Frequency-domain photothermoacoustic imaging contrast enhancement with a CW laser and non-linear frequency modulation chirps

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Abstract. The application of photoacoustic (PA) phenomena to medical imaging has been investigated for more than a decade. To implement this modality, one may choose between two types of laser sources, pulsed or continuous wave (CW). This selection will affect all features of the imaging technique. Nowadays pulsed lasers are the state-of-the-art technique in the PTA research. In this work we report frequency-domain photothermoacoustic imaging using linear and non-linear frequency chirps with a CW laser. The images produced using turbid tissue phantoms with subsurface inclusions were compared according to their contrast and depth resolution of absorbing lesions. In the CW method, in addition to the image produced by the amplitude of the cross-correlation between input and output signals, another image which is generated by the phase of the correlation signal is also available. The application of nonlinear frequency modulation instead of the standard linear frequency chirps introduced in our laboratory is demonstrated. These features are additional degrees of freedom uniquely available to the CW (but not to the pulsed laser) method.

1. Introduction

In the past decade photoacoustics (PA) has been the focus of intensive research as a promising technology for noninvasive, cost-effective medical imaging. Various biomedical applications have been investigated with this imaging technique, the most popular ones being breast cancer and brain tumors [1]. The strength of PA imaging lies in its ability to combine the contrast of diffuse optical tomography and the resolution of ultrasonic imaging. To implement this imaging technique, there is a possibility to choose between two types of laser sources, pulse or continuous wave (CW). To-date the pulsed laser has captured exclusive attention in PA research. The major reason for this choice is that the pulsed PA signal is stronger due to its high energy density and therefore is easier to detect and also it is easier to use because of its straightforward depth dependence. Despite these advantages, pulsed PA suffers from the requirement of a wide-band ultrasonic transducer which increases acoustic and thermal noise; also the presence of laser jitter noise may compromise the spatial resolution and lastly the required high peak power of laser pulses may cause an adverse health risk.

An alternative choice, the CW method, is based on a frequency-modulated or coded waveform energy source and facilitates frequency-domain signal processing [2]. The CW method not only can resolve most problems associated with a pulsed laser, but also does provide more control over the bandwidth and signal shape and superior diagnostic potential due to the phase imaging channel [2].
The present study investigates additional optimizing features of the CW technique: Introduction of linear and non-linear frequency sweeps (chirps) is examined, and the phase signal is employed to filter the amplitude image or generate a separate image.

2. Methods

In the pulsed method the acoustic pressure is generated by high power nanosecond laser pulses and the depth of the chromophores is perceived according to the time of flight of the acoustic signals. In the CW technique the acoustic waves can be generated by frequency modulated or coded laser irradiation. Various signal processing methods are available to convert frequency-domain to time-delay-domain signals: One method is to acquire the cross-correlation of input and output signals which can be implemented either in the time domain or more efficiently in the Fourier domain. When a coded input signal like linear frequency modulation (LFM) is used, the method is called matched filter compression [3]. Matched filter compression can give the highest signal to noise ratio (SNR) for an input signal buried in white noise, provided that the response is matched to the input signal [3]. This means that if the pressure response was an exact replica of input we could obtain the highest SNR; deviation from that condition will reduce the SNR.

As depicted in Fig. 1, the multiplication of the transducer output signal \( s(t) \) by the complex conjugate of the input signal is computed in frequency domain. The input signal \( r(t) \) is a replica of the reference signal which is the intensity modulated laser waveform (chirp). The bandwidth of the input waveform is controlled by the shape of the chirp (here 200 kHz to 800 kHz) and a Tukey window [4] is used to suppress all signals incoherent with the reference bandwidth. Inverse Fourier transformation of the result will generate the cross-correlation of the transducer output with respect to the reference signal (that is a real value and therefore the imaginary part will be zero after IFFT). The same procedure can be performed by substituting the input signal with its Hilbert transform which will generate the cross-correlation of the output signal with respect of the quadrature of the reference signal. The total cross-correlation amplitude and phase can be obtained by using the two calculated cross-correlations (in-phase and quadrature). The delay times of the resulting amplitude peaks reflect the delays of the acoustic transients, which correspond to the depths of particular chromophores. The resulting phase of the cross-correlation signal is caused by acoustic delays following PA energy conversion. The PA system depends on many parameters such as optical and acoustic properties of the media and the characteristics of the ultrasonic transducer. Despite the fact that the evaluation of these parameters individually is impractical, the value of the correlation phase should remain unchanged for a fixed position of the specimen-transducer distance and in the absence of noise. Therefore, if the experiment is repeated by using a continuous sequence of chirps at each coordinate point, the standard deviation (SD) of the phase can be used as an indicator of the presence of a signal-producing chromophore: small SD values express statistical fluctuation in a real signal and large values reveal noise. The process of averaging will also augment the amplitude SNR in proportion to the number of averages [5]. In the experiments presented in the next section (CW methods), 800 averages are used.

3. Experiments

The instrumentation and experimental set-up employed in this study are described elsewhere [6] and the applied laser intensities are according to the safety standard limits [7]. The following experiments...
illustrate the contrast capabilities of each technique (CW and pulsed). In Fig. 2, four images produced with the same phantom sample are shown. The phantom is made of PVC plastisol with a curved inclusion at 9 mm depth. The optical properties of the surrounding plastisol and the inclusion are mentioned in the caption. Associated with each image there is a signal trace in the location of the inclusion (X= 12 mm; on the image). Fig. 2a is generated from the amplitude of the cross-correlation signal. In the signal trace two main peaks are visible which correspond to the surface of the plastisol and to the inclusion. The insets indicate the contrast factor for each mode. Two deeper and much weaker peaks are also recognizable which are related to the echoes reflecting from the other side of the phantom. Fig. 2b illustrates the image produced by the inverse of the SD of the phase signals. In the signal trace four peaks are observable. Fig. 2c presents the image produced by filtering the amplitude signal using the phase signal, which significantly enhance the contrast. To achieve it, the amplitude signal is multiplied by the inverse of SD of the phase signal. Fig. 2d is the image produced using a pulsed Nd:YAG laser, otherwise under identical configuration to the CW irradiation. Despite the strong signal of the acoustic transient, the contrast is quite poor. This is an inherent feature of pulsed laser excitation and scattered photon interference with the transducer in the back-scattering configuration. The contrast factor in each signal is computed as the ratio of the inclusion peak divided by the average value of the signal outside the peaks area and is presented in the signal traces.

![Figure 2](image-url)  
**Figure 2.** Comparison of images and the signal trace on the inclusion generated by different methods: a) the cross-correlation amplitude, b) the inverse of SD of the phase signal, c) the cross-correlation amplitude which is filtered by the phase signal, d) pulsed method. (Sample properties are, surroundings: $\mu_s=3.1 \text{ cm}^{-1}$, $\mu_a=0.2 \text{ cm}^{-1}$ and Inclusion: $\mu_a=2 \text{ cm}^{-1}$)

Another experiment investigated how deep a chromophore position the aforementioned imaging techniques can detect in a scattering medium consisting of 0.47% Interalipid solution with the chromophore being plastisol with absorption coefficient 4 cm$^{-1}$. In Fig. 3, absorption peaks are shown: they weaken with increasing Interalipid solution overlayer thickness. Since the position of the sample with respect to the transducer was fixed, the delay time of the peaks remained constant [6]. Figures 3a are the cross-correlation amplitude traces generated by applying a LFM. Fig 3b shows the traces of the inverse of the phase SD obtained using a nonlinear chirp. Nonlinear chirps can be used to increase the generated PA energy, but they will also broaden the correlation peak. In a manner similar to pure...
ultrasound methods the LFM provides the best SNR [8]. On the other hand, since the broadening of the correlation peak is less pronounced in the SD phase signal, nonlinear chirps can be used to improve the contrast in the cross-correlation phase signal. Fig 3c is the signal trace generated by filtering the amplitude signal by the phase as discussed before. Fig 3d is the PA response to a pulsed laser. The contrast factors' of all the signal traces are presented beside them to assist in the comparison.

**Figure 3.** The signals detected in different depths of the 0.47% interalipid solution. The absorption coefficient of the chromophore material is 4 cm⁻¹. a) The cross-correlation amplitude, b) The inverse of the SD of the phase signal, c) The cross-correlation amplitude filtered by phase signal, d) The pulsed laser response signal.

### 4. Conclusions

Several features of Fourier domain PA with respect to contrast optimization are demonstrated and compared with pulsed method. It is shown that despite the strong signal generated in the pulsed technique which facilitates deeper detection, the CW method has superior contrast factor and at least similar depth resolution capability. The contrast of the CW method can further be improved by using the phase signal as a noise filter and the ability to control the bandwidth and the shape of the input waveform. It is confirmed that the phase signal contains valuable information that can be used to generate a separate image or filter the amplitude image and suppress the noise level with that. Furthermore the use of nonlinear frequency modulation can increase the contrast in the phase signal but not in the correlation amplitude signal.
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