Research Article

Algorithms and Results of Eye Tissues Differentiation Based on RF Ultrasound

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Algorithms and software were developed for analysis of B-scan ultrasonic signals acquired from commercial diagnostic ultrasound system. The algorithms process raw ultrasonic signals in backscattered spectrum domain, which is obtained using two time-frequency methods: short-time Fourier and Hilbert-Huang transformations. The signals from selected regions of eye tissues are characterized by parameters: B-scan envelope amplitude, approximated spectral slope, approximated spectral intercept, mean instantaneous frequency, mean instantaneous bandwidth, and parameters of Nakagami distribution characterizing Hilbert-Huang transformation output. The backscattered ultrasound signal parameters characterizing intraocular and orbit tissues were processed by decision tree data mining algorithm. The pilot trial proved that applied methods are able to correctly classify signals from corpus vitreum, blood, extraocular muscle, and orbit tissues. In 26 cases of ocular tissues classification, one error occurred, when tissues were classified into classes of corpus vitreum blood, extraocular muscle, and orbit tissue. In this pilot classification parameters of spectral intercept and Nakagami parameter for instantaneous frequencies distribution of the 1st intrinsic mode function were found specific for corpus vitreum blood, orbit and extraocular muscle tissues. We conclude that ultrasound data should be further collected in clinical database to establish background for decision support system for ocular tissue noninvasive differentiation.

1. Introduction

Ultrasound scanning of eye is a well-known instrumental investigation [1–3]. Ultrasound B-scans help to visualize internal structure of the tissues. In ophthalmology, B-scans are used to show cross-sectional view of the eye by displaying an image of ultrasound signal intensities originating from nonhomogeneities within tissue. The ultrasound methods combined with optical methods are of high importance in diagnosis and management of eye tumors [4, 5]. Limited set of B-scan based-measurement parameters (mostly geometrical: height, cross-sectional areas, and shape, microstructure homogeneity, and reflection intensity) are used for diagnostics of intraocular tissues and tumor in conventional diagnostic systems [6–8]. Statistical B-scan texture analysis-based parameters are also used for intraocular tumors [9] and thyroid tissue characterization [10].

The conventional ultrasound B-scan diagnostic systems use video (demodulated) signals to represent diagnostic images. This means that large part of information which is possibly embedded in raw or radio frequency signal (RF) representing backscattered ultrasound waves is thrown away. The information extracted from RF signals, however, could be successfully used for tissue characterization and development of quantitative ultrasound diagnostic systems [11]. For example, one-dimensional ultrasound RF signals, that is, A-scan signals are used to estimate tumor thickness, internal reflectivity, spontaneous vascular pulsation parameters [12, 13]. RF A-scan signal parameters (mean spectral frequency, the width of power spectrum, effective values of correlation function, and backscattering coefficient) can be successfully
used for followup of brachytherapy treatment and character-
ization of malignant melanoma of choroid [14, 15].

RF ultrasound signals from B-scan-diagnostic systems
were also analysed. Spectral analysis was used to obtain
parameters such as the size of acoustic scatterer, acoustic
concentration of scatterers, spatial variability, backscatter-
ing coefficient, attenuation coefficient and root mean
square velocity fluctuation, spectral slope, and intercept.
These parameters of RF signals were used as the pro-
gnostic indicators for uveal melanoma [16], correlated with
microcirculatory patterns in uveal melanomas [17] and used
for modeling of intraocular tumor tissues [18]. The effective
scatterer size, acoustic concentration, intercept, and slope of
3D regions of interest calculated from spectral parameters of
RF signals were used for characterization of cancerous lymph
nodes [19] and for characterization of mammary tumors
[20]. Two-dimensional spectrum analysis of RF signals was
applied in ocular tumor diagnosis [21].

The literature survey shows that ultrasound RF signals
are analyzed using statistical, nonparametric (Fourier), and
model-based spectral analysis methods by fitting approx-
imated backscattered spectrum model. These spectrum
estimation methods suffer when data is highly nonstationary
as is the case in RF ultrasound signals. Hilbert-Huang
transform (HHT) [22] is a promising tool for nonstationary
analysis. To the best of our knowledge, HHT-based methods are not yet used in the field of ultrasound-based eye tissue characterization.

The aim of this research is to develop parameterization
algorithms for backscattered ultrasound RF signals
received from eye tissues and to provide supplementary
B-scan parametric maps, which could improve ultrasound
colorization and differentiation of intraocular tissues.

2. RF Ultrasound Data

The hardware used for acquisition of raw RF signals com-
prising ultrasound B-scans was described in [23]. Briefly,
the hardware system could be specified as follows. The
ultrasound B-scan system is Mentor Advent A/B (Advent,
Norwell, MA, USA), with mechanically scanning 15 MHz
descansor. The original ultrasound scanner is supplemented
with signal acquisition extension [23]. Data acquisition sys-
tem was prototyped using computerized digitizer PICO 5203
(Pico Technology, Cambridgeshire, UK) having 32 MB of
buffer memory, 8 bits in amplitude resolution, and 250 MHz
of sampling frequency.

3. Algorithms for Characterization of
Backscattered Signals

Empirical mode decomposition (EMD) and ensemble
empirical mode decomposition (EEMD) followed by Hilbert
transform (Hilbert-Huang transform) were used for synthe-
sis of parametric maps and tissue characterization [22, 24].
Both EMD and EEMD methods extract so-called intrinsic
mode functions (IMFs) from the raw RF ultrasound B-scan
signals. IMFs serve as an input to Hilbert transform, which
outputs analytical (complex) signals. By taking modulus
and argument of complex signals, analytical amplitude and
phase are extracted from each IMF. Finally, distributions of
instantaneous frequency (derivative of analytical phase) and
amplitude are calculated for each IMF.

In order to characterize instantaneous amplitudes and
frequencies, Nakagami distribution was used since it has
been found to be suitable for ultrasound signal characteriza-
tion previously [25]. Nakagami distribution is parameterised
by two parameters: scaling parameter $\Omega$, which reflects
distribution of signal power, and $m$, which determines
the shape of the distribution. The Nakagami distribution
parameters were estimated from the 1st EMD IMF and 2nd
EEMD IMF. Both instantaneous amplitudes and frequencies
were parameterized for all B-scan RF signal lines.

Two additional parameters, spectral slope and intercept
[26], were calculated for characterization of echograms
inside the regions of interest (ROI). The signals were divided
into segments and then windowed using Hamming windows.
Fourier transform-based estimates of power spectrum were
averaged in order to reduce spectrum dispersion. The parameters (intercept and slope) were obtained after linear
fitting of calibrated spectral function in frequency band 5–
18 MHz. One more method to characterize nonstationary
RF signal by mean instantaneous frequency (MIF) and
mean instantaneous bandwidth (MIB) was used as described
previously in [23].

The newly developed software allows opening and
processing of raw RF ultrasound data files obtained by
ultrasound diagnostic scanner. At first, RF ultrasound one-
dimensional signals (A-scans) comprising B-scan sector are
demodulated and mapped from sector data to raster data as
a greyscale B-scan image (see grayscale images in Figure 1).
Then two ROIs are selected interactively by dragging cursors.
The first ROI is primarily meant to mark the suspicious tissue
and the second ROI—the healthy tissue. Selected regions
(matrixes of raw RF ultrasound data) are passed to parameter-
ization algorithms. The results of parameterization by
selected algorithm are added as a new layer to B-scan at
locations of selected ROIs (the colored boxes in Figure 1).

RF ultrasound (B-scan) signals were registered for 57
clinical cases. An experienced ophthalmologist has selected
two ROIs for each B-scan case. The size of ROIs was kept
to cover the area of the image with B-scan amplitude as
uniform as possible. In order to achieve uniformity of
B-scan amplitude, the ROI size was varied from 1.1 mm to
1.8 mm in depth (the mean being 1.5 mm) and from 5 to 12
echoscopy lines in width (the mean being 8.6). Then the RF
signals of both ROIs were processed by the parameterization
algorithms, and calculated parameters were stored into the
database.

4. Visualization of Tissue-Characterizing
Parameters

The “rose” or “radar” type diagrams were used in order to
present all sixteen parameters (see Table 1) in one diagram.
Such presentation of parameters that characterize the tissue
could be useful during visual preliminary analysis, that
is, before application of automatic classification algorithms such as rule-based classifiers or neural networks.

The whole set of 57 clinical cases of eye B-scan signals were parameterized. The general view of these parameters is presented in Figure 2. The parameter array (dimensions $57 \times 16$) was obtained from signals backscattered in healthy tissue of orbit, and the same size array was obtained in case of suspicious tissues inside the eyeball.

Close analysis of diagrams in Figure 2 shows that the distributions of the parameter values are different for healthy and suspicious tissues. For example, $\Omega$ for 1st IMF and $\Omega$ for RF signal parameters are distributed widely in suspicious tissues regions, while the same parameters in healthy orbit tissues are uniformly close to zero. The wide spread of values of the parameters could be noted as common feature of signals backscattered from intraocular suspicious tissues. The smaller variability of parameters from healthy tissues of the eye orbit could be explained by uniformity and similarities of these tissues. Therefore, in future, the tissues of eye orbit could be used as the reference backscattering target of eye.

Several clinically confirmed cases of healthy (extraocular muscle) and pathologic (intraocular blood) tissues were analyzed in order to investigate the power of proposed technique to differentiate between types of ocular tissues. The obtained illustrative diagrams (Figures 3(a) and 3(c)) indicate some differences among parameters characterizing ultrasound signals backscattered from intraocular blood or extraocular muscle. It can be also observed that parameters estimated from healthy orbit tissues exhibit similar values and patterns of radar type diagrams (Figures 3(b) and 3(d)).

The multitude of extracted parameters makes visual analysis difficult in case of subtle differences among eye tissues.
Automatic data mining analysis methods and classification techniques could potentially increase the accuracy of tissues differentiation.

5. Automatic Classification of Ocular Tissues

The computer software for data mining, see 5.0/C5.0 [6], was applied for automatic classification of RF ultrasound B-scan signals in the database. In total, 26 cases have been analyzed. The same sixteen parameters were used from each of 26 signals representing different clinical cases. We used predictive modeling algorithm for classification. This algorithm forms a decision tree or a set of rules understandable by a human. Classification of cases into three classes (intraocular blood, healthy orbit tissue, and extraocular muscle) was performed with decision tree of size...
Our method estimates quantitatively these ultrasonographic characteristics using set of RF signals processing algorithms, similarly as was reported in [16, 19, 21]. Related study [4] proposed to use the identification of extraocular muscle as a reference to avoid misinterpretation of extrascleral growth of intraocular tumor. Internal blood was also assessed [4] as another important factor when discriminating hemorrhagic lesion from choroidal melanoma. In rare cases choroid hemangiomas may grow in spite of benign histology [27]. These pathologies were found hard to differentiate which complicates decision on the best treatment. In such cases ultrasonic followup should be provided for evaluation of changes in formation size and internal reflectivity [27]. Therefore, improvement of internal blood differentiation is important. The extremely high internal reflectivity typical for choroid hemangioma should be verified with biopsy. Fledelius [27] also has described the classical CT-scan error miss interpreting oblique section of inferior rectus muscle. Supplementary ultrasonography of external eye muscles was found valuable in ophthalmologist’s evaluation. Therefore improvement of muscle differentiation is also important. Our results confirm forecasted [28] advantages of the RF-based quantitative analysis, allowing additional digital manipulation for overcoming certain limitations of qualitative interpretation. The second issue of our approach was application of complex algorithms for tissue characterization in relation with backscattering spectra model-based methods [18, 29, 30] and empirical or statistical estimation methods [25]. The backscattering models were theoretically and practically tested [29] with regard to the properties of the observed backscattering spectra. The estimated sizes of acoustic scatterers quite well correspond to the dimensions of observed histological structures. Our study showed that complex evaluation of backscattering spectra model based methods together with empirical or statistical estimation methods provides additional information and allows for better tissue characterization.

In conclusion, RF ultrasound signal analysis can be used to differentiate different ocular tissues. The critical problem in decreasing the tissues classification error is the availability of representative database having sufficient amount of annotated ultrasound data. One possible application of proposed method is the differentiation of intraocular tumors.

### 6. Discussion

The algorithms and software for eye tissues differentiation were developed using the analysis of modulated (RF) ultrasound B-scan signals. The algorithms parameterize the RF ultrasound signals in frequency and joint time-frequency domains. The classical Fourier and relatively new Hilbert-Huang transforms were employed to characterize the signals from selected regions of eye tissues. In particular, the following parameters were calculated: B-scan envelope amplitude (dB), approximated spectral slope (dB/MHz), approximated spectral intercept (dB), mean instantaneous frequency (MHz), mean instantaneous bandwidth (MHz), and Nakagami distribution parameters $m$ and $\Omega$ characterizing Hilbert-Huang transformation output. The extracted signal parameters were processed using data mining software and used to build the decision tree for automatic tissue classification. The pilot trial to automatically differentiate among *corpus vitreum* blood, extraocular muscle, and orbit tissues resulted in classification error of 3.8% in the database of 26 clinical cases of ocular tissues.

Our research is limited due to lacking of comparison with gold standard imaging modality such as MRI or with histological confirmation. However, application of the proposed method could be compared to similar research of eye tissue differentiation. In this pilot study we first evaluated differentiation of the simplest ocular tissues. As discussed by Fu et al. [4], the differentiation of eye tissues is often performed using the following ultrasonographic characteristics [4]: shape of lesion, reflectivity (low, medium, and high), internal structure consistency or irregularity, acoustic shadowing, and attenuation (from negligible up to high). However, this subjective and qualitative interpretation of B-scan images of eye tissue is hard to quantify and to use in automatic tissue differentiation algorithms. Output of our method estimates quantitatively these ultrasonographic characteristics.

| Extraocular muscle | Classified as | True class |
|--------------------|---------------|------------|
| Intraocular blood  | 9             | Extraocular muscle |
| Orbit              | —             | —          |
| —                  | 4             | Intraocular blood |
| —                  | 12            | Orbit |

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