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Simulation of dynamic contrast-enhanced ultrasound sequences using example-based texture generation

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Abstract

Simulation of dynamic contrast-enhanced ultrasound sequences with known perfusion characteristics and speckle characteristics that are consistent with those observed in experimental data would provide a useful tool for the evaluation of new perfusion quantification and image-processing techniques. A framework is proposed to simulate such perfusion data. It is based on the use of an example-based texture generation method. The generated texture of noise is compared to experimental data in terms of its statistical distribution and spatial correlation. Results show that the example-based method generates data that are closer to the experimental data than those obtained using a conventional parametric simulation method (33 to 80% smaller Hellinger squared distance). This fast and simple method allows simulation of dynamic contrast-enhanced ultrasound data for complex perfusion patterns, and should be useful for the validation of registration, segmentation or perfusion quantification methods.

1. Introduction

Dynamic Contrast-Enhanced Ultrasound (DCE-US) is based on the nonlinear detection of microbubbles that can be used as tracers of microvascular flow. Currently DCE-US is applied in the clinical setting for classification of liver lesions based on vascular patterns and for assessment of myocardial perfusion [1]. Its feasibility has also been shown for evaluation of microvascular flow during follow-up of anti-angiogenic therapy [2,3]. The technique can currently be limited, however, by motion, attenuation or flow estimation variance under low signal to noise conditions [4,5].

Solutions for these limitations are often sought by correlating DCE-US measurements made from *in vivo* data sets with information obtained in the same tissues with reference techniques (histology, contrast-enhanced CT, microsphere). Such comparisons are complicated by the differences in spatial sampling and by the different natures of information characterized by DCE-US and many of the reference techniques. Data sets providing a controlled variation of perfusion parameters and knowledge about the ground truth values for blood volume and flow would facilitate evaluation and optimization of novel techniques for flow quantification from DCE-US.

Software is available for the simulation of ultrasound data for a defined arrangement of scattering structures and sound propagation conditions, such as Field II developed by Jensen and Svendsen [6] or CREANUIS presented in Varray et al. [7]. Such software simulates linear and non-linear propagation and scattering of ultrasonic waves based on detailed scatterer maps. To simulate dynamic ultrasound sequences from microbubbles in a complex vascular network, the time-varying distribution of the flowing microbubbles would need to be mapped to simulate each frame of the sequence. Although this could be of considerable interest, modeling flow in a microvascular network would be very computantionally demanding and no such simulation has been reported using Field II or CREANUIS.

The objective of this work is to propose an alternative and simpler approach to simulate DCE-US sequences representative of data observed in tissues with complex microvascular

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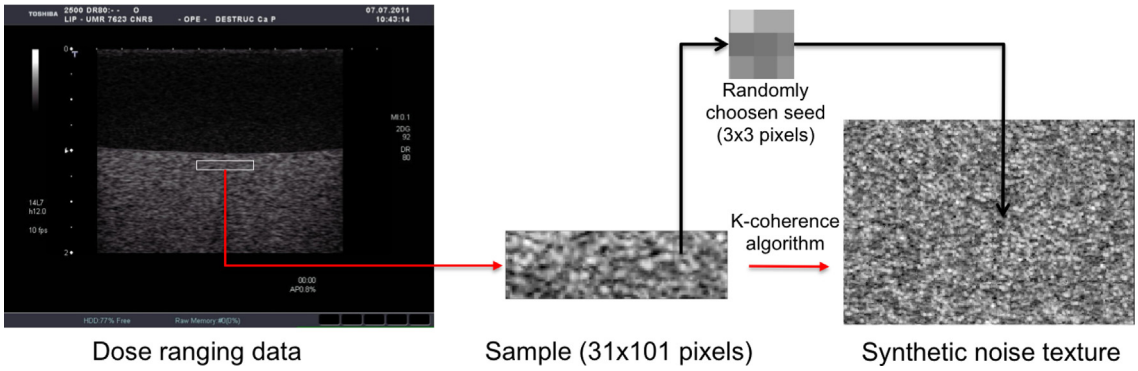

Fig. 1. The use of the dose-ranging data in the context of *K*-coherence. From a selected image for each contrast microbubble concentration, a region was selected in the superficial portion of the contrast solution (box outlined in white on the image). A seed was randomly extracted from this sample and the *K*-coherence algorithm was run to generate a synthetic acquisition.

networks. This technique could be useful for the simulation of DCE-US sequences to evaluate quantification, motion compensation algorithms or attenuation correction models.

The original approach proposed to simulate DCE-US perfusion data reposes on an example-based algorithm [8]. Example-based texture generation methods allow construction of arbitrarily large textures based on a sample and preserve spatial structure and intensity distribution. The quality of the texture of DCE-US noise obtained with such an algorithm is assessed in terms of its spatial correlation and distribution. A framework combining these simulated textures with data describing the evolution of contrast agent concentration as a function of time at each pixel is developed to provide a simple but realistic in terms of its spatial correlation and distribution model of DCE-US data.

2. Materials and methods

2.1. Dose-ranging data

2.1.1. Acquisition

DCE-US data were obtained from calibrated-concentration solutions of ultrasound contrast agent to provide the reference images for the example-based texture generation algorithm, from which the sample image and the seed will be extracted and to provide calibrated data with which to compare subsequent simulated DCE-US. Dose-ranging was conducted using the experimental ultrasound contrast agent BR38 (Bracco Suisse SA, Geneva, Switzerland). DCE-US dose-ranging data were acquired with an Aplio 50 imaging system and a PLT-1202-S linear probe (Toshiba Medical System, Tochigi, Japan). The mechanical index was fixed at a low level ($MI = 0.1$) and the transmit frequency was set to 7 MHz in Contrast Harmonic Imaging mode (CHI). Details of the experiment are described in Payen et al. [9]. The ultrasound contrast agent was reconstituted prior to the experiment in 5 mL of physiological solution (0.9% NaCl), to yield approximately 2×10^8 microbubbles/mL. Data were acquired for six concentrations from 0 microbubbles/mL, no contrast agent, to 4×10^5 microbubbles/mL. At each concentration, images were acquired during 10 s at 4 frames/s, giving a total of 40 images for each concentration. The size of the image pixel is 0.06×0.06 mm. Sequences were acquired in raw data format, which is a format specific to the Aplio 50 imaging system that is free of compression and thresholding. These data were converted into contrast echo-power data (the square of the linearised amplitude of the contrast signal) using custom software describe in Payen et al. [9].

2.1.2. Sample and seed extraction

One of the 40 images at each dose was randomly chosen to be used for sample and seed extraction. The other 39 were then used for evaluation. From the selected image, a sample of 31×101 pixels was selected close to the solution's surface, in an area where the signal was homogeneous and not significantly attenuated. From this sample, a 3×3 pixels seed was randomly selected and used to initialize the *K*-coherence algorithm (Fig. 1).

2.2. Simulation of DCE-US sequences

2.2.1. Signal model

To consider additive noise, dominant at low concentrations, the contrast echo-power at x at time t_i, $f_x(t_i)$, is modeled as the signal anticipated from the perfusion dependent contrast concentration, or the perfusion signal, u, corrupted by a multiplicative speckle-noise term, υ, and an additive baseline noise term, ε:

$$f_x(t_i) = u(t_i).\upsilon(t_i) + \varepsilon(t_i). \quad (1)$$

The speckle-noise, υ, is due to the random fluctuations of the power detected from the distributions of sub-wavelength-sized contrast microbubbles. The additive baseline noise ε is due to electronic noise, which is present with and without contrast agent. The perfusion signal that is assumed to describe the variation of the contrast echo-power as a function of contrast agent concentration. Therefore, the speckle-noise term is normalized to have a distribution with a mode value equal to 1. The distributions and the spatial correlation properties of the terms ε and υ are assumed to be constant.

2.2.2. K-coherence noise generation

Equation (1) includes a speckle and a baseline noise component. In order to realistically simulate these, an example-based