Trends in Time Series of Parameters from Ultrasonic Images due to Metabolic Activities of the Human Liver

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Abstract. Being the biggest inner organ of humans, the liver contributes decisively to metabolism. Hereby, liver activities result from reactions on ingestion and digestion and are assumed to influence the acoustical properties of the liver tissue. In this work we present initial results of the investigation of aforementioned reactions by observing the liver in-vivo with ultrasound during several hours. After extracting various parameters from the recorded radio frequency data sets, time series of these parameters are analysed in order to find relations between a supervised ingestion and changes in the computed time series.

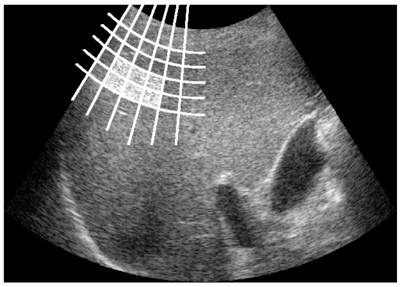
1 Introduction

The liver (*greek: hepar*) is the biggest inner organ of humans performing different metabolic functions. The main tasks of the liver are detoxication of blood, composition, decomposition and modification of metabolites and storage of glycogen. In its function as an exocrine gland the liver also produces biles, which is stored in the gallbladder. The blood supply of the liver is secured from two independent vessel systems. On the one hand the vena porta brings in fresh blood from the gastrointestinal tract (70 % of oxygen supply), on the other hand the arteria hepatica provides a second inflow (30 % of oxygen supply).

Up to now, the human liver has been examined concerning different perspectives and questions using all prevalent imaging modalities. Especially diagnostic ultrasound has become popular due to its flexible, non-ionising and inexpensive application. Ultrasonic research has been done on focal and diffuse lesions (i.e. cysts, cancer, cirrhosis etc.) utilizing tissue characterisation, flow analysis, ultrasound contrast agents, elastography and more. Nevertheless, all investigations were focused on spatial considerations and not on inspections of temporal changes in the (healthy or pathological) liver due to metabolic processes. Thus, the analysis of trends in temporal parameter-charts of ultrasonic data is a novel approach to investigate activities of the liver.

Fig. 1.

(a) Ultrasound imaging, using a custom made belt to fasten the ultrasound probe.



(b) Liver ultrasound image. Segmentation into ROIs and combination of ROIs in an AOI.

The objective of this work is, therefore, the derivation of a relation between a supervised ingestion (activation of the liver) and a change in the corresponding time series computed on parameters that are commonly used in ultrasonic tissue characterization [1]. Such a change in the time series according to a variation in the acoustical properties of the tissue could result from different reasons [2], e.g. an increase of secretion activity, an increase of blood perfusion or changes in pressure due to contraction of the gallbladder.

2 Methods

2.1 Data Acquisition

For a period of three hours the livers of four volunteers (normal weight, according to body mass index, BMI) have been scanned using a Siemens Sonoline Antares ultrasound system (probe: curved array C5-2, center frequency: 3.25 MHz, bandwidth: 5.5 MHz, depth: 13 cm, focus: 6 cm, field of view: 70.5 °, scan lines: 300). In combination with this system we used the Axius Direct Ultrasound Research Interface (URI) to obtain unprocessed, beamformed RF-data with 16 bit resolution and 40 MHz sampling rate. During the aforementioned three-hour-period, one data-frame was acquired and stored every minute.

The ultrasound scans were conducted intercostally on the seventh segment of the liver (upper right corner of the liver). This segment turned out to be particularly suitable for tissue characterisation and functional analysis, since only few larger vessels are crossing. This property results in particular homogeneous tissue. In order to spatially stabilise the data acquisition, the ultrasound transducer was fastened on the probands with a custom made belt (Fig. 1 (a)). Furthermore, probands were instructed to exhale completely before each acquisition. Thus, the imaged liver intersection could be maintained throughout the examination.

Each proband was scanned twice, both times in the morning: The first day completely fasting, the other day fasting in the beginning and then after ingestion of a hardboiled egg to stimulate the liver by lipids.

2.2 Parameter Extraction

For parameter extraction, parts of an existing system for tissue characterization was used [1, 3]. Every data set was subdivided into up to 3000 *Regions Of Interest* (ROIs). The ROIs consisted of 128 sample points in the transducer axial direction and of 16 scan lines in the lateral direction. Their axial and lateral overlaps were 75 % and 50 %, respectively. Thus, each ROI comprises an area of approximately 5.0 mm × 7.0 mm at focal depth (schematic scetch: Fig. 1 (b)).

Up to 130 parameters were calculated for each ROI. These parameters can be divided into two larger groups, i.e. spectrum parameters and texture parameters. *Spectrum parameters:* On the one hand, spectrum parameters were calculated using Fourier transformation after applying a Hamming window to the radio frequency data (RF data) of each ROI. On the other hand, an autoregressive model (AR model) was used to estimate the power spectrum. The order of this model was 15, according to the results achieved by the Akaike information model [4]. For both cases, spectral results of adjacent scan lines were averaged to obtain unbiased estimators. *Texture parameters:* Both first order and second order texture parameters were computed. Hereby, computations were performed on envelope detected data using Hilbert transform. First order texture parameters consisted of different estimates of echo amplitude evaluating the grey value histograms. Second order parameters (i.e. cooccurrence parameters) incorporate spatial relations between grey scale pixels according to [5, 6]. However, those parameters were computed for different distances of the cooccurrance matrix, but only for axial direction to account for the sector geometry of the transducer.

For the last step of parameter extraction a particular homogeneous area within the imaged seventh segment of the liver was chosen and called the *Area Of Interest* (AOI). This AOI comprised an area of approximately 1.6 cm × 2.3 cm at focal depth and, therefore, consisted of 105 ROIs. The values of each parameter (one per ROI) were averaged within this AOI. Admittedly, before averaging the values of the ROIs, an elimination of outliers was performed by using the MAD criterion (*Median Absolute Deviation*). Here, those ROIs of a parameter were neglected whose absolute deviation from their median was greater than six times MAD.

The technique of averaging several small, overlapping ROIs and, hence, merging them to one bigger AOI (instead of directly extracting one parameter per AOI) was conducted in order to achieve unbiased estimations.

2.3 Time Series Analysis

Stringing all computed values of one parameter together and plotting them over time, one time series per parameter is obtained. Several statistical techniques were carried out for time series analysis [4, 7]. However, this analysis was only performed in time domain, so far. In order to compensate for noise effects and to better detect changes in time series, we smoothed the series by using moving average filters of different window-length, smoothing splines by incorporating a smoothing-parameter of 15 and linear regression models of different orders. Before accomplishing these smoothing techniques, temporal median filtering was conducted using a window-length of five, in order to reduce the contribution of outliers.

Furthermore, the time series were analysed in intervals, dividing the series in time segments with respect to their local trends. This division has been conducted by automatically detecting trend reversals [7] and fitting a first order linear regression model within these intervals.

3 Results

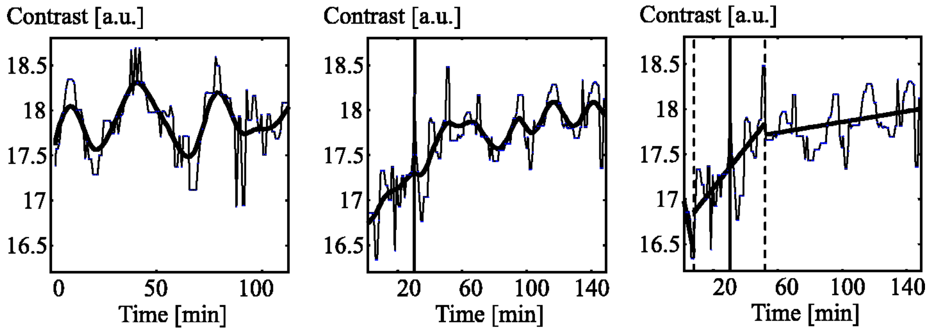
The analysis of the computed time series showed that a first group of parameters (consisting of both texture and spectral parameters) are not affected by the lipid-stimulation. A change or trend reversal can neither be detected in the fasting nor in the non-fasting time series. However, in addition to this first group a second group of parameters (consisting of both types of parameters, too) showed a trend reversal in their non-fasting time series, while the results obtained from the fasting series featured no trend reversal.

In figure 2 the median-filtered time series of the normalised second order texture parameter *Contrast* [5, 6] are exemplarily shown for the fasting (a) and the non-fasting (b,c) case of one proband (activation 31 minutes after the start of the examination, BMI = $20.8\,\mathrm{kg/m^2}$). In order to smooth the time series, the fasting (a) as well as the non-fasting charts (b) were processed using smoothing splines. Apparently, the fasting series stays stationary, oscillating on a constant level. However, the non-fasting series appears to change its level over time. Performing the detection of trend reversals on the non-fasting series (c), a trend reversal can be found 21 minutes after the ingestion. This delay corresponds to the time of an increase of portal blood circulation after an ingestion and, hence, seems to be also reasonable from a medical point of view.

4 Conclusion

The described results encourage for further investigations. Currently, a larger data base is built up by scanning more probands. However, future examinations will be conducted using an ECG trigger (ECG: electrocardiogram) in order to enhance the stabilisation of data acquisition. Investigations have to be made to ensure that computed trends are deterministic (i.e. result form lipid stimulation) and not stochastic. In particular examinations with no activation have to be analysed concerning the observed oscillations. For the next step, parameters will be combined to reduce their large number by applying principal component analysis. Furthermore, future investigations will be conducted not only in the

Fig. 2. Time series of normalised second order texture parameter *Contrast*.



(a) No activation. Median-filtered series (thin) and smoothing splines (bold).

(b) 31 minutes activation (vert. line). Median-filtered series (thin) and smoothing splines (bold).

(c) 31 minutes activation Median-filtered (thin), trend reversals (dashed), first order regression (bold).

time domain, but also in the frequency domain. Therefore, analysis using joint-time-frequency techniques [8] are considered promising.

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