**Placental H-scan Sonography Demonstrates Feasibility of an Ultrasound-Based Method for Generation of a Placental Biomarker**

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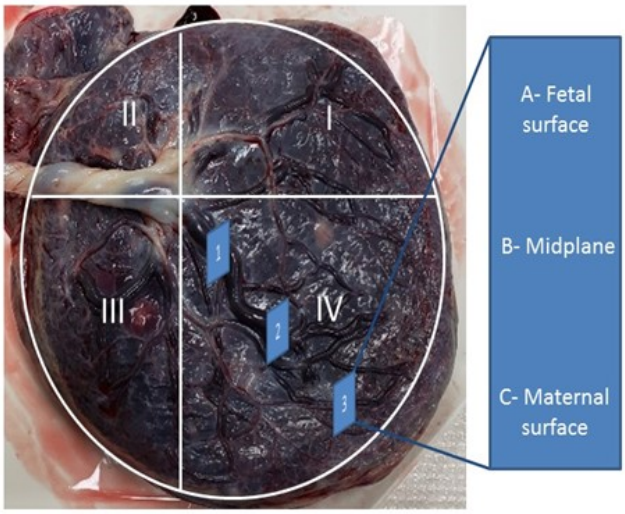
**Objective:** To demonstrate the validity of H-scan— a sonographic method of quantifying scattering associated with tissue microstructure and displaying the results as a colormetric overlay to the standard B-mode image — as a novel method of quantifying the scattering sites within the placentae. Our goal is to identify easily reproducible, direct, and non-invasive, placental biomarkers based on H-scan imaging to detect and predict placenta-related disease.

**Study Design:** Prospective, descriptive cohort study of unselected women presenting for obstetric care at a tertiary medical center. Patients enrolled antenatally for post-delivery placental collection and ex vivo ultrasound on Siemens S3000 research platform with acquisition of raw acoustic echos and post-processing to generate H-scan images. Raw RF data were acquired in triplicate with the placenta in a water bath at physiologic temperature over a variety of acquisition conditions. H-scan results were compiled to describe the range of measurements within and between placentae and to generate a three dimensional map of placental H-scan measurements.

**Results:** 14 term patients enrolled for *ex vivo* placental ultrasound with 36 regions analyzed in triplicate across 4 assigned quadrants in 3 acquisition conditions representing a total of 1294 RF sequences. Excellent precision was demonstrated in all acquisition conditions however the heterogeneity of the placental tissue is apparent in the high level of intraplacental variability (Figure 1). The percentage of smaller scatterers was also quantified across and between radial circumferences (Figure 2).

**Conclusion:** H-scan quantification of placental tissue demonstrates high precision with serial sampling across a variety of acquisition strategies including with artifact modeling conditions of antenatal assessment. While intra-placental variability was pronounced, radial ratios across zones demonstrate potential for within tissue correction. Both the precision and ability to generate this quantification from the B-mode RF signal support the feasibility of our novel imaging with H-scan as a placental biomarker.

## Figure 1: Precision and Intraplacental Variation Across Acquisition Strategies Demonstrated by Standard Error of the Mean (SEM)




**Acquisition Strategies**

| 1: Ideal | 2: Handheld | 3: Abdominal Phantom |
|---|---|---|
| Mounted and stabilized probe with unobstructed characterization of tissue | Examiner may inadvertently deform tissue, introduces probe movement artifact | Uses an abdominal phantom to models tissue obstruction and deformation in addition to handheld variability |

**Precision**

| | Acquisition Strategy | | |
|---|---|---|---|
| | 1: Ideal | 2: Handheld | 3: Abdominal Phantom |
| Range of SEM | 0-0.92 | 0-0.7 | 0-0.69 |
| SEM<0.5 | 97% | 99.26% | 96% |
| SEM <0.25 | 91.84% | 94.85% | 93.65% |
| SEM <0.1 | 90.48% | 88.97% | 92.86% |
| SEM <0.05 | 87.76% | 71.32% | 85.71% |

*N=3 per ROI*

**Intraplacental Variation**

| | Acquisition Strategy | | |
|---|---|---|---|
| | 1: Ideal | 2: Handheld | 3: Abdominal Phantom |
| Range of SEM | 0.07-1.05 | 0.04-1.1 | 0-0.86 |
| SEM<0.5 | 67% | 77% | 72% |
| SEM <0.25 | 10.26% | 49% | 23% |
| SEM <0.1 | 5.13% | 12.82% | 12.82% |
| SEM <0.05 | 0.00% | 5.13% | 7.69% |

*N=12 per ROI*

## Figure 2: H-Scan Small Scatter Percentage Across the Surfaces and Depths of the Human Placenta in A Variety of Acquisition Conditions

**Small Scatter Percentage**

| | Acquisition Strategy | | |
|---|---|---|---|
| | 1: Ideal | 2: Handheld | 3: Abdominal Phantom |
| Proximal to the Cord Insert (Zone 1) | 56.52% ± 2.77% (0.23) | 54.32% ± 2.86% (0.25) | 52.51% ± 2.65% (0.23) |
| Mid-Circumference (Zone 2) | 56.59% ± 3.00 (0.25) | 54.43% ± 2.92 (0.26) | 52.54% ± 2.68 (0.24) |
| Marginal (Zone 3) | 56.46% ± 3.24% (0.27) | 56.67% ± 3.41% (0.31) | 52.62% ± 2.89% (0.25) |
| Ratio Zone 3:1 | 0.999 ± 0.042 (0.003) | 0.989 ± 0.046 (0.004) | 1.011 ± 0.066 (0.014) |
| Ratio Zone 2:1 | 1.002 ± 0.036 (0.003) | 1.002 ± 0.0294 (0.003) | 1.012 ± 0.042 (0.009) |
| Ratio Zone 2:3 | 1.003 ± 0.040 (0.003) | 1.015 ± 0.044 (0.004) | 1.006 ± 0.084 (0.017) |

*N=130 per ROI; Mean ± STD (SEM)*