Assessment of longitudinal changes in placental transverse relaxation time in normal murine pregnancy using compartmental analysis

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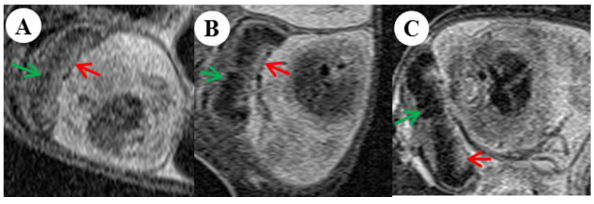
Introduction: The placenta is a highly vascularized organ that forms the interface between the mother and her fetus. A growing body of evidence supports the concept that various complications of pregnancy (e.g. intrauterine growth restriction, preeclampsia) may be the outcome of placental vascular underperfusion, hypoxia and/or ischemia. Magnetic resonance imaging (MRI) based tissue transverse relaxation (T2) parameter has been shown to correlate with micro-vascular perfusion status of tissue in humans [1]. Murine models of pregnancy are important means of studying and understanding the etiology of conditions due to their functional similarities with the human placenta [2]. Mice placenta consists of two major regions, the labryinth zone and the junctional zone. Commensurate with the developing fetus, there are marked changes in the placenta, and the different regions show differential development. Consequently, placental T2 relaxation parameter also changes with gestational age [3,4]. However, it is not known how the T2 properties of the individual placental regions, labyrinth vs. junctional zone, change with gestational age, and which part contributes primarily to the overall change in the T2 value of the placenta. In different placental pathologies, the labyrinth and the junctional zone regions get affected differently [5], and hence, knowledge of normal gestational age related changes in the T2 properties of these compartments is important.

Purpose: To quantify the longitudinal changes in T2 relaxation parameter with advancing gestational age in the different regions of the mouse placenta, and to study their relative contributions to the overall change in placental T2 parameter.

Methods: The study protocol was approved by the Institutional Animal Care and Use Committee (IACUC) of Wayne State University. Timed-pregnant CD-1 mice (n=9) were obtained from Charles River Laboratories (Wilmington, MA). Mice were scanned on a 7.0T, 20 cm bore superconducting magnet on gestational day (GD) 13, GD15 and GD17. Prior to image acquisition, the animals were sedated using isoflurane, and kept under anesthesia throughout the scan time. The MR scans consisted of (A) T2 – weighted turbo spin echo for anatomical evaluation and (B) Multi spin echo for T2 mapping. The T2 maps were generated by fitting the multiecho signal to a mono exponential function on a pixel by pixel basis. Pixels with poor fit were threshold to zero. A total of three free hand drawn region of interests (ROIs) were used to map the placenta, the labyrinth and the junctional zone, from which the mean and standard deviation of the T2 values were recorded. The labyrinth and junctional zones were manually segmented based on the signal intensity on the T2 weighted image at TE – 43.2 ms. It is to be noted that regions included in the labyrinth and junctional zone were conservative, and the sum of these two did not account for the total area of the placenta. However, the ROIs were proportional to the respective compartment sizes. The longitudinal changes in the placental T2 values were then statistically compared for differences using a single factor ANOVA test. A $p<0.05$ was considered statistically significant.

Results: A total of 9 mice were analyzed on all three days, which included 35 individual placentas on GD13, 36 placentas on GD15 and 36 placentas on GD17. Figure 1 shows placentas on GD13 (A), GD15 (B) and GD17 (C), and the visualization of the labyrinth and junctional zones. The average T2 value, measured across various placentas were significantly different across the gestational ages ($p < 0.0001$), and was 45.92 ± 4.12 msec (mean±standard deviation) on GD13, 42.19±6.60 msec on GD15 and 39.05 ± 1.65 msec on GD17. The standard deviations quoted here represent the variation of the measured T2 value from one placenta to another. Similarly, the average T2 measured across the labyrinth zone was 60.53 ± 3.98 msec on GD13, 59.85 ± 5.77 msec on GD15 and 56.63 ± 3.66 msec on GD17. The average T2 measured across the junctional zone was 40.45 ± 3.64 msec on GD13, 37.23 ± 5.67 msec on GD15 and 34.26.63 ±1.97 msec on GD17. Figure 2 plots the change with gestational age in T2 values of a) the overall placenta, b) the labyrinth and c) the junctional zones. A statistically significant ($p<0.0001$) change was seen in the placental T2 values of the junctional zone between GD13 and GD17.

Discussion and Conclusion: The T2 relaxation parameter of the placenta decreases as a function of the gestational age and the development of the fetus. This is in agreement with what was seen in the human placenta and has also been reported in mice [3,4]. Furthermore, we show that while a longitudinal change in the T2 values is seen in both the labyrinth and junctional zones, it is the change in the size and the T2 value of the junctional zone that appears to drive the overall decrease in placental T2 with gestational age. The T2 value of the labyrinth zone mostly remains constant. This longitudinal study establishes the baseline T2 values of these compartments for GD13, GD15 and GD17, the knowledge which is important for the investigation of T2 parameter differences in various placental pathologies.



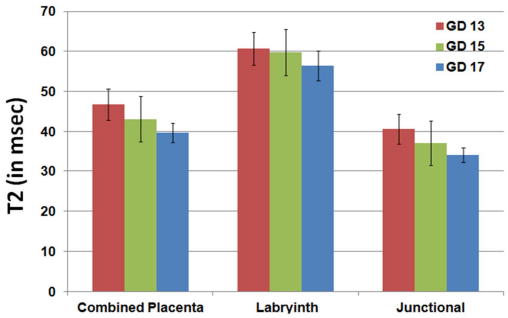


Figure 1. T2 weighted images showing the placenta and the corresponding fetus (A: GD13, B: GD15, C: GD17). The regions composing the placenta are marked: green arrows – junctional zone, red arrows - labryinth zone.

References:

[1] An, H., et al., Stroke, 2009; [2] Georgiades, P., et al., Placenta, 2002; [3] Krishnamurthy U.,et al., ISMRM 2013; [4] Wright, C., et al., Placenta, 2011;[5] Bobek G., et al., PLoS ONE, 2013.