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Research Article

Optimal self-calibration of tomographic reconstruction parameters in whole-body small animal optoacoustic imaging

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ABSTRACT

In tomographic optoacoustic imaging, multiple parameters related to both light and ultrasound propagation characteristics of the medium need to be adequately selected in order to accurately recover maps of local optical absorbance. Speed of sound in the imaged object and surrounding medium is a key parameter conventionally assumed to be uniform. Mismatch between the actual and predicted speed of sound values may lead to image distortions but can be mitigated by manual or automatic optimization based on metrics of image sharpness. Although some simple approaches based on metrics of image sharpness may readily mitigate distortions in the presence of highly contrasting and sharp image features, they may not provide an adequate performance for smooth signal variations as commonly present in realistic whole-body optoacoustic images from small animals. Thus, three new hybrid methods are suggested in this work, which are shown to outperform well-established autofocusing algorithms in mouse experiments *in vivo*.

1. Introduction

Optoacoustics offers unique *in vivo* imaging capabilities for preclinical research [1]. However, achieving optimal resolution and contrast as well as associated quality measures in optoacoustic tomographic images implies accurate calibration of the reconstruction parameters. The position and orientation of the ultrasound sensors, spatial variations of the speed of sound (SoS), attenuation and other acoustic properties of the propagation medium may all significantly affect the collected optoacoustic responses [2] and therefore must be correctly accounted for in the image reconstruction process. For example, cross-sectional optoacoustic systems based on single-element [3,4] or arrays of cylindrically focused transducers [5,6] are commonly employed due to important advantages derived from reducing the optoacoustic problem into two dimensions. For accurate tomographic reconstructions, the location of all detection points in the imaging plane needs to be precisely known or determined experimentally, the latter by, *e.g.*, imaging a calibration phantom having a uniform and known SoS. Once the acquisition geometry is properly calibrated, the correct values of the acoustic propagation parameters must still be taken into consideration, ideally with the use of an algorithm accounting for acoustic heterogeneities [7–11]. In many practical cases, the map of SoS variations in the imaged medium is not available a priori nor can be extracted experimentally so representative reconstructions are obtained by considering a uniform heuristically fitted SoS [12,13].

Dependence of SoS on the temperature of the surrounding matching medium is yet another uncertainty that must be accounted for, *e.g.* by continuously monitoring, the temperature throughout duration of the experiment [14]. Indeed, even subtle temperature variations lead to substantial changes of SoS in water of 2.6 m/s/°C [15]. Consequently, if the water temperature cannot be properly controlled during a prolonged experiment, dynamic calibration of the SoS becomes essential. In addition, local discrepancies between sound propagation velocity in the water and the imaged sample, even under assumption of uniform acoustic properties, may raise the necessity in additional SoS calibration on a per-slice basis. Moreover, fast automatic calibration of the SoS is of high importance in real-time imaging systems, where GPU-accelerated reconstruction algorithms now allow for real-time optoacoustic visualization of the sample in the course of the experiment [16].

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Determining autofocusing (AF) parameters for biological images has been a wide area of research and diverse families of methods have been reported for digital microscopy [17–19], shape from focus [20] and cytogenetic analysis [21]. Some simple AF approaches based on sharpness metrics [22] may perform equally well for optoacoustics, especially when high frequency strongly contrasting image features such as high resolution subcutaneous are present in the images. However, they may not provide an adequately robust performance for smooth or ultrawideband signal variations as commonly present in realistic whole-body optoacoustic images from small animals, especially when considering quantitative model-based reconstructions that preserve low-frequency information [23].

In this work, we discuss on the performance of a number of different AF algorithms for automatic SoS calibration in cross-sectional optoacoustic tomography. Along with investigating a number of measures extensively reported in the literature, we propose additional efficient hybrid focusing metrics employing pre-processing to enhance the focusing performance. The proposed methods further incorporate key improvements, *viz.* edge detection and diffusion, making them optimal for application in optoacoustic SoS self-calibration.

2. Materials and methods

2.1. Autofocusing algorithms

The workflow for a typical SoS calibration procedure is depicted in Fig. 1. Optoacoustic images corresponding to selection of different values of the SoS in a certain reasonable range are tomographically reconstructed from the recorded signals. Thereafter, the reconstructed images are processed with the AF algorithm and focus measures are employed to determine the best matching SoS. The fitted SoS, as obtained from the calibration method, is then fed back as a parameter for the reconstruction of the dataset/frame. The algorithms described in this section can be classified into three main groups, namely intensity-based (i and ii), gradient-based (iii and iv) and edge-based (v–vii) measures, where the last group of metrics simultaneously correspond to the hybrid approaches suggested in this work. In order to enable comparison between the different methods, all focus measures are readjusted so that the global minima represent the most focused image. The focus measure is normalized to the maximum value in the SoS range considered. Focus metrics were calculated on the interval from 1460 to 1580 m/s, corresponding to a typical range of SoS in water and soft tissues, with step size of 1 m/s, and processed with smoothing Savitzky–Golay denoising filter (with polynomial order of 0 and window size of 5 points) [24]. The algorithms tested are presented below.

2.1.1. Maximum pixel intensity

The maximum pixel intensity represents the most intuitive and computationally efficient focus measure. The method is inspired by the tendency of the user to look for the brightest spots in the focused image as well as the largest image contrast so that it is assumed that a given structure has the highest intensity value when it is focused. As such, this metric is expected to perform better with high signal-to-noise-ratio (SNR) images rich with high-contrast features, but is the most artifact-prone if noise and other image artifacts yield these high-intensity features. The focus measure is defined as

$$F_{MI} = -\max_{x,y}[f(x,y)], \quad (1)$$

where $f(x,y)$ is a function of two variables representing the gray level intensity in the cross-sectional image. The negative sign is added so that the global minimum represents the most focused image, as mentioned above.

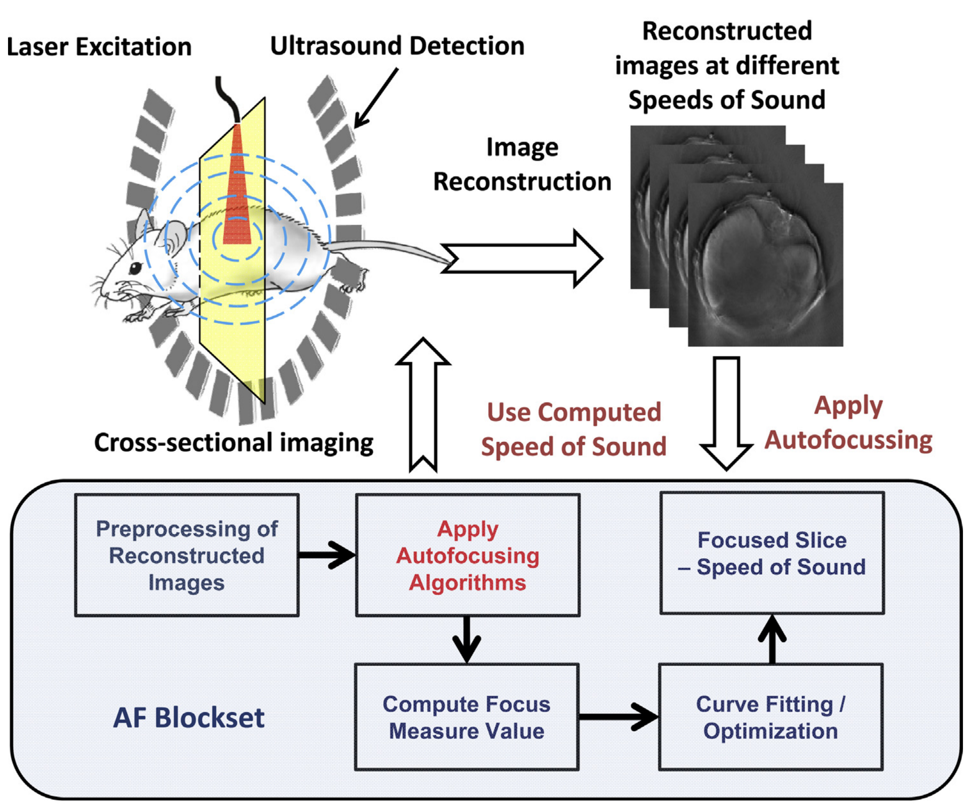

Fig. 1. Basic principle of the application of the autofocusing in the optoacoustic reconstruction workflow. The autofocusing (AF) blockset illustrates the post-reconstruction autofocusing algorithm employed to automatically calibrate speed of sound.