Early Predictors of FASD
&
General Health of Children and Young Adults with PAE

PAE and Nailfold Capillary Morphology in Children Aged 3–17 Years: Preliminary Results

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Learning Objectives

1. Understand how a simple, painless fingertip test that reveals tiny blood vessels may signal long-term health risks.

2. Recognize early physical signs linked to PAE, detectable in children as young as age 3, before potential disease develops.

3. Discover how early detection could lead to better monitoring and support for children and families affected by PAE or FASD.

Background

- **Adults with FASD or PAE experience higher rates of chronic conditions**—e.g., hypertension, diabetes, obesity, hypercholesterolemia, and autoimmune disorders.
- **Early signs of these adult diseases → detected in children and adolescents with PAE → accelerated risk trajectories** compared to unexposed peers.
- However, **biomarkers that allow individuals with FASD to be stratified based on these risks remain unidentified**.

Sub-Study Purpose

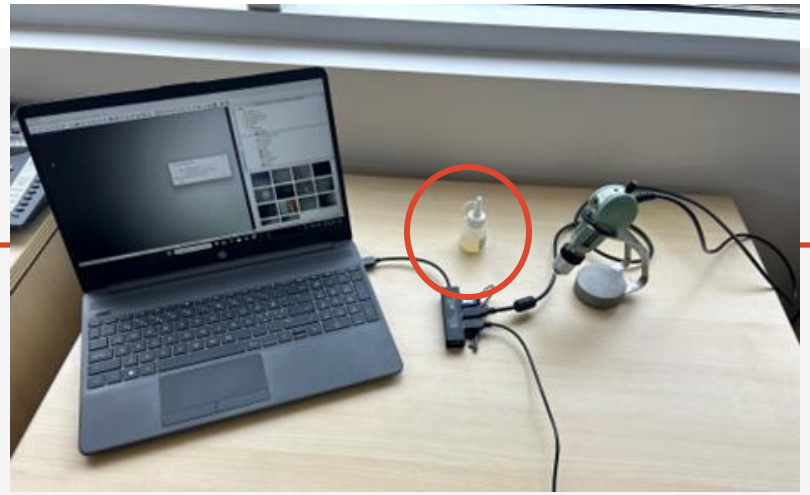
Examine whether children with PAE show indicators of clinical or subclinical vascular and metabolic compromise by assessing differences in structural microvasculature, including alterations in nailfold capillary morphology.

→ Nailfold Capillaroscopy Changes as a Potential Biomarker of Cardiometabolic Risk in Children with PAE.

Experimental evaluation using **quantitative and qualitative** assessments of nailfold capillaries → characterize patterns in **shape, density, width, and inter-capillary distance** → signal early microvascular changes.

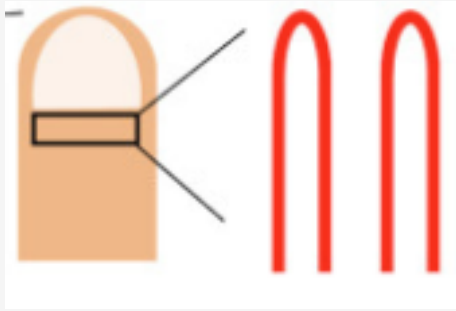
Identifying these early patterns (e.g., microvascular alterations) in children with PAE may support timely pediatric screening and prevention strategies, potentially mitigating long-term health risks.

Nailfold Capillaroscopy – What is this?



- **Nailfold Capillaroscopy → non- invasive** microscope with a larger magnification lens coupled with a digital video camera and a laptop for data encoding and analysis → **provides a window into the digital microcirculation.**

- The child removes fingernail polish + wash hands.
- Hands flat on the table.
- Drops of vegetable oil (e.g., cedar oil) are placed on 3 fingers (not thumbs) to reduce light reflection.



Nailfold Capillaries

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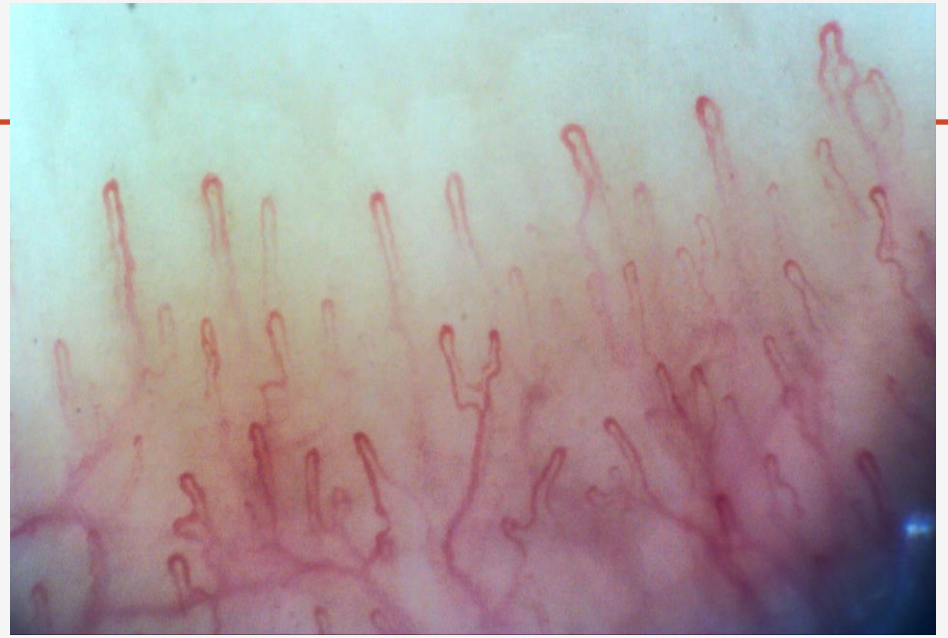
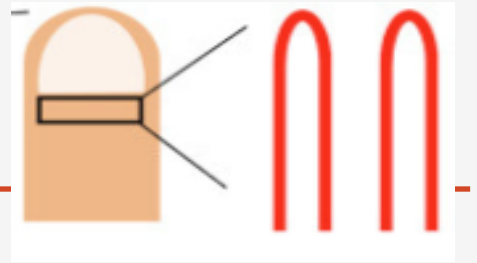
FASD United



Examples that were not successful ⊗

Nailfold Capillaroscopy - Background

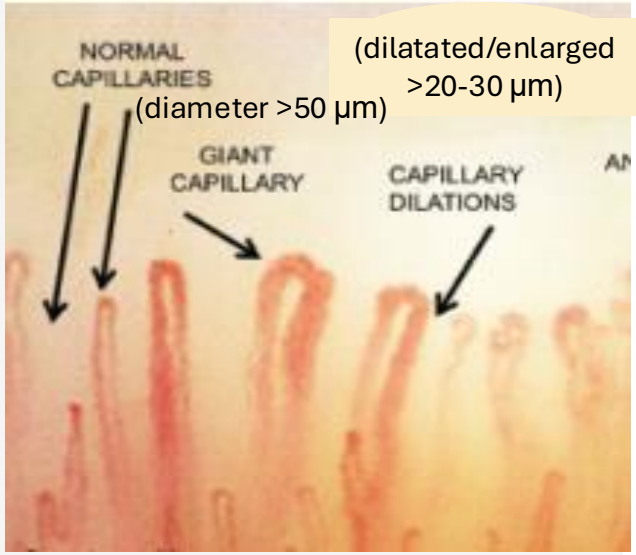


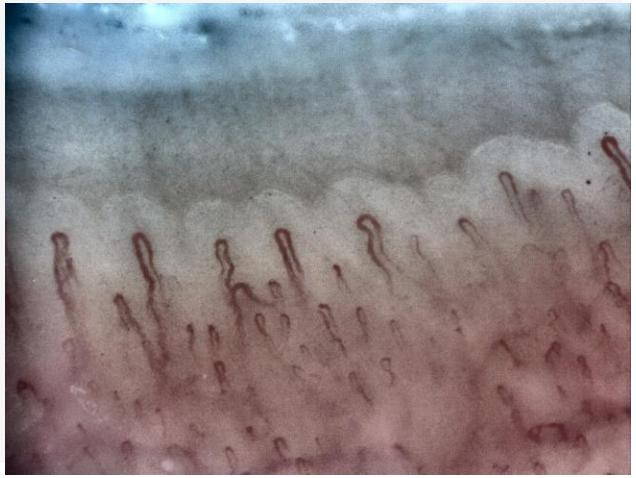
- **Reduced density + larger capillaries → pre-hypertension, metabolic conditions** (e.g., obesity and diabetes), **inflammation, and autoimmune conditions** (e.g., systemic sclerosis) in **adults**, less is known about the microvasculature in individuals with FASD.

- Primary use in **pediatric** populations → **rheumatologic disorders** (e.g., **lower density and higher dilatation**).

- **Nailfold capillaries changes → life factors and behavioral characteristics →** poor diet, smoking, sleep deprivation, and psychological stress → contribute slow blood flow (e.g., twisted loops, lower density).

- No norms for adults or children → **Only thresholds** (i.e., < 7 caps/mm) **defined as abnormal/deviant in adults.**
  → There is **not** an agreement upon threshold **for children**, as the use in children is much more limited.





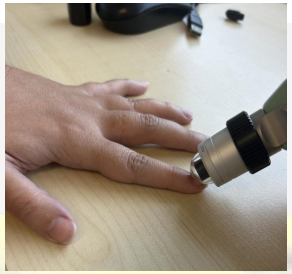
Methods

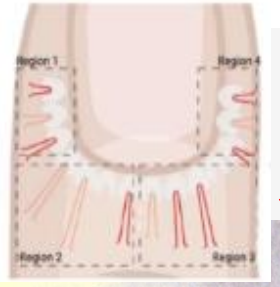
Measures

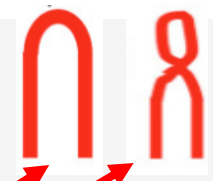
Microvascular structure in nails:

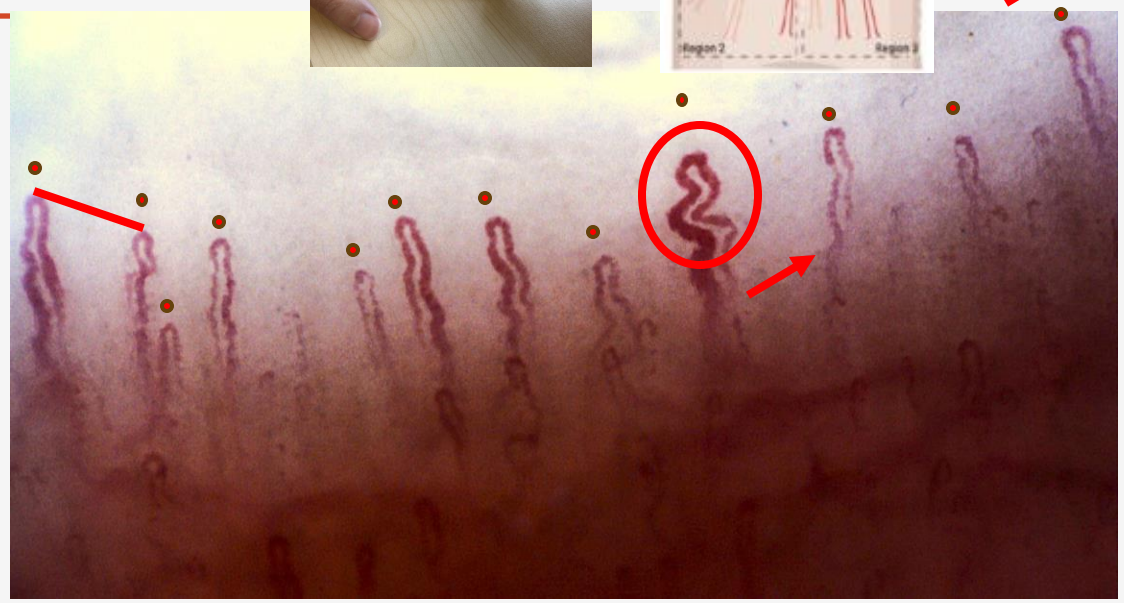
- Overall Capillary density
- Average Width
- Inter-capillary distance
- Morphological abnormalities:
  - Enlarged
  - Branched
  - Crossed
  - Multi-crossed
  - Broken

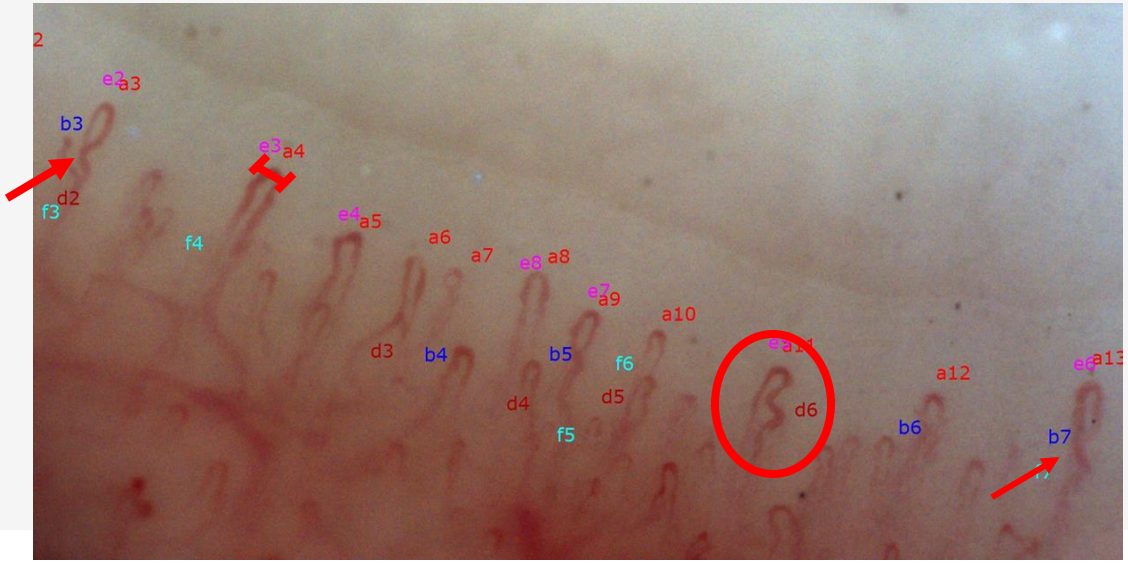
Inter-rater (2 raters) agreement across capillary metrics (>0.80).











Preliminary Results

Sample Characteristics

Main study-UCSD and Emory N~200.
120= PAE and 80= no/minimal PAE
(age 3-17 years old).

N=37: n=27 PAE and n=10 Controls

	PAE n=27 N (%)
FAS	1 (3.7%)
Partial FAS	4 (14.8%)
ARND	7 (25.9%)
PAE	15 (55.5%)

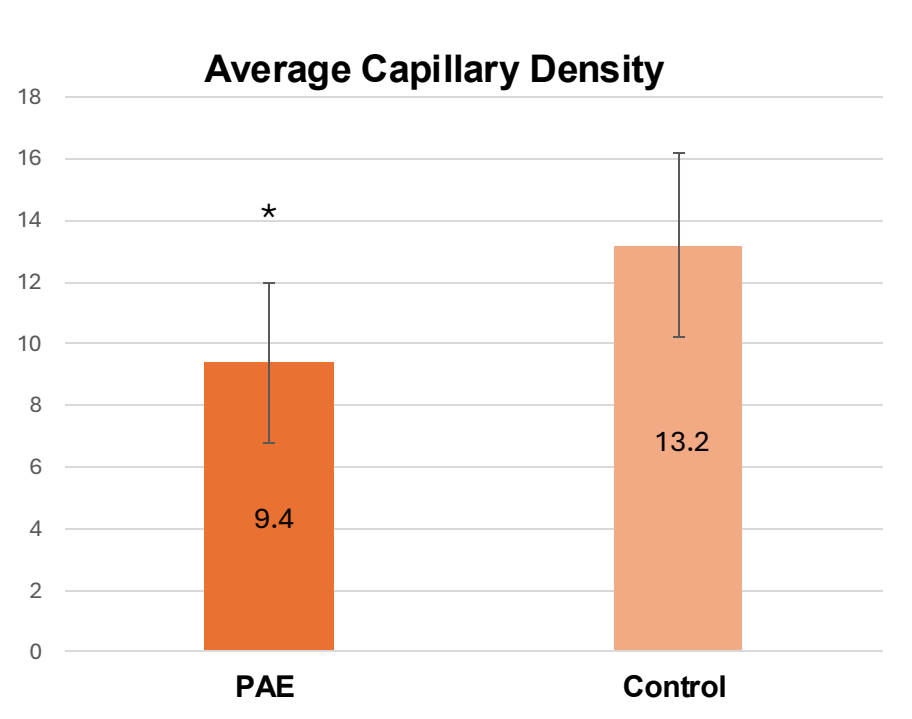
Drs. Jones and/or Del Campo diagnoses/referrals
(+ Caregiver Interview Questions)

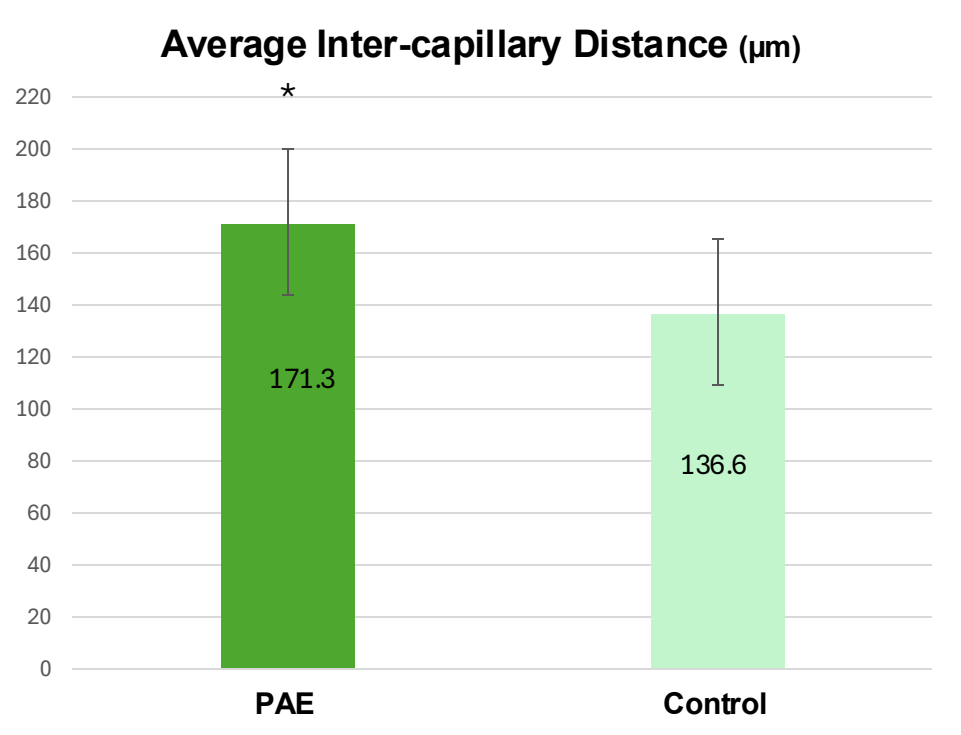
Table 1. Participant Sociodemographic Characteristics by Prenatal Alcohol Exposure (N= 37).

	Prenatal Alcohol Exposure n=27	No Prenatal Alcohol Exposure n=10
	Mean (SD)	
Age	8.3 (4.0)	11.2 (4.7)
Sex	n (%)	
Female	13 (48%)	5 (50%)
Male	14 (52%)	5 (50%)
Race		
White	19 (70%)	7 (70%)
Asian	2 (7%)	0 (0%)
Native American	3 (11%)	2 (20%)
More than one	1 (3.7%)	1 (10%)
Other	2 (7.41%)	0 (0%)
Ethnicity		
Hispanic	18 (67%)	4 (40%)
Non-Hispanic	9 (33%)	6 (60%)

https://www.mayoclinic.org/diseases-conditions/fetal-alcohol-syndrome/diagnosis-treatment/drc-20352907

Preliminary Results





-Children with PAE (mean age 8.3 yrs) had **lower** capillary density than controls (mean age 11.2 yrs) — an interesting finding, as younger children are expected to have *higher* density.

⇩

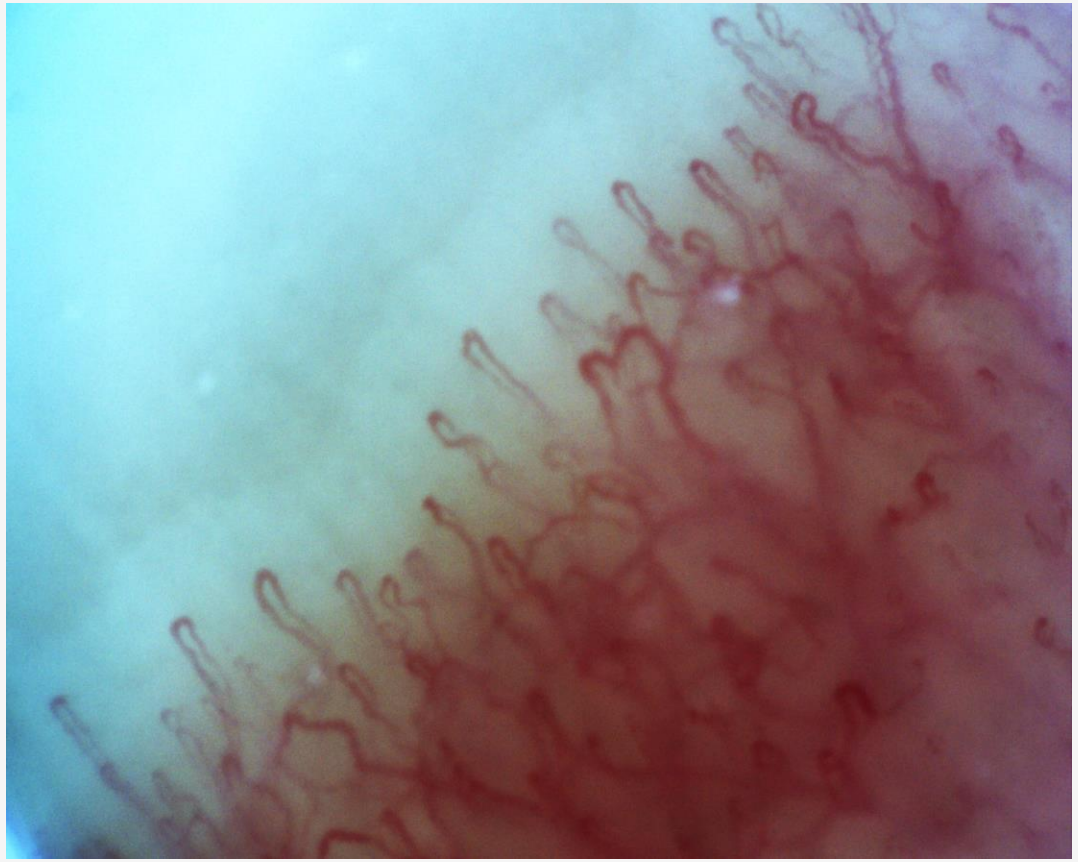
-Age showed a negative association with density ($p = 0.045$), density decreases with increasing age.

(NOTE: Bars show unadjusted means, also tested using adjusted regression models and results remained significant. Residual diagnostics confirmed normality assumptions; sensitivity analysis conducted where necessary).

Examples PAE vs Control

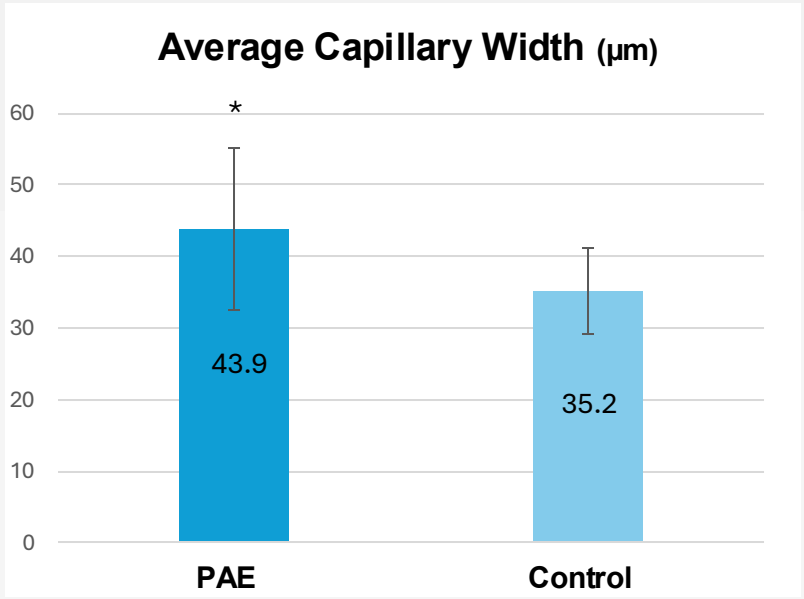
PAE

(lower density)

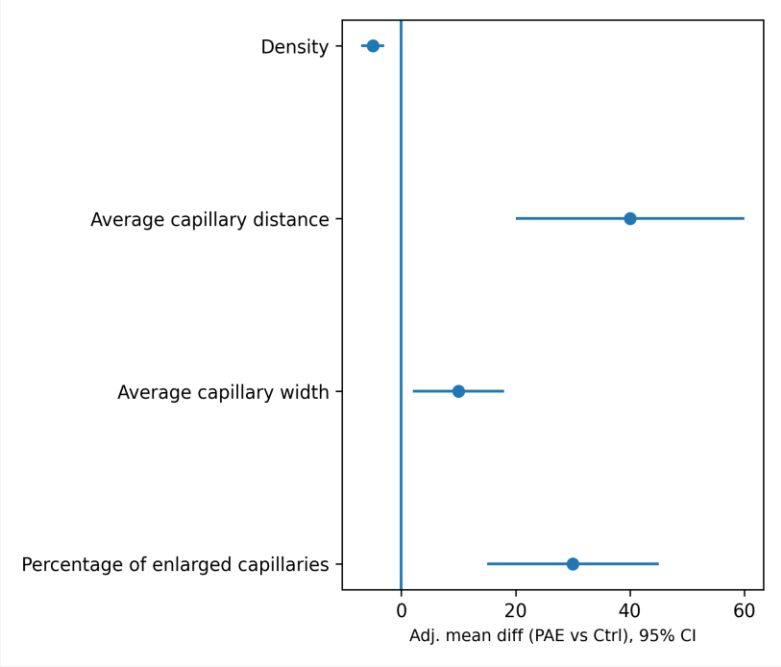


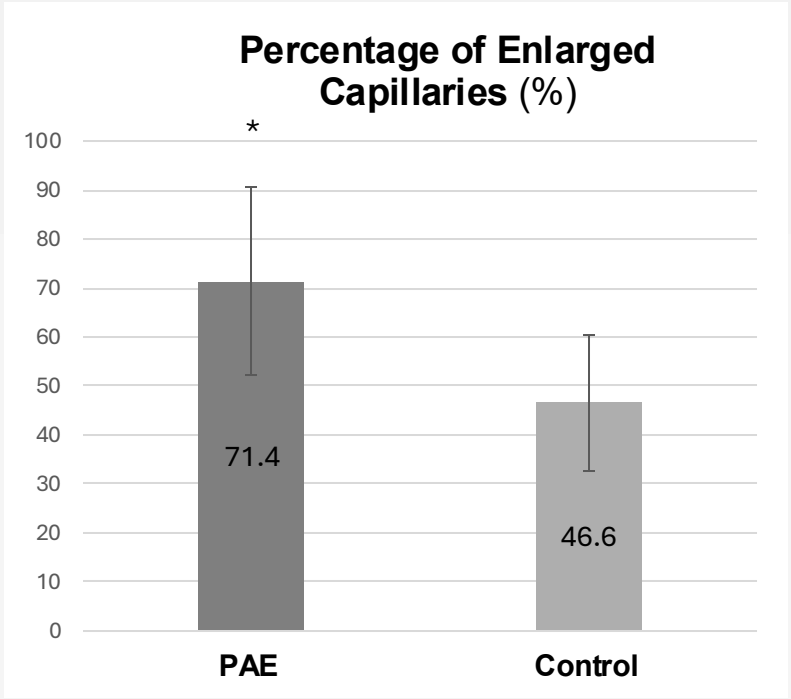
Control

Preliminary Results



-Child's sex was associated with width (p = 0.012), with females exhibiting wider capillaries overall.





-Linear regression models estimating adjusted mean differences in capillary morphology associated with PAE (adjusted for age and sex). Points represent β coefficients with 95% confidence intervals.

Preliminary Results

Other morphological indicators did not differ significantly between groups.

Table 3. Capillary Morphology Within Each Participant by Prenatal Alcohol Exposure (N = 37)		
	Prenatal Alcohol Exposure n=27	**No Prenatal Alcohol Exposure n=10**
	Mean of individual level proportions (SD)	
Broken	37.4% (21.8)	26.0% (15.5)
Branching	27.5% (18.9)	20.8% (17.1)
	Median of individual level proportions (IQR)	
Crossed loops	18% (11.1-38.5)	26% (0.0-33.3)
Multi-crossed	0.0% (0.0–0.0)	0.0% (0.0–0.0)
Note: Values represent the average percentage of capillaries per participant that displayed each morphological characteristic (e.g., branched, crossed).		

Discussion

KEY FINDING: Children with PAE show **lower density, greater inter-capillary distance, wider** and more **enlarged** capillaries.

EARLY BIOMARKER POTENTIAL

Microvascular differences may serve as **early indicators of physiological alterations in children with PAE** and merit further investigation as **potential biomarkers** of cardiovascular or metabolic risk (e.g., pre-hypertension).

TRANSLATIONAL POTENTIAL

They may also have **translational potential** for future screening in general practice using this **simple and non-invasive** method.

Findings can lead to recommendations for clinical assessments, as well as early interventions in children or adolescents with FASD to help prevent progression of potential disease.

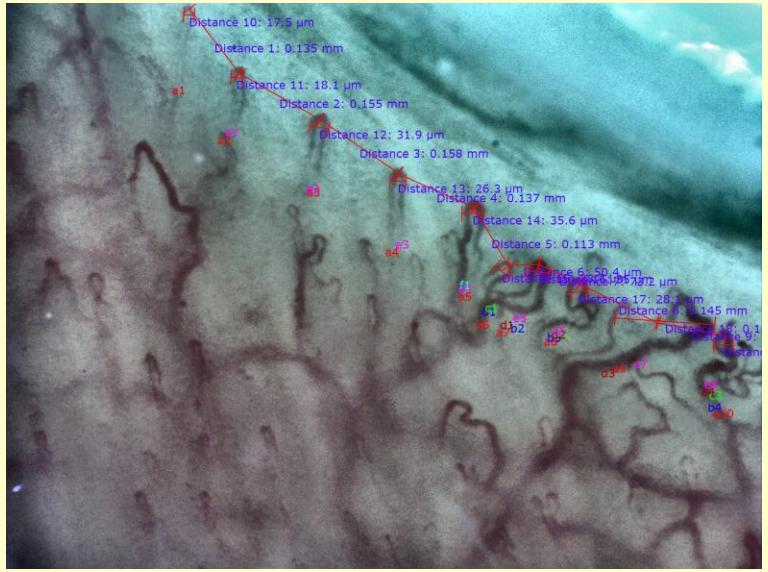
Discussion

Future work

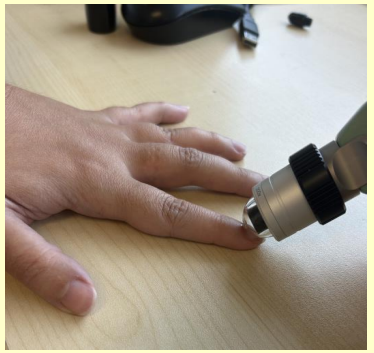
- Examine associations/correlations with:
  - Blood pressure
  - Blood lipids
  - Life factors: sleep, physical activity, diet
  - Growth measures (e.g., children size, BMI)
- Expand findings across the diverse multi-site samples Emory + UCSD
- Compare with adult populations
- Possibly transitioning to automated analysis (could facilitate large-scale prospective studies using capillaroscopic parameters as possible biomarkers of chronic diseases)

LIMITATIONS: Small sample, currently n=70; findings are preliminary. Microvascular differences may reflect other unmeasured influences (e.g., genetics, postnatal environment, life factors/habits, fingertip temperature).

Thank you!



PAE



No PAE

Funded by NIAAA and conducted within the CIFASD consortium.

Alcohol Screening – Caregiver Questions

1. Before your child was born, were they exposed to any alcohol during the pregnancy?

Yes *No Suspected Don't Know

*If No, stop here.

If yes, please indicate when and approximately how much you estimate was consumed:

	Any Alcohol at all? **Yes, No, Suspected, DK**	How many *drinks on a typical day when drinking?	How many *drinks per week?
In the month before conception			
1st Trimester			
2nd Trimester			
3rd Trimester			

*By "drink", we mean a 12 ounce can or glass of beer or cooler, a 5-ounce glass of wine, or a drink containing 1 shot of liquor (such as vodka, tequila, whiskey, or gin).

***Only* IF #1 is Yes or Suspected:**

1. Has your child ever been diagnosed with a Fetal Alcohol Spectrum Disorder, such as Fetal Alcohol Syndrome (FAS) or Alcohol-related Neurodevelopmental Disorder (ARND)?

Yes No Unsure

If yes, what was the diagnosis? _____

Normality Assessment

- Normality of all outcome distributions was assessed using both graphical and formal methods. Visual inspection of histograms and Q–Q plots was complemented by four formal tests: **Shapiro–Wilk, Kolmogorov–Smirnov, Cramér–von Mises, and Anderson–Darling.**

- Three outcomes, Density, Percentage Enlarged, and Capillary distance, met normality assumptions. All formal tests were non-significant ($p > 0.05$) and visual inspection confirmed approximate symmetry in each case.

- **Width** was the only outcome showing deviation from normality ($p < 0.01$), with right skew observed particularly in the exposed group. **Residual diagnostics from the linear regression** model identified this violation as driven by a **single outlier** (Cook's $D > 1$), rather than a distribution problem.

- -A **sensitivity analysis** was conducted excluding the outlier. Results were comparable to the primary analysis ($\beta = -8.06$, $p = 0.013$), confirming robustness. Given this finding, Width was retained on its original scale without transformation.

Preliminary Results

Table 2. Participant Nailfold Microvascular Characteristics by Prenatal Alcohol Exposure (N= 37).			
	Prenatal Alcohol Exposure n=27	**No Prenatal Alcohol Exposure n=10**	**p-value**
	Mean (SD)		
Capillary density	9.4 (2.6)	13.2 (3.0)	p < 0.001
Average Capillary distance	171.3 (28.9)	136.6 (27.3)	p < 0.01
Average capillary width	43.9 (11.4)	35.2 (6.1)	p < 0.01
Percentage of enlarged capillaries	71.4 (19.1)	46.6 (13.8)	p < 0.001

Table 2. 1 Adjusted associations between prenatal alcohol exposure and vascular outcomes (N = 37)	
Outcome	**β (95% CI)**
Density	−4.43 (−6.46, −2.40), p < 0.001
Average capillary distance	38.18 (16.01, 60.36), p < 0.01
Average capillary width	9.87 (2.24, 17.51), p < 0.01
Percentage of enlarged capillaries	28.17 (14.09, 42.25), p < 0.001
NOTE: All models adjusted for age (continuous) and sex. Reference group: control (No PAE).	

Discussion

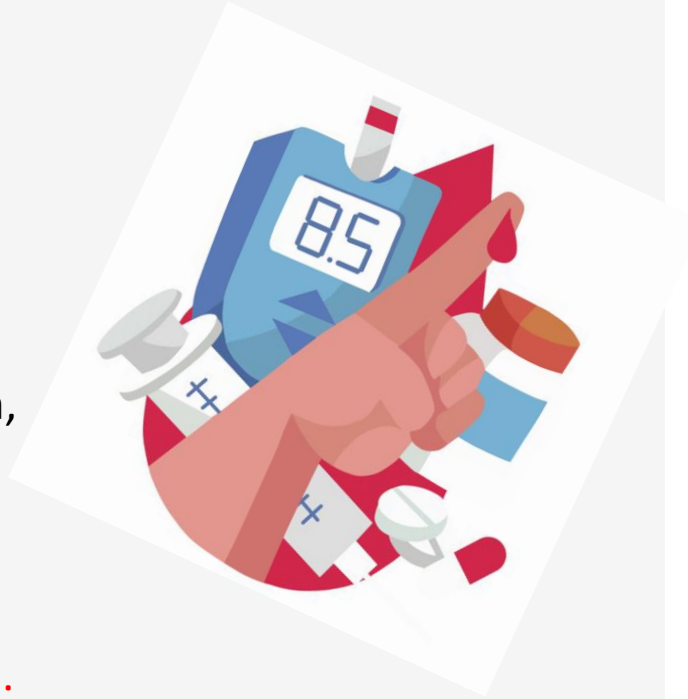
What this means for families and communities?

1. This painless, minutes-long, non-invasive test could give **families and doctors** an early heads-up before any potential disease appears.
2. **For individuals with FASD and families**: it shifts the focus from treating problems to preventing them through early care and support— starting in childhood.
3. **For communities and policymakers**: it supports the case for early screening and continued health monitoring in children with PAE, so support reaches families long before potential complications arise.

Early Predictors of FASD – Main Study

Continues the work started in Ukraine.

Other Clinical Visit Components (single session):



- 9 health questionnaires for parent/guardian (dietary intake/eating habits, physical activity, sleep, anxiety, depression and adverse childhood experiences).
- Physical exam of the child by study Pediatrician (growth measures, blood pressure, hearing/vision screening).
- Blood sample (glucose, lipids, blood count, hemoglobin A1C, C-reactive protein, iron, thyroid levels, miRNAs, telomeres and cytokines), saliva sample, tooth sample.
- NIH-Toolkit (cognitive assessments).
- 3D facial images.
- Nailfold capillaroscopy (non-invasive imaging with high-resolution video microscope; Optilia Instruments, Sweden). → TODAY'S PRESENTATION

EXTRA Preliminary Results, Presented at RSA 2025

PAE (n=22), we did not have controls at that time, and we also do not yet have the pediatric clinical data (e.g., blood pressure, blood lipids) ready for analysis for our updated n=37/n=70 samples.

- A significant positive correlation was observed between diastolic blood pressure and capillary width (ρ = 0.53, p = 0.014).

- Capillary width was also positively correlated with triglyceride levels (ρ = 0.50, p = 0.028).

- In an age-adjusted linear regression model, diastolic blood pressure was significantly associated with capillary width (β = 1.04, SE = 0.35, p = 0.008), indicating that each 1 mmHg increase in diastolic BP corresponded to a 1.04 μm increase in capillary width. Age was not a significant predictor (p = 0.26). The model explained 33% of the variance in capillary width (R^2 = 0.33).

Discussion: These preliminary findings suggest that **nailfold capillary width may reflect underlying cardiovascular and metabolic status in this sample of participants with PAE**. As the study progresses, the inclusion of unexposed comparison children will allow us to better clarify differential risk.