Post-Partum Relaxation Parameter Mapping of Human Placentas at 1.5T : Differences Between Pre-Eclamptic and Healthy Pregnancies

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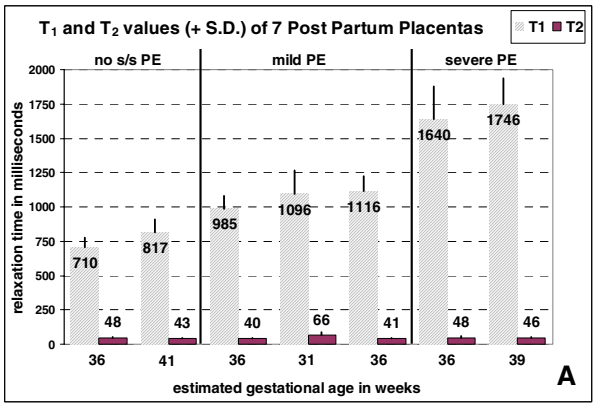
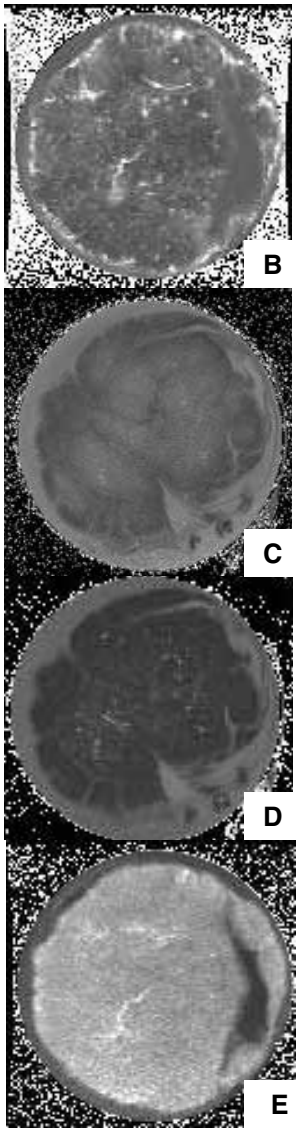


Introduction: Although pre-eclampsia (PE) was first described more than two thousand years ago, both the cause of and a cure (other than delivery of the fetus and removal of the placenta) for this complicated and life threatening disease evade researchers and medical caregivers to this day. In the United States, PE occurs in roughly 10% of pregnancies each year: the incidence of this disease has remained unchanged since the late 1970s. PE is responsible for at least 20% of maternal deaths and 15% of premature births in the U.S. every year, worldwide these numbers are much higher.(1) Several lines of evidence point towards poor placental implantation and subsequent malformation and dysfunction as a root cause of this disease.(2) Since MR imaging is a sensitive modality with which we can study the *in vivo* placenta with minimal risk to the fetus, and since very little is known about the magnetic properties of the human placenta at 1.5 Tesla, this study of the relaxation parameters of the *post partum* human placenta was undertaken on seven different singleton pregnancies. Placentas were collected and their T_1 and T_2 relaxation times calculated: two from healthy pregnancies, three from pregnancies exhibiting mild PE, and two from pregnancies exhibiting severe PE. Our goal is to gain some knowledge of the magnetic properties of the placenta in order to improve clinical prediction and basic scientific knowledge of the human placenta and development of PE.

Methods: All research performed was IRB approved. Placentas were collected with parental consent, rinsed with saline water, and secured in a container of 0.5% NaCl water within 12 hours of birth. Included in the container was a 15 mL tube containing 3% agar, 0.5% NaCl and 12 % NiCl, by weight. Basic information about the gestational age of the newborn, and of the severity of maternal pre-eclampsia was collected from the patients' charts. MR scans were performed at room temperature in a 1.5T GE Signa scanner within 24 hours of birth. A single channel body coil used for transmit was paired with an 8 channel head coil for signal reception. All image sets consisted of five 10mm slices with 5mm spacing through the placenta, roughly in plane from the fetal side through to the maternal side, with NEX=1 and 256x256 data points. The T_1 image sets consisted of TRs (25, 50, 75 & 100 ms) all with a minimum full TE (14 ms) and a total scan time of 18 min. The T_2 image sets consisted of TEs (2, 1, 1/2, 1/4 & 1/8 sec), with a TR of 2 sec for a total scan time of 36 min. Relaxation times were calculated from the least squares fit to the characteristic equations. Slice by slice, regions of varying sizes but completely within the placenta were chosen by hand, and average relaxation times were computed as the mean of relaxation times pixel by pixel within each region, along with the average S.D. of these times within each region.



Figures: **Figure (A)** Plot of post-partum placental T_1 and T_2 values, grouped in no, mild, and severe PE. T_2 values vary from 40 to 66 ms, with mean of 46 ms and S.D. of +/- 7 ms. No significant relationship between T_2 and PE is present. T_1 values vary from 710 to 1746 ms, with mean of 1490 ms and S.D. of +/- 70 to 280 ms. T_1 appears to increase with increasing severity of PE. **Image (B)** T_1 and **Image (C)** T_2 maps of a single slice through the 39 week PE placenta plotted on the far right in Figure A. **Image (D)** T_1 and **Image (E)** T_2 maps of a single slice through the 36 week healthy placenta plotted on the far left in Figure A. No trends linking gestational age (from 31 to 41 weeks) with relaxation times is apparent.

Discussion: There is limited value in concluding anything about the T_2 measurements on these post partum placentas, as spin-spin relaxation is influenced heavily by the oxidative and metabolic state of the tissue, and therefore will vary drastically from *in vivo*, to the first few minutes and hours after birth. That said, there were no differences in the T_2 times which could be linked to the pathology of PE. In contrast, average T_1 times were more than two-fold higher in placentas from two severe PE pregnancies versus two normal pregnancies (averaging 1693 ms vs. 764 ms, respectively). Including the mild cases of PE, T_1s do appear to correlate with the severity of PE in this small and unmatched data set. The S.D. of T_1 was also higher in the PE group (averaging 280 ms PE vs. 70 ms non-PE). Since spin-lattice relaxation is related more to inherent structural characteristics, such as cellular structure and vasculature, (which are altered in PE), T_1 would be less likely to dramatically change post partum, with the caveat that the process of labor and/or separation from the uterine wall does not bring about changes(3) which differ in the normal and PE placentas. In any case, standard myosin/eosin staining of the two placentas shown in Images B through E revealed dramatic changes in cellular arrangement and sub-cellular structures (data not shown), and these differences may be reflected by the differences in spin-lattice relaxation time. Previously published work performed by Gowland et. al. (4) found that both T_1 and T_2 decrease with gestational age and with occurrence of PE (and IUGR). However, their study was performed *in vivo*, at 0.5 Tesla, and with lower spatial resolution. Current work on this project includes development of a fast (< 2min) T_1 mapping protocol so that these measurements can be repeated in the pregnant patient *in vivo*, and includes recruitment of a matched patient population.

References: (1) "Revised 1990 Estimates of Maternal Mortality: A New Approach by WHO and UNICED". *WHO*, Geneva, 1996. (2) SJ Fisher "The Placental Problem: Linking abnormal cytotrophoblast differentiation to the maternal symptoms of Preeclampsia" *Reprod Biol Endocrin* 2:53 2004 (3) MO Pulkkinen et.al. "Proton NMR Spectroscopy of the Phospholipids in Human Uterine Smooth Muscle and Placenta" *Gynecol Obstet Invest* 46:220-24 1998 (4) PA Gowland et.al. "In vivo Relaxation Time Measurements in the Human Placenta Using Echo Planar Imaging at 0.5T" *MRI* 16:241-47 1998

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