A Quantitative Ultrasound Approach for Detecting Placenta-Mediated Diseases

Farah Deeba*, Ricky Hu*, Victoria Lessoway‖, Jefferson Terry†, Denise Pugash‡,
Jennifer A. Hutcheon§, Chantal Mayer§ and Robert Rohling*¶
*Department of Electrical and Computer Engineering, University of British Columbia, Vancouver, British Columbia, Canada
‖Department of Ultrasound, BC Women's Hospital, Vancouver, Canada
†Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, British Columbia, Canada
‡Department of Radiology, University of British Columbia, Vancouver, British Columbia, Canada
§Department of Obstetrics and Gynaecology, University of British Columbia, Vancouver, British Columbia, Canada
¶Department of Mechanical Engineering, University of British Columbia, Vancouver, British Columbia, Canada
Email: {rohling, farahdeeba}@ece.ubc.ca

***Abstract*—In this work, we apply a quantitative ultrasound approach to detect placenta-mediated diseases. We measure the quantitative ultrasound parameters: attenuation coefficient estimate, integrated backscatter coefficient and effective scatterer diameter from 46 *ex vivo* placentas collected from normal pregnancies and pregnancies affected by intra-uterine growth restriction and preeclampsia. Preliminary results show the potential of quantitative ultrasound to distinguish between health and diseased placentas.**

***Index Terms*—Attenuation Coefficient Estimate, backscatter coefficient, effective scatterer diameter, quantitative ultrasound, placenta**

I. Introduction

The placenta is the critical interface between the fetus and the mother. This dynamic organ goes through structural and functional changes throughout the pregnacy. Any abnormalities during the dynamic developmental process of the placenta would impact the health of the mother and the fetus, both during and beyond the prenatal period. Specifically, the placenta plays a major role in the pathogenesis of many pregnancy complications such as preeclampsia (PE) and intra-uterine growth restriction (IUGR). These placenta-mediated complications are often the late manifestations of a chronic pathological process, preceded by a long sub-clinical phase [1]. This sub-clinical phase, which often involves characteristic changes in underlying microstructure, presents a window for early detection and intervention with a potential for improved pregnancy outcome. However, there is a lack of currently available clinical tools for the *in vivo* assessment of placenta microstructure.

Quantitative ultrasound (QUS) is emerging as an important clinical tool for biological tissue characterization and disease detection, which has found a wide range of applications, including fatty liver disease identification and monitoring [2], [3], cancer detection in prostrate and lymph nodes [4], cervical ripening detection [5], and breast lesion characterization [6]. QUS parameters can be expressed as functions of acoustic and mechanical properties of interrogated tissue, which are often found to be related to the pathological states. Additionally, QUS parameters are both user independent and system independent, and therefore are helpful to establish baseline values for healthy tissue and differentiate between healthy and diseased tissue across patients at different point of time. In this work, we identify three QUS parameters, attenuation coefficient estimate (ACE), integrated backscatter coefficient (IBC) and effective scatterer diameter (ESD), the combination of which has previously been used for improved diagnosis of hepatic steatosis [3]. ACE is a measure of the ultrasound energy loss with propagation depth due to the combined effect of scattering and absorption. Backscatter coefficient measures the ultrasound intensity that is scattered in the backward direction. IBC is a measure of the backscatter strength, which is estimated by integrating the backscatter coefficient in the effective frequency band of the transducer. Backscatter coefficient can further be used to estimate the ESD of the dominant sub-resolution scatterer, where the size limit is determined by the incident ultrasound frequency [2].

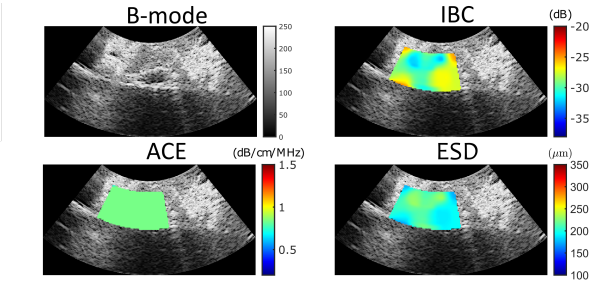

Fig. 1: ACE, IBC and ESD maps overlaid on ultrasound B-mode image for an example placenta.

Currently, multiple multinational research initiatives have been undertaken to develop non-invasive and *in utero* placenta imaging techniques [7]. Compared to other imaging techniques, such as MRI, the role of QUS in placenta imaging is less studied. The few QUS studies on the placenta are limited to the characterization of normal placental tissue [8]. The objective of this proof-of-concept study is to investigate

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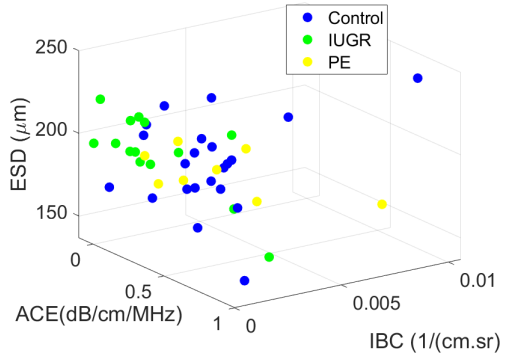

Fig. 2: Scatter plot of QUS measures representing control, IUGR and PE cases.

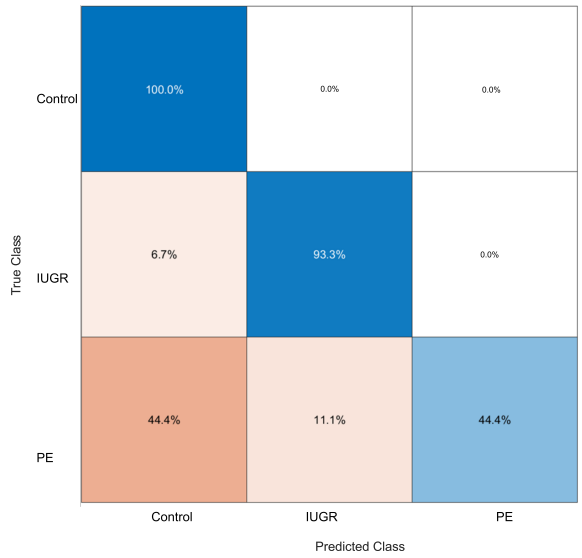

Fig. 3: Cross validation matrix for Fine Gaussian Support Vector Machine (SVM) classifier.

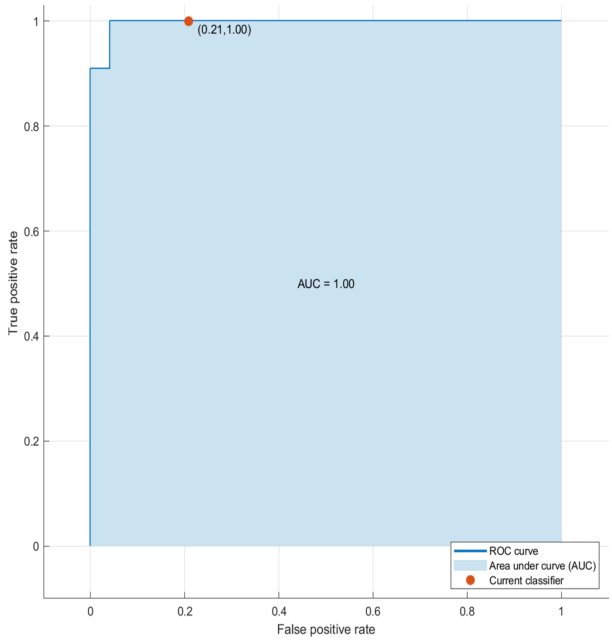

Fig. 4: Receiver operating characteristic curve.

the ability of QUS to differentiate between placentas from normal and complicated pregnancies. To achieve this objective, we have employed a previously developed spatially weighted three dimensional regularization method that yielded superior QUS reconstruction performance with improved resolution-precision trade off in presence of tissue heterogeneity [2]. We apply the QUS method on the placentas *ex vivo* obtained from both normal pregnancies and pregnancies affected by preeclampsia (PE) and/ or intrauterine growth restriction (IUGR). Finally, we present the preliminary classification results and discussions.

II. Method

In this study, 46 placentas were collected from a group of women who delivered via cesarean delivery at BC Women's Hospital, Vancouver, Canada. The study (H17-00331) was performed under written informed consent of all participants after approval by the University of British Columbia Children's and Women's Research Ethics Board. We included 24 placentas from pregnancies affected by PE and/ or IUGR and 22 placentas from healthy pregnancies. Among the diseased placentas, 15 were affected by IUGR only. The rest were affected by both PE and IUGR, or PE only. PE was defined as the presence of gestational hypertension with proteinuria and a pregnancy was considered to be complicated by IUGR if the fetal abdominal circumference is below the 10th percentile measured from routine ultrasound examination.

The placentas were stored at 4°C until the examination. Before examination, layers of acoustic absorbing pad (Aptflex F28, Precision Acoustics, UK) were placed beneath the maternal surface of the placenta disc to reduce reverberation artifacts. The placenta was secured using two rubber bands at the edges to the absorbing pad layers and then placed in a rigid plastic container to minimize any deformation while transporting from one imaging modality to another. The ultrasound data from the placentas were acquired with an Ultrasonix

SonixTouch machine (Analogic, Richmond, Canada) and a m4DC7-3/40 curved array transducer (Ultrasonix, Richmond, BC, Canada). The placenta fixed within the container was submerged in a constant-temperature water bath (Cole-Parmer, Montreal, QC, Canada) with temperature set at 37°. The transducer was submerged in the water bath with a few millimetres between the transducer face and the fetal surface. Volumetric ultrasound radio-frequency data were captured and stored for offline processing to reconstruct QUS maps: ACE, IBC, and ESD.

To compute ACE, BSC and ESD, the data acquired from the tissue were normalized by the data from a well-characterized reference phantom, manufactured by CIRS (Northfolk, VA, USA), acquired using the same transducer and system settings. With a piece-wise continuous assumption in all the three directions, we applied a 3D total variation regularization approach to reconstruct ACE and IBC maps [2]. We utilized a Gaussian form factor [9] to express the backscatter coefficient as a function of ESD and measure the ESD map. Finally, we applied a fine Gaussian support vector machine classifier using the mean of the three QUS maps as the feature.

III. Results

We show example QUS maps overlaid on the B-mode images for a placenta *ex vivo* in figure 1. The combination of QUS parameters can distinguish among different placenta groups. We demonstrate the scatter plot of QUS measures for control, IUGR and PE group (figure 2). Using a fine Gaussian support vector machine classifier with a multi-class classification approach, we were able to attain an overall accuracy of 87%, while the area under the receiver operating characteristic curve (AUROC) was equal to 1.0 (figure 4). Specifically, the classifier was able to correctly identify 100%, 93.3% and 44.4% cases in the control, IUGR and PE group, respectively (figure 4).

IV. Conclusion

The is the first study to show the application of quantitative ultrasound to classify placenta-mediated diseases. In this work, we found that the combination of attenuation coefficient, integrated backscatter coefficient and effective scatterer diameter could distinguish the placentas from normal pregnancies from those affected intrauterine growth restriction and preeclampsia, with moderate accuracy. Further study is needed to relate QUS to patho-physiological changes in the placenta and improved classification performance.

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