OCT-based approach to local relaxations discrimination from translational relaxation motions

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ABSTRACT

Multimodal optical coherence tomography (OCT) is an emerging tool for tissue state characterization. Optical coherence elastography (OCE) is an approach to mapping mechanical properties of tissue based on OCT. One of challenging problems in OCE is elimination of the influence of residual local tissue relaxation that complicates obtaining information on elastic properties of the tissue. Alternatively, parameters of local relaxation itself can be used as an additional informative characteristic for distinguishing the tissue in normal and pathological states over the OCT image area. Here we briefly present an OCT-based approach to evaluation of local relaxation processes in the tissue bulk after sudden unloading of its initial pre-compression. For extracting the local relaxation rate we evaluate temporal dependence of local strains that are mapped using our recently developed hybrid phase resolved/displacement-tracking (HPRDT) approach. This approach allows one to subtract the contribution of global displacements of scatterers in OCT scans and separate the temporal evolution of local strains. Using a sample excised from of a coronary arteria, we demonstrate that the observed relaxation of local strains can be reasonably fitted by an exponential law, which opens the possibility to characterize the tissue by a single relaxation time. The estimated local relaxation times are assumed to be related to local biologically-relevant processes inside the tissue, such as diffusion, leaking/draining of the fluids, local folding/unfolding of the fibers, etc. In general, studies of evolution of such features can provide new metrics for biologically-relevant changes in tissue, e.g., in the problems of treatment monitoring.

Keywords: optical coherence tomography, relaxation, signal processing, speckle, tissue characterization

1. INTRODUCTION

Biological tissues are very complex media containing many different types of heterogeneities. In some cases implementation of the conventionally discussed OCT elastography (in which the tissue is characterized only by differences in the Young modulus) becomes problematic, because the reaction of the tissue to mechanical perturbations requires to take into account additional properties, such as viscosity, permeability of internal fluid, etc. In general, viscoelastic properties of the tissue can be characterized by evaluation of its relaxation parameters[1-5]. In some earlier studies the relaxation of the tissue is estimated by tracking the gradually varying displacement of the tissue surface (e.g. using phase-resolved Doppler techniques) after sudden unloading or after a mechanical impact[1,2]. However, the so-estimated relaxation time can be determined not only by local properties of the tissue, but influenced by the "global geometry" of the region where this relaxation is studied. For example, it is well known that in cracks filled with a liquid with the same viscosity and subjected to loading/unloading, the characteristic relaxation time is determined by the dimensions of the crack[6]. In the general case there can be a wide spectrum of various local relaxation processes inside the biological tissue.

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Local relaxation responses are assumed to be related to various biological processes in the tissue bulk, such as diffusion, leaking/draining, local folding/unfolding of the fibers etc. Parameters of local relaxation itself can be used as an additional informative characteristic for distinguishing the tissue in normal and pathological states over the OCT image area. Studies of evolution of such relaxation features can provide new metrics for biologically-relevant changes in tissue, e.g., in the problems of treatment monitoring.

Here we present an OCT-based approach to evaluation of inner local relaxation processes inside the tissue after a sudden change of its initial loading (pre-compression). For extracting the local relaxation rate we evaluate temporal dependence of local strains that are mapped using our recently developed hybrid phase resolved/displacement-tracking (HPRDT) approach[7]. This approach allows one to separate global and local motions of scatterers in the tissue and thus single out only local strains. We demonstrate that the observed relaxation of local strains can be reasonably fitted by an exponential law, which opens the possibility to characterize the tissue by a single relaxation time that can be extracted from the observed time-dependence of the inter-frame strains. In this report we present a preliminary description of the basic procedures. Details will be reported in a full-scale publication elsewhere.

2. OCT-SYSTEM PARAMETERS, EXPERIMENTAL SETUP AND SIGNAL PROCESSING

For the experimental demonstrations, we used a home-made spectral-domain OCT scanner described in our previous publications[5,7-14]. Briefly, it had a central optical wavelength of 1320 nm, bandwidth of 106 nm and a scan rate of 20 kHz for spectral fringes. The axial resolution of the system is 10 μm and in the lateral direction the full width half-maximum (FWHM) beam diameter is 20 μm. OCT system has 512 elements of spectrometer array in the axial direction. The complex-valued signal acquisition is based on the use of periodically modulated tunable reference arm. It means that at 20 kHz spectral fringes rate, the complex-valued A-scans are formed at 10 kHz rate.

In comparison with our previous OCE publications[7-10,12,13] where initial pressure was applied using the OCT probe itself, now we separate the probe and loading/unloading system. Probe operates in non-contact manner as it was performed in our works for mocrocirculation imaging[14]. Loading of the tissue was applied manually by locating flat metal plate on the tissue surface in the free area between OCT probe and the tissue. Sudden change of the loading state of the tissue was performed by rapid removal of the metal plate away from the tissue. This unloading approach has several advantages:

1. The moment of metal plate removal is naturally observed on OCT signal so the relaxation process can be observed from its beginning;
2. We naturally eliminate possible biases of estimations of the relaxation parameters that can be caused by the parasite relaxations of the probe system or whole mount system because the tissue relaxation happens in half-free space. It ensures that we observe tissue relaxation without admixing of another samples relaxations.

We perform 2D-dataset acquisitions that means we scan 512 B-scans from a single spatial plane. Each B-scan contains 512 complex A-scans and covers 2 mm in the lateral direction. For our OCT-system it means that acquisition takes ~25 sec. The relaxation actually is completed in for this period of time. Because the acquisition was performed in two directions the minimal time lag between each processed B-scan pair with the same parity is 0.1 sec.

It can be also noted that signal processing procedure used to discriminate local strains automatically subtracts translational motions of the tissue, so that the relaxation properties of the bottom substrate are also subtracted for each analyzed area. Nevertheless, tissue was located on the almost solid substrate that does not manifest any relaxation properties for the OCT inter-frame time.

Signal processing is based on HPRDT approach[7]. In details it was described in our previous publication[7]. Briefly, HPRDT utilize phase-differences between two processed B-scans that were calculated within the subset windows 16x16 pixels in size. The key point of HPRDT is to determine the gradient of this phase-difference in the axial direction using Kasai estimator within the subset window and applying least-square linear regression[7]. This gradient can be recalculated in local strain taking into account the OCT system parameters[7]. HPRDT approach also provides the subsets matching procedure even if they were shifted relative to each other due to translational motions[7]. As it was described in our previous publication[7] HPRDT is applied for OCT elastography to mapping the local strains for two B-scans. Here we apply this signal processing to estimate the temporal dependence of the local strain relaxation. Namely, for the fixed time lag between processed frames in the analyzed sequence, the local strains for the sequence of chosen matched subsets can be evaluated as a function of time. Here we emphasize that local phase gradients and strains are calculated for each pair of subsequently obtained B-scan with fixed time-lag between it. In details this scheme is described in our previous

publication[5] for speckle correlation approaches. In the present report the local strain evolution (instead of speckle decorrelation) describes the local relaxation function for each area. This provides much better separation of the local relaxations from the translational motions.

Because the local relaxation in general case can be multi-exponential[15] in the first step of the law estimation we test the obtained local strain evolution for compliance with the exponential law[15]. Then to extract local relaxation rates then least-square fitting of the exponential-function parameters is performed[1,2,5,15].

Thus, the proposed local relaxation evaluation consists of the following procedures:

1. Loading the tissue with the flat metal plate;
2. Unloading the tissue surface during the OCT-data acquisition;
3. Calculation of the local strains using HPRDT approach for several fixed time lags between processed scans;
4. Testing local strains evolution for compliance with the exponential law;
5. Fitting local strains evolution to determine the relaxation parameters.

Below we preliminary describe the procedure of comparing the local strains evolution with the exponential law. Other procedures in details will be published in a full-scale article elsewhere.

3. EVOLUTION OF LOCAL STRAINS: COMPARISON WITH AN EXPONENTIAL LAW

It cannot be stated a priori that relaxation of strains in biological tissue is dominated by a single process with a single relaxation time. In contrast, for materials with complex heterogenous structure, a broad spectrum of relation processes is typical[15], which results in formation of nearly logarithmic in time of power-law temporal evolution of perturbations towards equilibrium state of the material. However, in view of especially clear physical interpretation of single-relation-time model here we demonstrate how this simplified model can be applied to describe the local strain relaxation in some biological tissues based on experimentally obtained sequences of OCT scans. In such an approximation, the evolution of strain $s(t)$ in the initially perturbed tissue towards the equilibrium zero-strain state can be written in the following form:

$$s(t) = S_0 \cdot [1 - \exp(-t/T)], \tag{1}$$

where S_0 is the initial local strain caused by a flat metal plate pressed onto the tissue and released at $t = 0$; t is the current time and T is the characteristic relaxation time (so that $1/T$ has the dimension of frequency - relaxation rate). In principle it is possible to estimate the perturbation value S_0 by comparing the initial OCT scan corresponding to $t = 0$ with a sufficiently distant scan corresponding to $t >> T$ (say, several seconds or more), for which the tissue can be considered relaxed. However, for typical amplitudes S_0 on the order of several per cent, the speckle-structure decorrelation can be rather significant[11,12,13] and the corresponding displacements of scatterers in the compared scans can be on the supra-wavelength and even supra-pixel scale, which complicates the direct evaluation of the temporal evolution of the cumulative strain described by Eq. (1). In view of this it is more convenient to observe the temporal strain evolution using a sliding method, i.e. to perform comparison of a pair of scans separated by a fixed time interval (time lag) $\Delta t << T$ and to observe how such incremental strain $\Delta s << S_0$ evolves as a function of time. Since the inter-frame interval can easily be chosen much smaller than the relaxation time, $\Delta t << T$, the incremental strain can be made sufficiently small to avoid strong inter-frame decorrelation, which is helpful for reducing the decorrelation noise and improving strain-estimation accuracy.

If we assume that $s(t)$ obeys Eq. (1) with a single relaxation time, then the incremental strain $\Delta s = s(t) - s(t + \Delta t)$ is described by the following relationship

$$\Delta s = S_0 \cdot [1 - \exp(-\Delta t/T)] \cdot \exp(-t/T), \tag{2}$$

Since it is assumed that $\Delta t << T$ the exponential function can be expanded as $\exp(-\Delta t/T) \approx 1 - \Delta t/T$, such that

$$\Delta s \approx S_0 \cdot \Delta t/T \cdot \exp(-t/T) \tag{3}$$

Such incremental strains can be easily found experimentally by comparing sequential B-scans (e.g., scans with number n and $n+1$ or $n+2$, etc.) It is also clear from Eqs. (2) and (3) that if the relaxation is exponential in time $\propto \exp(-t/T)$, then for different time lags Δt_1 and Δt_2, the ratio of the corresponding incremental strains $\Delta s_1 = \Delta s(\Delta t_1)$ and $\Delta s_2 = \Delta s(\Delta t_2)$ should not depend on the current time:

$$\frac{\Delta s_2}{\Delta s_1} = \frac{1-\exp(-\Delta t_2/T)}{1-\exp(-\Delta t_1/T)} \approx \frac{\Delta t_2}{\Delta t_1} \neq f(t) \tag{4}$$

Certainly if relaxation of strain in the tissue essentially deviation from the exponential law with a single relaxation time (e.g., for a wide spectrum of relation times like considered in[15]), the ratio (4) of incremental strains should become time-dependent. Consequently, experimental confirmation of the fact that ratio (4) is time-independent can be used for verification whether the assumption about approximately exponential relaxation of strain according to Eq. (1) is reasonable.

We use these conclusions to verify the applicability of the exponential law to describe the relaxation of local strains as a function of time using samples of coronary vessels. We process adjacent B-scans, then B-scans with skipped one frame or two frames. For the used OCT system, the corresponding time lags are $\Delta t_1 = 0.1$ sec, $\Delta t_2 = 0.2$ sec, and $\Delta t_3 = 0.3$ sec. Relaxation laws $\Delta s_i(t)$ found for the incremental strains with different time lags Δt_j are presented in Fig. 1. Panel (a) represents the time dependence of the incremental local strains for these three cases. It is clearly seen that functional dependence of the local strain $\Delta s_i(t)$ as a function of time. Panel (b) shows the experimentally determined ratios $\Delta s(t,\Delta t_3)/\Delta s(t,\Delta t_1)$ and $\Delta s(t,\Delta t_2)/\Delta s(t,\Delta t_1)$. It is seen from Fig. 1 that these ratios remain fairly constant within the observation intervals $\sim 1-2$ sec. Furthermore, quantitatively these ratios appear to close to $\Delta t_3/\Delta t_1$ and $\Delta t_2/\Delta t_1$ as expected from Eq. (4). This means that the parameters of the relaxation process remain fairly constant in different parts of the relaxation curve, so that the estimated characteristic relaxation times are fairly independent of the amplitude of the initial perturbation. This conclusion is very important, because it indicates that the characteristic relaxation times obtained in different experiments (with eventually different amplitudes of the initial strain perturbations) can be compared. All three relaxation curves shown in Fig. 1a can be fairly well fitted by the exponential law of the form (2), which gives the following estimate for the relation time: $T = 0.6 \pm 0.05$ sec. The above-mentioned features of the observed relaxation processes indicate that for time intervals $\sim 1-2$ sec., the observed time evolution of the local strains in the released tissue indeed can be fairly reasonably approximated by an exponential law with a single relaxation time (which agrees with similar conclusions as in previous publication[5], where another correlation-based technique was used to observe relaxation processes in the tissue).

Additionally, we have evaluate the lateral variations of local relaxation rate inside the coronary vessel wall on the depth ~ 150 mcm from the top of the vessel surface. Panel (a) Figure 2 shows spatial distribution of the relaxation rate along indicated dashed line on the structural image presented on Panel (b).

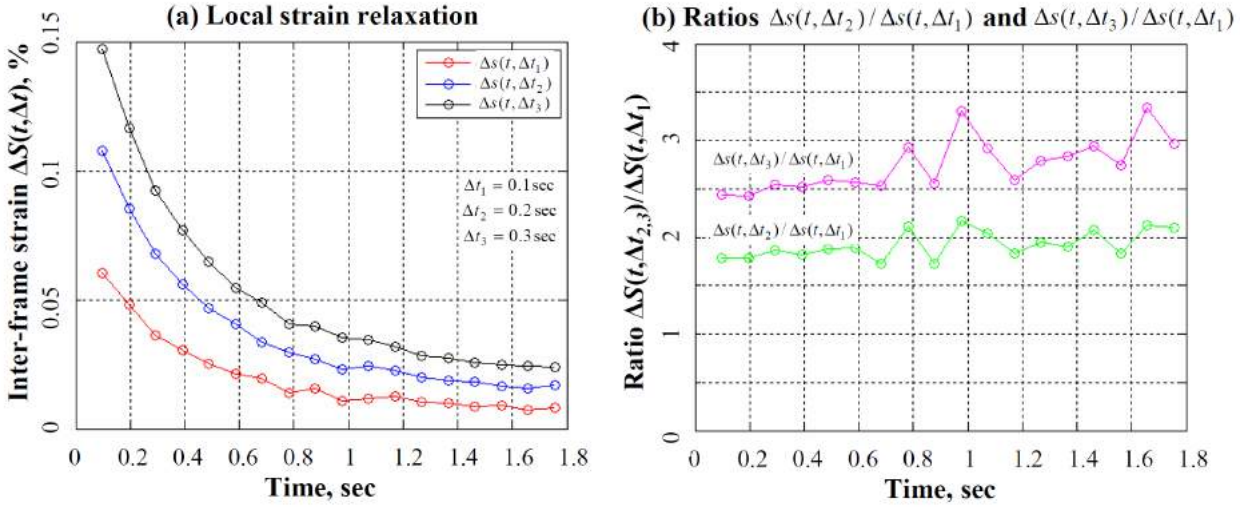

Fig.1. Local inter-frame strain $\Delta s(t,\Delta t)$ relaxation for various time lag between processed scans. Panel (a) represents the time dependence of the incremental local strains for these three cases. Panel (b) shows the experimentally determined ratios $\Delta s(t,\Delta t_3)/\Delta s(t,\Delta t_1)$ and $\Delta s(t,\Delta t_2)/\Delta s(t,\Delta t_1)$.

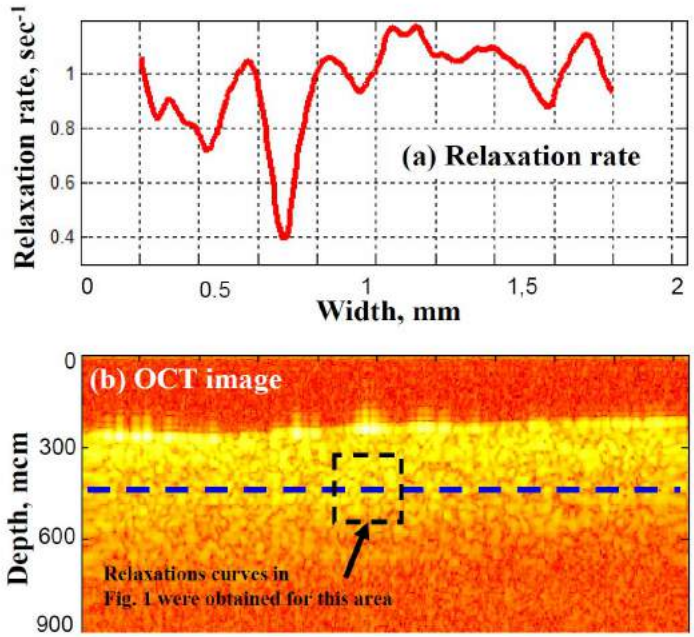

Fig.2. Spatial distribution of the relaxation rate. Panel (a) represents variations in the lateral directions of local relaxation rate inside the coronary vessel wall on the depth ~ 150 mcm from the top of the vessel surface. This cross-section is indicated by dashed line on Panel (b) represents OCT image (B-scan). Relaxation curves plotted in Fig. 1 were obtained for the area indicated by dashed square.

4. DISCUSSION AND CONCLUSION

The above-presented results demonstrate that the phase-resolved technique developed in our previous publication[7] for estimating local strains is practically operable for studying relaxation of strains in biolological tissues on the scales from tens of milliseconds to several seconds. This technique allows one to separate local relaxation phenomena depending on local characteristics of the tissue from "global" relaxation phenomena (that depend on the entire size of the studied region and somehow averaged tissue properties over this fairly large region).

We have verified for a sample of coronary vessel that for the considered time intervals ~ 0.1-1 sec., the observed strain relaxation can be fairly accurately approximated by an exponential law with a single relaxation time (deviation from this law may also become a new indicator in some cases). This relaxation time can be locally (in practice, within a chosen size of the processing window) estimated quantitatively. We have verified that in different parts of structural OCT scans, the extracted relaxation times can differ several times, which means that the developed approach is sensitive enough to ensure mapping of the spatial distribution of relaxation time. The so-obtained "relaxograms" should give an additional information to elastographic strain maps that are conventionally discussed in the context of compressional OCT-based elastography.

An important advantage of the so-obtained relaxograms is that the relaxation times can be compared not only relatively within the same OCT scan, but can be readily compared for different samples. For conventional strain maps such a comparison between different samples is much more difficult, since the conventionally reconstructed strain maps are relative in their nature and require application of non-trivial calibration procedures to relate dimensionless strains and the actual elastic moduli of the tissue. Therefore the above-described OCT-based "relaxography" is a promising technique that can further expand possibilities of multi-modal OCT systems.

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