Vision Grant Report

Date of report: ☐ This is a progress report ☒ This is a final report

Recipient Information

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Grant Details

Project name	Early Assessment of Pregnancy Complications: Placental Characterization based on Ultrasound Images and Numerical Biomechanical Models			
Original grant amount & period	$ 20K	From: 01/2020 (month & year)	To: 12/2020 (month & year)	
Has an extension been granted?	☒ Yes ☐ No	*If yes*, what is the current grant period?	From: 01/2020 (month & year)	To: 12/2022 (month & year)
Dates covered by this report	From: 01/2020 (month & year)	To: 12/2022 (month & year)		

Project Aims & Accomplishments

Short description of project & aims:
The main goal of this project was to shed light on the relationship between placental structure and hemodynamics and placental pathologies, to better understand the underlying biomechanics of preeclampsia. The aims of this project were: (1) To correlate placental transport capacity from in-silico models with in-vivo data. (2) To correlate placental density with in-vivo ultrasound echotexture and (3) To estimate the risk of developing preeclampsia (PE) using routine 2nd trimester scans.

Did you meet the aims you set out to achieve?
☒ Yes ☐ No

Please explain:
The 1st aim of the project was successfully completed by a recruited M.Sc. student (Mr. Tirosh Mekler) at the school of Mechanical Engineering, Tel Aviv University. Tirosh generated 3D models of a fully grown placental lobule based on a generic morphology. The main structure of the villous tree within the intervillous space (IVS) was constructed while the terminal villi were assumed to be a porous medium residing inside the IVS. To estimate the oxygen concentrations and subsequent transport to the fetus due to the changes in placental morphology, a given volume averaged tissue porosity was chosen and kept constant while the inner distribution of the lobule was altered. To distribute the porosity properly, we used a transition zone (TZ); the results of this study have been recently published in the leadin journal 'Placenta'

(Mekler et al., 2022). Furthermore, we also examine the effect of asymmetrical morphology by altering the locations of the decidual veins (DVs). Our results showed that the local villi density has a significant impact on the flow field and oxygen uptake. The location of DVs and their asymmetric distribution are shown to have a major effect on the oxygen distribution within the IVS. Our model was verified against published data.

The 2nd aim is still part of an ongoing work. Due to the poor resoultion of ultrasound scans we decided to shift the project to MRI imaging, a promising tool for pregnancy management and diagnosis. A MATLAB code was written to extract the density field of fetal tissues inside the human placenta in histological sections. The resulting data is to be implemented into the numerical models developed in aim 1. The models will be correlated with MRI density maps.

The 3rd aim is a future work, and will be developed once the 2nd aim is achieved.

Have there been any significant changes to the original project plan over this reporting period? If so, how well have the project team managed these changes?
Yes, in the 1st aim the morphology that was examined represented a fully grown healthy placentome (lobule) where the values that represented the terminal villi density were in the healthy range instead of the pathlogical range. Furthermore, a study of the DVs impact on the oxygen uptake by the fetus was added in order to expand our knowledge on placental structure and hemodynamics

In the 2nd aim a shift to MRI imaging was established by a new collaboration with MRI experts (Prof. Michal Neeman from the Weizmann Institute of Science and Prof. Dafna Ben-Bashat from Tel Aviv University)

Has the project faced any new ethical issues in the past year? If so, how well has the project addressed these?
No

What did you accomplish during this reporting period?
Please see the details in the "For Final Report Only" section"

For Final Report Only

What new information does this contribute to the field of preeclampsia?
Our study highlights the importance of placental structure and density for a proper perfusion of the IVS and subsequent transport of nutrients. Evidence has shown that preeclampsia is characterized by a less dense placenta with fewer terminal villi, which from our results will result in higher blood flow velocities and lower oxygen concentrations within the IVS.

Have you or do you plan to present this information at any meetings? Have you or will you submit a manuscript for publication?
The work described in this report was presented in the following two conferences and part of it was recently published in the journal "Placenta". In both the conferences and the publication the Preeclampsia Foundation Vision Grant Award was acknolowledged.

Journal Paper:
Mekler, T., Plitman Mayo, R., Weissmann, J., & Marom, G. (2022). Impact of tissue porosity and asymmetry on the oxygen uptake of the human placenta: A numerical study. Placenta, 129, 15–22. https://doi.org/10.1016/j.placenta.2022.09.008

Conference Presentations:

1. Mekler, T., Marom, G., & Plitman Mayo, R. (2021) Numerical Modelling of Spatial Porosity Impact on Maternal Blood Flow and Oxygen Transport in the Placenta.Talk. Israel Society for Placental Research (ISPR), December 2021. Rehovot, Israel. 2. Mekler, T., Marom, G., Plitman Mayo, R. (2022). Numerical Modelling of Spatial Porosity and Asymmetry Impact on Maternal Blood Flow and Oxygen Transport in the Placenta.Talk. Israel Association for Computational Methods in Mechanics (ISCM) – 49th Annual Meeting, March 2022. Be'er-Sheva, Israel.
What other impact has receiving this award had on you, your career, colleagues, and/or the field of preeclampsia? This award has helped to foster my independent career, build new collaborations, expand the field of placenta and pregnancy research in Israel, improve my supervising, writing and oral skills. Wishfully, our work is helping to elucidate placental physiology and the important role of biomechanics in in placental pathologies.
Please provide a plain language summary of findings. This will be listed on the Preeclampsia Foundation website. *(350 words or less)* The findings of this study demonstrate the significant impact that placental morphology has on the nutrient transport to the fetus. Furthermore, for the same macrostructure of the placenta, the inner tissue distribution can be significantly different thereby affecting the oxygen distribution and transport. We have introduced a novel multiscale approach where the microstructure is incorporated numerically making the in silico models more biologically relevant. Finally, the decidual veins location and number were investigated for the first time, assessing their impact on the oxygen uptake. Interestingly, they were found to have a major impact on the maternal-blood circulation and oxygenation patterns demonstrating that their role in placental physiology is far from negligible.

Please email this completed Word document and financial report to eleni.tsigas@preeclampsia.org
If you have any questions, please email or call 321-421-6957