Biomedical Signal Processing and Control 44 (2018) 67–74

Contents lists available at ScienceDirect

Biomedical Signal Processing and Control

journal homepage: www.elsevier.com/locate/bspc

# Variable speed of sound compensation in the linear-array photoacoustic tomography using a multi-stencils fast marching method

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ARTICLE INFO

*Article history:*
Received 29 January 2018
Received in revised form 19 March 2018
Accepted 15 April 2018

*Keywords:*
Linear-array photoacoustic tomography
Variable speed of sound
Delay and sum
Multi-stencils fast marching method

ABSTRACT

Despite the promising clinical application of linear-array photoacoustic tomography, it has been shown the variable speed of sound would severely affect the photoacoustic imaging quality, resulting in the target deterioration and inaccurate depth positioning in the conventional constant speed assumed delay and sum (DAS) reconstruction. By contrast, multi-stencils fast marching (MSFM) method is able to produce accurate time delay map for the tissue with inhomogeneous acoustic speed. This study explored the combination of DAS reconstruction algorithm with the MSFM approach to reduce the imaging distortions due to the speed spatial variation, where the target structure and target position in depth could be measured more precisely. To validate the performance of the proposed method, numerical, phantom, and *in vivo* photoacoustic studies were conducted with the qualitative and quantitative analysis, especially in the detection of mouse deep brain tumor with an intact skull.



## 1. Introduction

Nowadays, photoacoustic (PA) imaging is a thriving biomedical imaging modality in preclinical research. Via the instant thermoelastic expansion effect of optical absorbable target, the PA signal could be generated, detected and then reconstructed to reflect the optical absorption properties of the tissue [1–3]. The most potential modality for clinical translation of PA imaging is the linear-array ultrasound transducer based photoacoustic tomography (PAT), which has the unique capability of visualizing optical absorbers with high acoustic spatial resolution to detect deep structures in biological tissue, revealing a tissue's anatomical, functional, metabolic, histologic and molecular properties [4–6]. However, a series of distortion factors, such as the variable speed of sound, acoustic attenuation, optical heterogeneity, and other unexpected experimental conditions [7–10], could affect the imaging quality and target position in the reconstructed photoacoustic image.

Besides the optical aspect, our current study focused on the correction of acoustic distortion, especially the spatial variation of the speed of sound (SoS) in the acoustic heterogeneous medium. Indeed, the speed of sound may vary considerably for different types of tissue within a range of 1400–1600 m/s, whereas the speed in the skull bone is around 2200–3000 m/s [11–13]. Beard et al. proposed an automatic sound speed selection using an autofocus approach [14]. Lutzweiler put forward an optoacoustic image segmentation method based on the signal domain analysis to account for the heterogeneous acoustic properties [15]. Optimal self-calibration was proposed by Mandal to smooth the signal variation in mouse whole-body PA imaging [16]. The speed of sound correction with the coherent weighted method was proposed by Yoon's group [17]. Concomitant speed of sound tomography [18] and passive element enriched PAT [19] were applied to compensate the speed variation with a prior knowledge of the object structure. A higher-order geometrical acoustic approximation [20] and finite element based method [21] also took the variable speed of sound into account.

However, most of current PA image reconstruction methods are iteration based approaches or theoretical analysis to find the optimal uniform and constant sound speed, rather than the realistic variable SoS map. Delay and sum (DAS) is considered as the most common reconstruction algorithm in the linear-array photoacoustic imaging [22–24], but it still assumes a fixed sound speed in the coherent calculation of the corresponding time delays between the

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https://doi.org/10.1016/j.bspc.2018.04.012
1746-8094/

transducer element and predefined imaging field of view [25,26]. This mismatch between the actual and predicted uniform speed of sound may extremely deteriorate the photoacoustic image quality and interfere the accuracy at the spatial positioning of the imaging target. Therefore, it is necessary to correct the sound speed in the conventional DAS reconstruction algorithm if this method was applied in the acoustic heterogeneous media, such as deep brain tumors, skull base surgeries and cerebral neuron modulation.

To solve this problem, herein the time delay map in the traditional DAS reconstruction was calculated by the multi-stencils fast marching (MSFM) method, where the spatially variable sound speed was accounted for. The MSFM method depends on the approximated nonlinear wave propagation equation, i.e. Eikonal equation, for the computation of delay time in the acoustic heterogeneous medium [27]. This method was originally used for tracking the evolution of an expanding wave front, where the front could be considered as the fastest sound wave front from a point acoustic source. Here we are proposing the time delay map which was computed at each predefined grid space by solving the Eikonal equation along several stencils, picking the solution that satisfies the shortest path. As a sequence, this method could obtain the arrival time of the wave front at the points of discrete lattices and then generate the corresponding time delay map accurately with the compensation of variable acoustic speed of different structures within the imaging field of view.

## 2. Methods

### 2.1. Theory of the DAS reconstruction compensated by the MSFM method

On the condition of thermal confinement and stress confinement, the laser irradiated biological tissue leads to the generation of PA waves. After the propagation in the acoustic heterogeneous medium, the PA signals could be detected by the linear array ultrasound transducer. Then the PA images, i.e. the initial PA pressure distribution, could be restored by properly delaying and coherent summing the signals received at the adjacent scanlines. The basic principle of DAS reconstruction is,

$$RF_{DAS}(i,j) = \sum_{k=0}^{N-1} RF(k, t - \Delta t_{i,j}) \tag{1}$$

Where $RF(k,t)$ is the detected PA signal at the $k$ th transducer element, $N$ denotes the total number of scanlines within the DAS accumulation. $\Delta t_{i,j}$ is the time delay adapted to the acoustic wave propagation time in the media, i.e. from each element of transducer to the predefined imaging pixels $(i,j)$, which in most cases is computed based on a constant speed (~1540 m/s). This fixed sound speed is obviously contradictory to the practical application. In real biological tissue, however, the acoustic properties deviate significantly from the idealized homogeneous characteristic, resulting in the deterioration and inaccurate positioning of the target in the PA image. The MSFM method assumes the front wave propagated along the normal direction, and the speed of sound could be different at every point in the imaging region of interest (ROI). At a given location, the motion of the front wave could be depicted by the Eikonal equation,

$$\|\nabla T(\tilde{x})\| F(\tilde{x}) = 1 \tag{2}$$

Where $T$ and $F$ are the time of flight and the speed of sound at point $\tilde{x}(i,j)$, respectively. To calculate the propagation of the PA wave fronts, the speed map which reflects the tissue acoustic properties in different tissue structures should be prepared in advance. All the grids in the ROI are classified as the known, narrow band, and far region, which separately reflect the fixed, uncertain, and the unknown arrival time at a specific point. If $\nabla T$ is approximated by a second-order finite difference scheme, the equation to calculate the arrival time of flight $T_{i,j}$ could be presented as [28],

$$\left[\max\left(\frac{3T_{i,j} - 4T_{i-1,j} + T_{i-2,j}}{2}, \frac{3T_{i,j} - 4T_{i+1,j} + T_{i+2,j}}{2}, 0\right)\right]^2 + \left[\max\left(\frac{3T_{i,j} - 4T_{i,j-1} + T_{i,j-2}}{2}, \frac{3T_{i,j} - 4T_{i,j+1} + T_{i,j+2}}{2}, 0\right)\right]^2 = \frac{1}{F_{ij}^2} \tag{3}$$

$$\left[\max\left(\frac{3T_{i,j} - 4T_{i-1,j-1} + T_{i-2,j-2}}{2\sqrt{2}}, \frac{3T_{i,j} - 4T_{i+1,j+1} + T_{i+2,j+2}}{2\sqrt{2}}, 0\right)\right]^2 + \left[\max\left(\frac{3T_{i,j} - 4T_{i+1,j-1} + T_{i+2,j-2}}{2\sqrt{2}}, \frac{3T_{i,j} - 4T_{i-1,j+1} + T_{i-2,j+2}}{2\sqrt{2}}, 0\right)\right]^2 = \frac{1}{F_{ij}^2} \tag{4}$$

As a result, the arrival time $T_{i,j}$ can be computed by minimum root of Eqs. (3) and (4), which separately represent the arrival time from the orthogonal direction and diagonal direction. Given the variable speed distribution, the acoustic propagation time from each element to each grid point $(i,j)$ at the imaging field of view could be derivated, assuming each element center as the boundary condition with an initial point source. Thus the calculated time delay map $T_{i,j}$ could be used to replace the $\Delta t_{i,j}$ in the conventional constant speed assumed DAS reconstruction algorithm, as shown below,

$$RF_{DAS+MSFM}(i,j) = \sum_{k=0}^{N-1} RF(k, t - T_{i,j}) \tag{5}$$

### 2.2. Numerical model

Numerical model was established first to validate that the MSFM method could obtain the accurate time delay map with spatially variable sound speed, revealing its capability to reduce the acoustic distortions due to the inhomogeneous acoustic properties of the medium. The k-Wave toolbox was chosen for the forward PA wave propagation simulation [29]. The photoacoustic simulation setup for the multi-layer variable sound speed is shown in Fig. 1(a), where the linear array transducer is placed just above the imaging object. The variable SoS map is presented in Fig. 1(b), and the sound speed in this multi-layer target is changing from 1500 m/s to 2000 m/s. It is worth noting that this multi-layer speed map is intentionally designed with a relatively large speed difference between each layer, being able to demonstrate the feasibility of the DAS-MSFM reconstruction in the acoustic heterogeneous media.

The presence of the skull would severely affect the imaging quality, which may cause serious interferences in delineating deep brain tumors [30]. The numerical model of PA detection of mouse deep brain tumor with an intact skull is illustrated in Fig. 2(a), and the corresponding variable sound speed map is shown in Fig. 2(b). The brown curved insert in the speed map could mimic the transmission sound speed (2800 m/s) in the skull, which was placed between the linear-array transducer and the point targets.

### 2.3. PA experiment setup

The feasibility of the proposed method was tested by the phantom and *in vivo* PA imaging of mouse brain tumor subsequently. A laser system (Vibrant HE532I, OpoTek, USA) with optical parametric oscillator (OPO) unit emits a 5 ns width laser pulse at the range of 680–1210 nm. The output laser was delivered through the fiber bundle to ensure the light uniform illumination to the object surface. The external trigger signal from the laser system was sent to synthesize the receive-only mode on the research ultrasound system (Vantage 64, Verasonics, USA) to collect the PA data, and the corresponding ultrasound image could also be acquired after a fixed trigger delay. All the ultrasound and photoacoustic (US/PA)