**, 56 (9).

- [28] Moein Mozaffarzadeh, Ali Mahloojifar, Mahdi Orooji, Karl Kratkiewicz, Saba Adabi, Mohammadreza Nasirivanaki, *Journal of biomedical optics* **2018**, 23 (2), 026002.
- [29] Moein Mozaffarzadeh, Ali Mahloojifar, Mohammadreza Nasirivanaki, Mahdi Orooji, in *Photonics in Dermatology and Plastic Surgery 2018*, International Society for Optics and Photonics, **2018**, p. 1046717.
- [30] Roya Paridar, Moein Mozaffarzadeh, Mohammad Mehrmohammadi, Mahdi Orooji, *Biomedical Optics Express* **2018**, 9 (6), 2544–2561.
- [31] J-F Synnevåg, C-IC Nilsen, Sverre Holm, in *Ultrasonics Symposium, 2007. IEEE*, IEEE, **2007**, pp. 1545–1548.
- [32] Giulia Matrone, Alessandro Stuart Savoia, Giosuè Caliano, Giovanni Magenes, *IEEE transactions on medical imaging* **2015**, 34 (4), 940–949.
- [33] Kathyayini Sivasubramanian, Vijitha Periyasamy, Rhonnie Austria Dienzo, Manojit Pramanik, *Journal of biophotonics* **2018**, 11 (5), e201700317.