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A new denoising method for improved parameter estimation in DCE-US

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Background

The major role of angiogenesis in cancer growth has led to the development of dynamic contrast enhanced (DCE) imaging methods to probe tumor angiogenic vasculature. In DCE-ultrasound (DCE-US), fitting mathematical perfusion models to measured time intensity curves (TICs) describing the echo power as a function of time enables the estimation of quantitative hemodynamic parameters. Quantification is facilitated by the linear relationship between contrast concentration and echo power (TIC) at typical contrast concentrations found in tissue [1]. When log-compression is applied by the scanner, data linearization is still possible, provided that sufficient dynamic range is used for acquisition [2]. However, parameter estimation remains challenging due to the noisy nature of DCE-US data. As a result, prior to applying curve fitting, a preprocessing step for TIC denoising is necessary and widely employed.

DCE-US images present the same type of speckle noise observed in conventional B-mode images [3]. In amplitude, noise can be described by a multiplicative noise model following a Rayleigh distribution [3]. In time, noise in consecutive frames can be considered to be independent due to the Brownian motion of DCE-US contrast particles over time [1]. By log-transforming the ultrasound data, the original multiplicative noise becomes additive, and the noise distribution can be approximated by a Gaussian distribution [4], enabling the application of standard low-pass linear filters for temporal denoising.

Recently, contrast ultrasound dispersion imaging (CUDI) was proposed and tested for prostate cancer (PCa) localization with promising results [5]. In CUDI, fitting the modified local density random walk (mLDRW) model to DCE-US TICs enables the estimation of the local dispersion parameter κ , which provides a characterization of the microvascular architecture. However, parameter estimation after standard low-pass filtering in time-domain has shown limited results, requiring the addition of spatial filtering, and therefore reducing the spatial resolution of the method. Motivated by the model fitting limitations caused by high noise levels, here we propose a novel preprocessing method for DCE-US based on wavelet denoising, and we evaluate the ability of this method to improve parameter estimation

in CUDI.

Methods

Based on the convective dispersion equation, the evolution of the contrast agent concentration at each pixel over time, $C(t)$, is described by the mLDRW model as [5]

$$C(t) = \alpha \sqrt{\frac{\kappa}{2\pi(t-t_0)}} e^{-\frac{\kappa(t-t_0-\mu)^2}{2(t-t_0)}}, \quad (1)$$

with $\kappa = v^2/D$ being the dispersion-related parameter, t_0 the theoretical injection time, μ the contrast mean transit time, and α the time integral of $C(t)$. Fitting the measured TICs by (1) enables the estimation of the dispersion parameter κ , which characterizes the microvascular architecture.

In CUDI, before curve fitting, a preprocessing step is applied to reduce the TIC noise level. Up until now, this consisted of a FIR (finite impulse response) low-pass filter in time domain with cut-off frequency of 0.5 Hz, proven sufficient to represent any perfusion TIC in the prostate [5]. In this work, we propose a novel preprocessing method, based on wavelet denoising. By this method, an outlier removal procedure is first performed to locally remove low value outliers. This enables the use of standard denoising methods, optimized for Gaussian white noise, based on the approximation of the log-transformed signal amplitude to a Gaussian distribution [4]. The noise level is then estimated at each wavelet decomposition scale. Lastly, the wavelet coefficients at each scale are thresholded, removing low-value noise-related coefficients and preserving dominant signal coefficients.

In order to evaluate the ability of the proposed denoising method to improve parameter estimation, 95 noisy TICs were simulated by the mLDRW model with multiplicative noise obeying a Rayleigh distribution. The signal-to-noise ratio (SNR) of the simulated TICs was -1.4 dB, and the parameter κ was varied from 0.1 s^{-1} to 2 s^{-1} , covering the range of values typically found in the prostate [5]. The estimation performance was evaluated by calculating the determination coefficient R^2 of the fit with respect to the clean simulated TIC, and the normalized mean error (NME) in the estimation of the parameter κ .

The proposed method was also tested on DCE-US loops from 6 patients with biopsy-proven PCa, acquired after an intravenous peripheral bolus injection of 2.4-mL SonoVue® (Bracco, Milan, Italy) with an iU22 ultrasound scanner (Philips Healthcare, Bothell, WA) in power modulation mode at low mechanical index (MI=0.06). The data was collected at the Academic Medical Center, University of Amsterdam, the Netherlands. All the patients signed informed consent. The fitting performance on patient data was evaluated by calculating the mean R^2 of the fit with respect to the filtered TIC, and the

percentage of voxel with successful fit ($R^2 > 0.75$).

Results

Table 1 reports the results of the simulations, comparing the estimation performance of wavelet denoising (WD) filtering with FIR low-pass (FIR-LP) filtering. Table 2 reports the results obtained in patient data, comparing the fitting performance obtained after WD filtering, FIR-LP filtering, and without any preprocessing. Figures 1a and 1c show an example of TIC together with the corresponding FIR-LP and WD filtered curves for simulated and patient data, respectively. Figures 1b and 1d compare the fit obtained after FIR-LP and WD filtering with the clean TIC, for simulated data, and with the filtered TIC, for patient data.

Table 1. Results in simulated data

Filtering	FIR-LP	WD
R^2	0.74 ± 0.1	0.98 ± 0.1
NME (%)	-4.71 ± 16.4	-0.91 ± 6.16

Table 2. Results in patient data

Filtering	none	FIR-LP	WD
R^2	0.78 ± 0.04	0.86 ± 0.06	0.88 ± 0.06
Percentage fit (%)	0.04	42.7	54.7

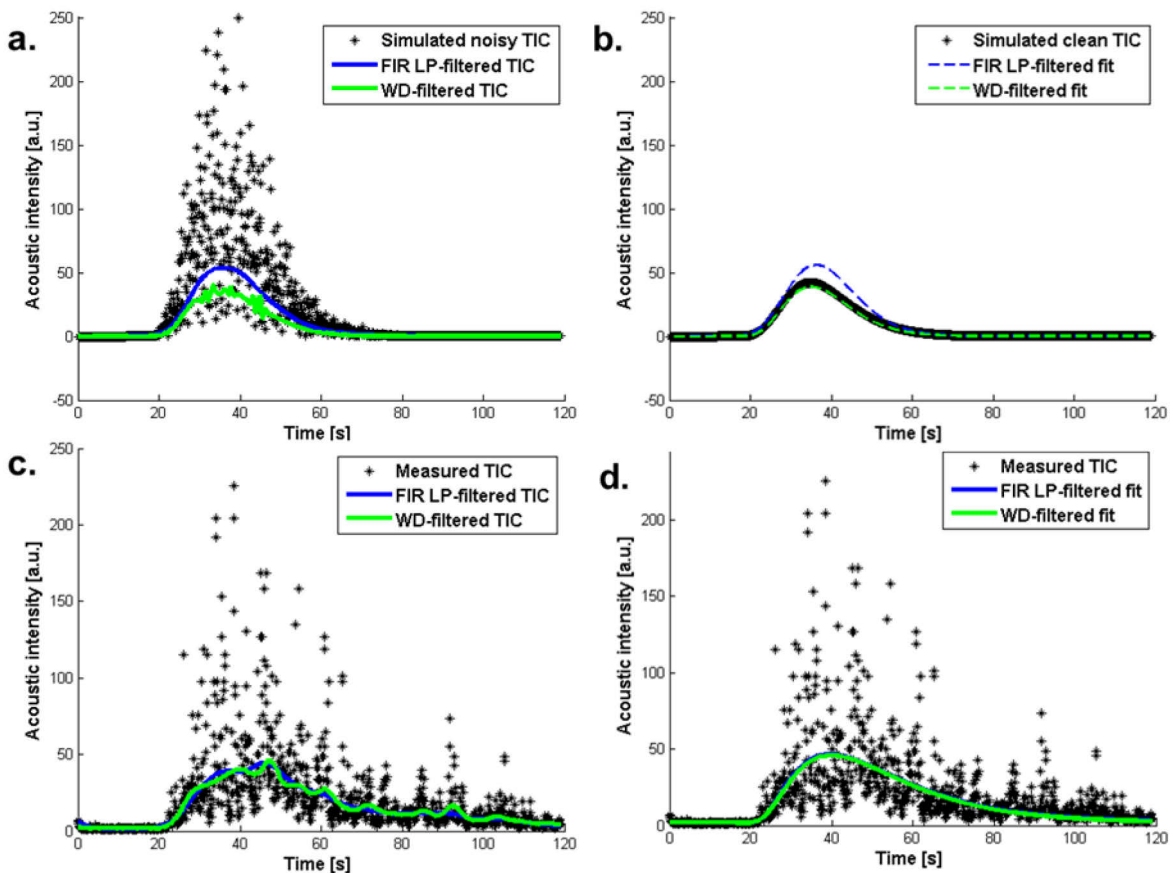


Fig. 1 a. Simulated noisy TIC with corresponding TIC after FIR-LP and WD filtering. b. Simulated clean TIC with corresponding fits obtained after FIR-LP and WD filtering. c. Experimental TIC with corresponding TIC after FIR-LP filtering and WD filtering. d. Experimental TIC with corresponding fits obtained after FIR-LP filtering and WD filtering.

Discussion and conclusions

Denosing in the temporal domain is a necessary step for parameter estimation in DCE-US, as demonstrated by the very low (0.04%) percentage of pixel TICs which can be fit without any filtering in time-domain. In this work, a novel preprocessing step based on wavelet denoising was presented and tested for improved parameter estimation in CUDI; a comparison with standard FIR-LP filtering is also provided. By simulations, the proposed method showed a significant reduction in the estimation error and a significant R^2 increase (p -value<0.01). Moreover, the analysis in patient data showed a significant improvement in R^2 and in the percentage of pixels with successful fit (p -value<0.01). The promising results suggest that time filtering based on wavelet decomposition might be well suited for temporal denoising of DCE-US loops, reducing the need for spatial low-pass filtering and thus leading to a better compromise between fit accuracy and spatial resolution.

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