

RESEARCH QUESTION

- Are there **Placental Chorionic Surface Vascular Network (PCSVN)** features that distinguish placentas of increased risk for ASD from those in the general population?

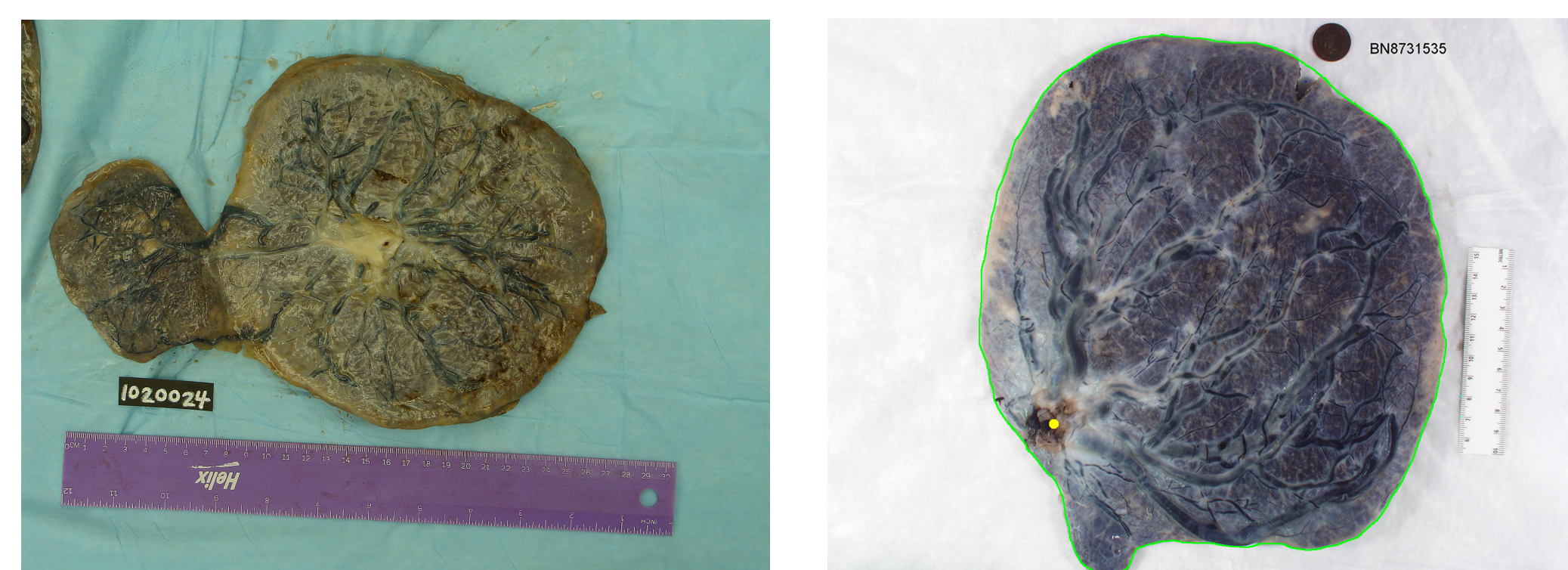


Figure: Sample images of Early Autism Risk Longitudinal Investigation (EARLI) & National Children's Study (NCS) placentas.

DATA SET

- 89 EARLI placentas.** EARLI is an autism enriched-risk pregnancy cohort that focuses on the prenatal and early life periods of children who have biological siblings already diagnosed with ASD. **HIGH RISK** for ASD.
- 201 NCS placentas.** NCS is a population-based cohort with pregnancies at unknown risk for ASD. **LOW-RISK** for ASD.
- 8 shape-related, 28 arterial, and 28 venous PCSVN features were computed.
- Results only on the arterial network due to a higher level of precision and accuracy.

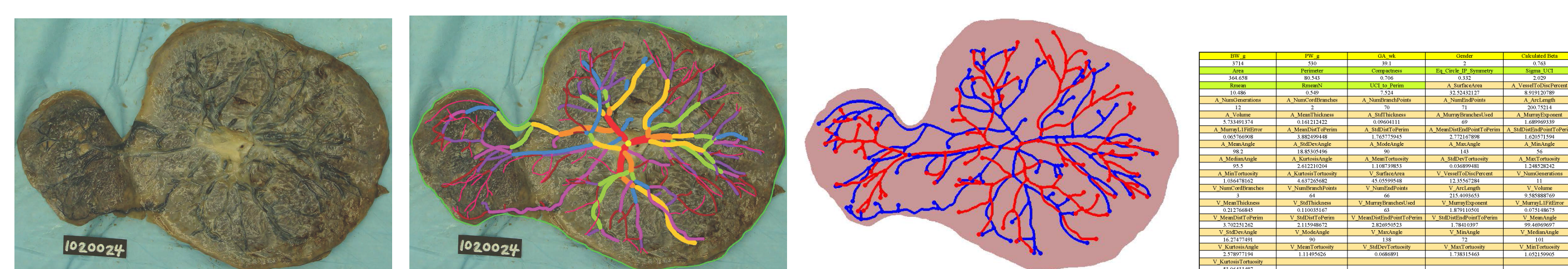


Figure: Left to right: (A) raw EARLI placenta. (B) traced image of (A). (C) skeletonisation graph of (B). (D) PCSVN values obtained from (C).

METHODS & RESULTS

Step 1: Boruta Algorithm: Select all-relevant PCSVN features

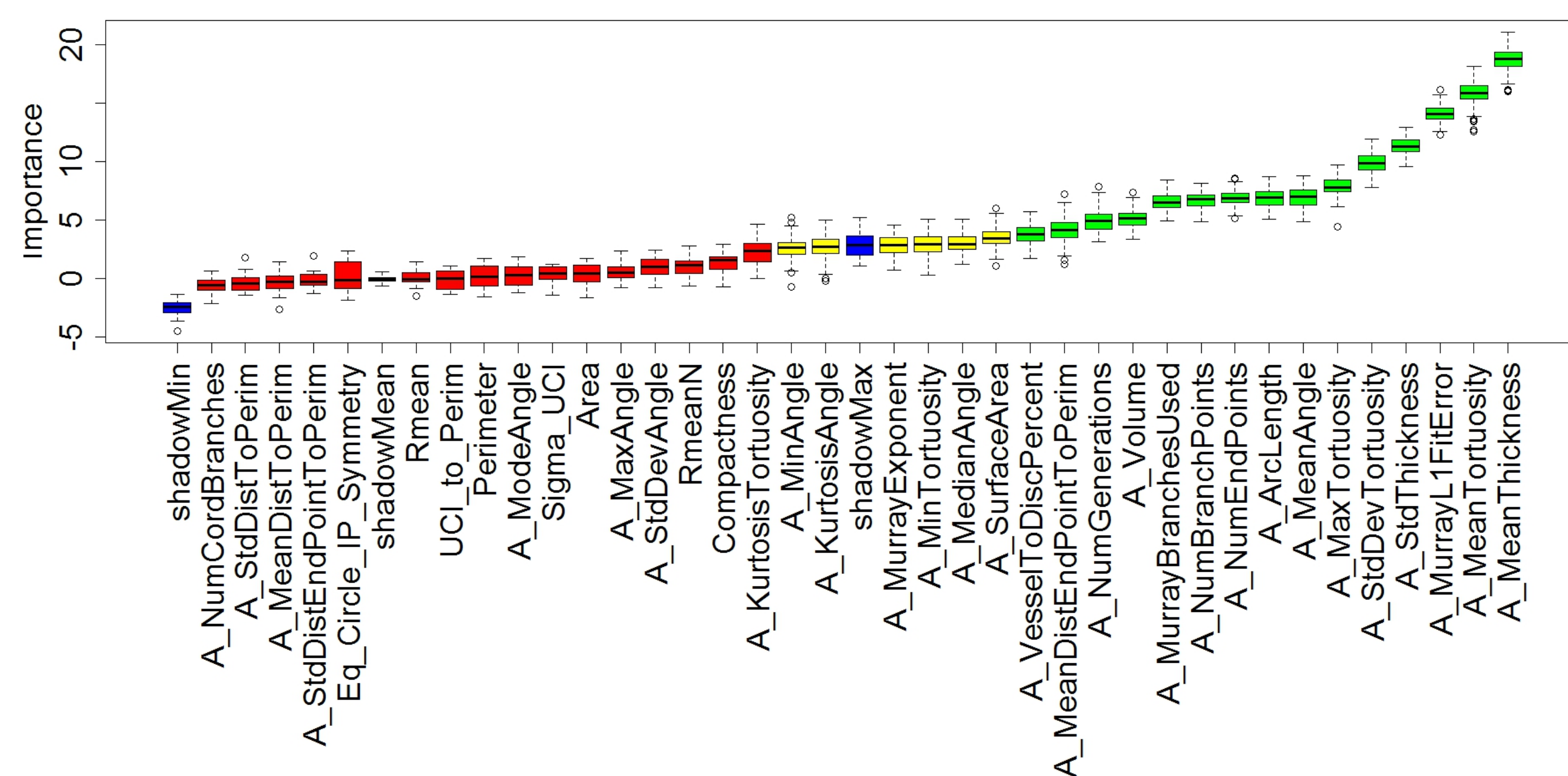


Figure: Importance scores (vertical axis) for each of the arterial vascular features (horizontal axis) returned by the Boruta algorithm.

METHODS & RESULTS

Step 2: Principal Component Analysis (PCA): Identify groups of biological effects of villous growth in different ASD risk categories

Boruta Ranking	Vessel Features	PC1	PC2	PC3	PC4	PC5
1	A_MeanThickness	-0.1582	-0.4747	0.1035	0.0651	-0.0089
2	A_MeanTortuosity	0.0002	0.0575	0.5347	-0.0979	0.0013
3	A_MurrayL1FitError	-0.256	-0.3903	0.0438	0.0139	0.0397
4	A_SidThickness	-0.1566	-0.4762	0.0701	-0.0046	0.0196
5	A_SidDevTortuosity	0.0029	0.0812	0.5912	-0.0641	0.1449
6	A_MaxTortuosity	0.0948	0.0724	0.5459	-0.0264	0.1709
7	A_MeanAngle	-0.0611	0.0704	0.2028	0.2135	-0.936
8	A_NumEndPoints	0.4251	-0.0298	-0.0132	0.0153	-0.005
9	A_ArcLength	0.3773	-0.1259	-0.0035	-0.0163	0.0116
10	A_NumBranchPoints	0.4254	-0.0301	-0.0125	0.0146	-0.0038
11	A_MurrayBranchesUsed	0.4254	-0.0301	-0.0125	0.0146	-0.0038
12	A_Volume	0.1444	-0.4823	0.065	0.0502	-0.0368
13	A_NumGenerations	0.3182	-0.0237	0.014	0.2178	-0.0619
14	A_MeanDistEndPointToPerim	0.0055	-0.0323	0.0545	0.905	0.2124
15	A_VesselToDiscPercent	0.255	-0.3502	0.0031	-0.2561	-0.1457

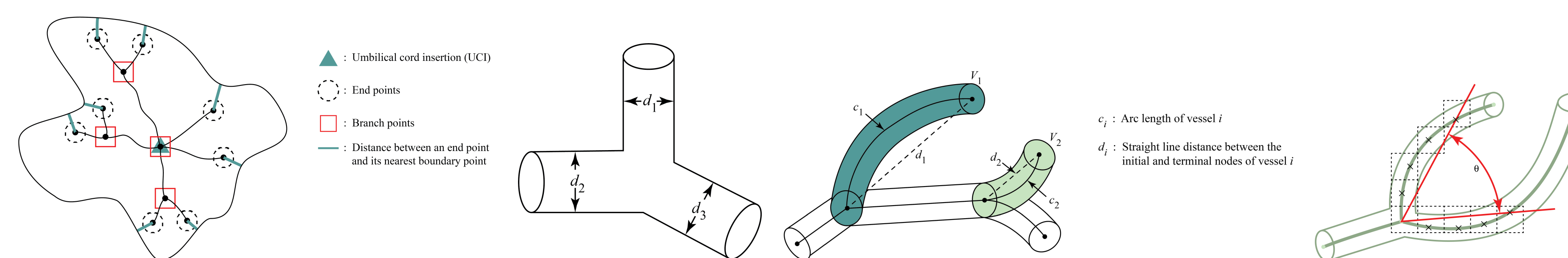
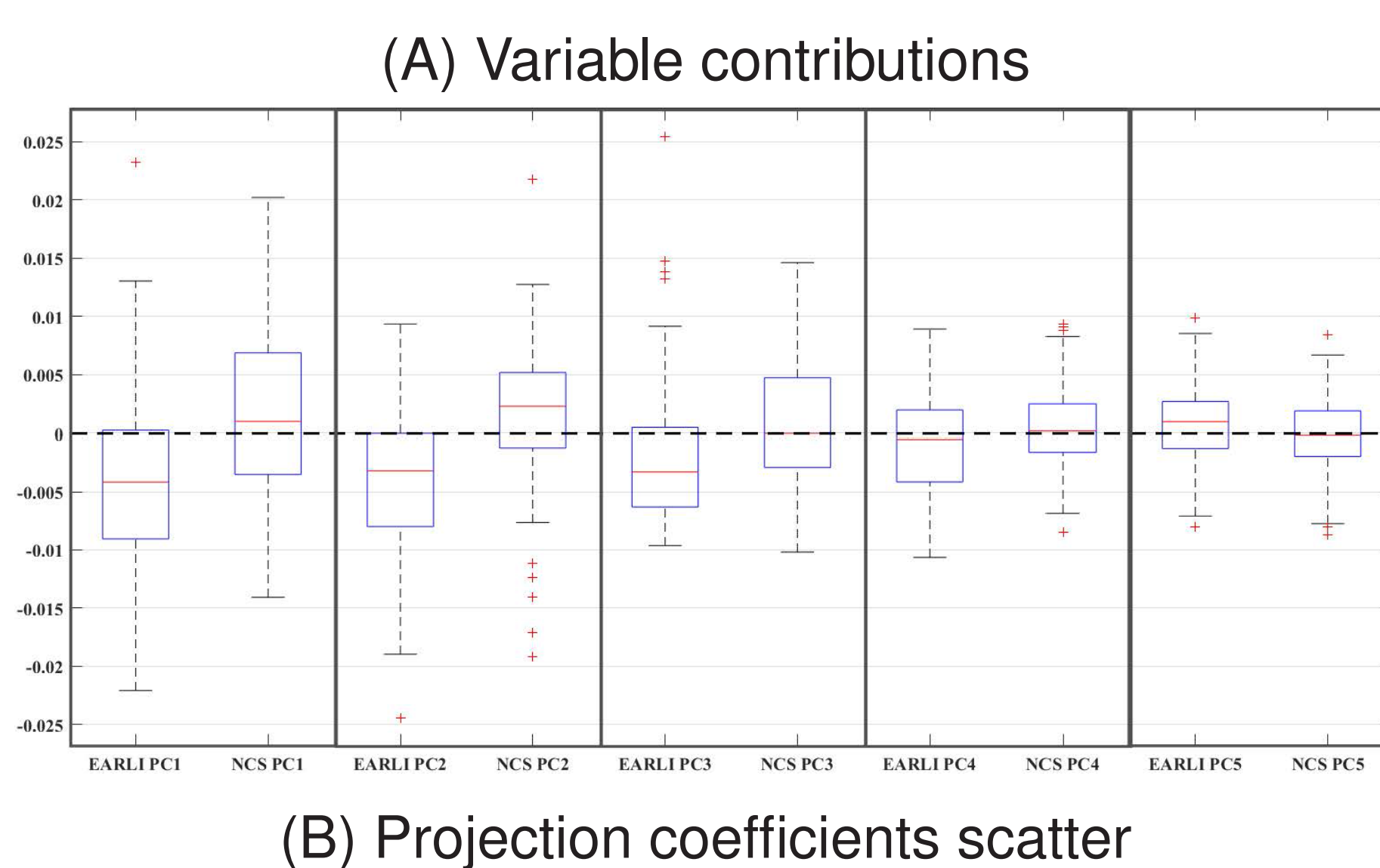
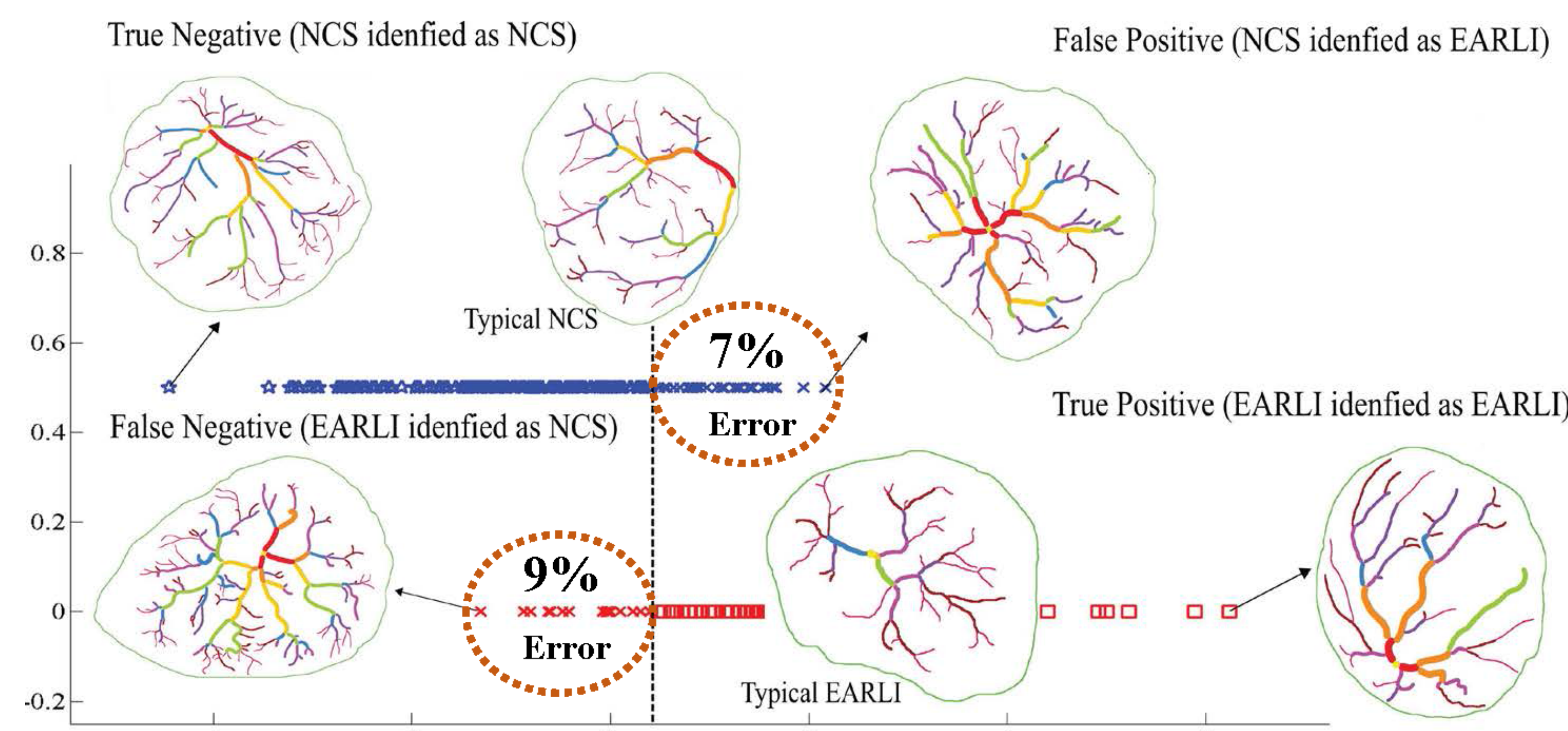


Figure: Visual definitions for the five principal features.

Step 3: Linear Discriminant Analysis (LDA) with 10-fold cross validation: Produce classification statistics



DISCUSSIONS

- The difference in high and low ASD risk is better explained by the vascular features alone.
- PCSVNs associated with placentas of high-risk ASD pregnancies generally had **fewer branch points, thicker and less tortuous vessels, better extension to the surface boundary, and smaller branch angles** than their population-based counterparts.
- A major contribution of our work is **the creation and validation of a model to discriminate placentas associated with children in a high-risk ASD group against a population of unknown ASD risk based on automatically selected PCSVN features.**
- Our work can potentially be used to **establish a hierarchy of importance** when studying the connection between various environmental/genetic factors and fetal outcomes as reflected in the PCSVN geometry.
- Questions to ask next: **what environmental or genetic factors cause this group of 5 parameters to vary together and whether these variables stabilize in their permanent state early in gestation.**
- Searching for the types of geometric signatures that are measurable and capable of providing **accurate readings in 3-dimensional imaging environment** is going to play a vital role in early risk assessment and intervention for ASD.
- The study presented here should motivate **a pursuit of additional PCSVN features** which might be correlated with various dichotomous health outcomes as long as information on outcome classification is available.
- We anticipate that **some PCSVN features will be correlated with outcomes** such as diabetes and obesity or other "fetal origins" disorders, including autism and schizophrenia, once **reliable and automated vessel extraction methods are established** to allow analysis of PCSVNs in large cohorts.

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