GENT253

Fetal Fraction Amplification Yields Sufficient Fetal Fraction to Enable cfDNA Screening with a Low Screen-Failure Rate Between 8-10 Weeks Gestation

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Background

- In November of 2024, prenatal cell-free DNA (pcfDNA) screening for chromosomal abnormalities became available beginning at 8 weeks gestation via a whole genome sequencing (WGS) assay that utilizes fetal fraction amplification (FFA).
- Here, we report on the laboratory experience with pcfDNA screening with FFA between 8w0d and 9w6d gestation for samples received in the first months following availability.

Methods

- Data from pcfDNA screens ordered between 11/19/2024 and 03/31/2025 were considered for analysis.
- Number of orders received, screen-positive results, and screen failures were calculated.
- Fetal fraction (FF) medians and first and third quartiles (Q1, Q3) for the 8- and 9-week gestational age period were calculated. Where provided, BMI information was analyzed.

Results

- During the study period, 13,316 orders were placed for patients between 8w0d and 9w6d.
- 287 were screen-positive, for a screen-positive rate of 2.16% (**Table 1**).
- Results could not be generated for 42 samples, resulting in a screen-failure rate of 0.32% (**Table 2** and **Table 3**).
  - 18 samples (0.14%) were screen-failures due to insufficient FF (**Table 2**).

Table 1. Screen positive results

Result type	287 screen positive reports (2.16% screen positive rate)
Aneuploidies	
Trisomy 21	**61** (21.25%)
Trisomy 13	**25** (8.71%)
Trisomy 18	**17** (5.92%)
Sex chromosome aneuploidy (SCA)	**93** (32.40%)
Rare autosomal aneuploidies (RAA)	**94** (32.75%)
Microdeletions	
1p36	**2** (0.70%)
22q11.2	**2** (0.70%)
15q11.2	**2** (0.70%)
5p	**2** (0.70%)
4p	**0** (0.00%)

*11 were screen positive for multiple abnormalities

- Median FF across the cohort was 15.3% (Q1=11.3%; Q3=20.1%). For samples ordered in the 8th week of pregnancy, median FF was 13.6% (Q1=10.3%; Q3=17.9%) and for samples ordered in the 9th week of pregnancy, median FF was 16.9% (Q1=12.7%; Q3=21.7%) (**Figure 1**).
- For samples in which BMI could be assessed (n = 8,130, 61% of study samples), the proportion at BMI ≥30 was 35.0% (n = 2,847). For those with BMI ≥30, median FF was 12.3% (Q1=9.2%; Q3=15.9%) (**Figure 2**).

Table 2. Screen failure rates for weeks 8 and 9 combined

Reason for failure	42 total screen negative reports (0.32% screen failure rate)
Insufficient FF	**18 samples** (0.14%)
Other QC metrics	**24 samples** (0.18%)

Table 3. Screen failure rates by week

Week	Rate
Week 8	**0.34%**
Week 9	**0.27%**

0.32% overall screen failure rate

Figure 1. Fetal Fraction distribution at 8 and 9 weeks

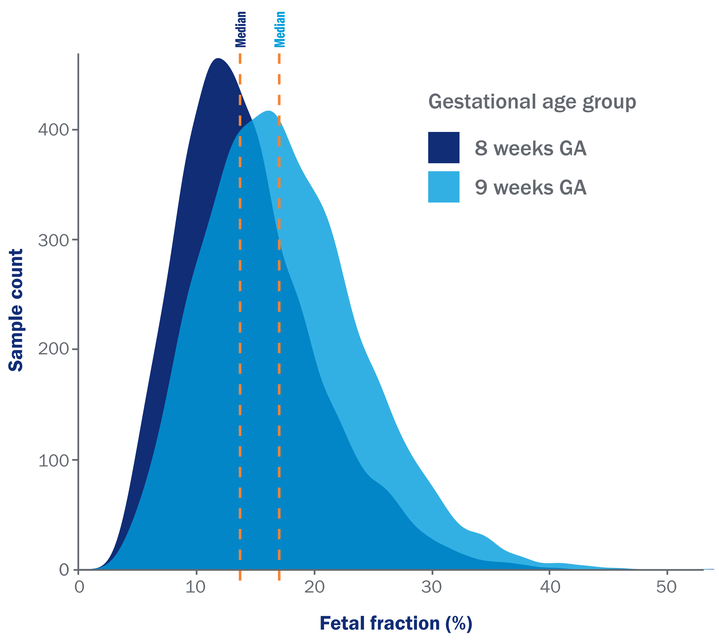
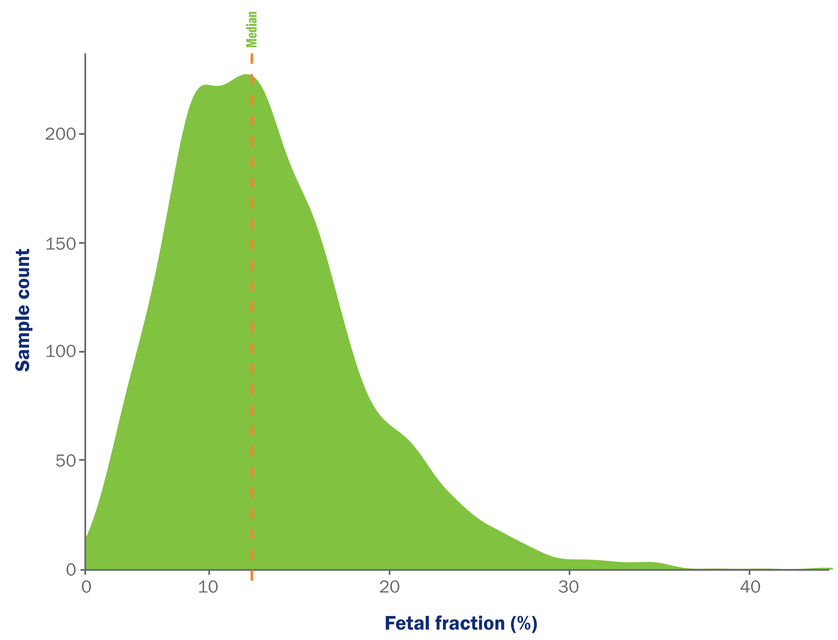


Figure 2. Fetal Fraction distribution at high BMI ≥30



Conclusions

- Laboratory experience with pcfDNA screening for pregnancies from 8w0d to 9w6d demonstrated sufficient FF for analysis while maintaining a low screen-failure rate across a broad population including patients with high BMI.

Disclosures: All authors were employees of Myriad Genetics, Inc. at the time of this study and received salaries and stock as compensation.

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