A noninvasive prenatal screen with >4% fetal fraction in all samples

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INTRODUCTION

- For millions of pregnant patients, noninvasive prenatal screening (NIPS) based on cell-free DNA (cfDNA) detects whether their pregnancies are at elevated risk for fetal chromosomal abnormalities.
- Fetal fraction (FF), the proportion of cfDNA originating from the placenta, can impact the accuracy of NIPS, and many laboratories fail samples with low FF, commonly defined as FF <4%.
- FF has been shown to negatively correlate with body mass index (BMI), pregnancies with trisomy 18 or 13, and early gestational age, resulting in higher test failure rates in these populations.
- A whole-genome sequencing (WGS)-based NIPS that employs FF amplification (FFA) technology for all samples has been shown to increase FF by 3.9-fold for samples with low FF.[1]

METHODS

- We retrospectively analyzed results from 19,464 patients who underwent NIPS with FFA during a two-month period.
- The FFA technology increased FF by preferentially sequencing short cfDNA fragments, known to be enriched for fetal-derived cfDNA. FF was assessed for patients who received a screening result (N= 19,433).
- BMI data were available for 12,579 patients.

RESULTS

- Median maternal age was 31 years and median gestational age was 12 weeks.
- Fetal fraction increased overall by >2-fold with FFA as compared to standard NIPS without FFA (Figure 1).
- No patients had FF results <4%. Ninety-nine percent of patients had FF >8.1% (Figure 2A).
- In patients with BMI ≥30 (N=4,429), 99% of patients had FF >7.1%. Even in patients with BMI ≥40 (N=1,060), 99% had FF >6.2% (Figure 2B).

Figure 1. Fetal Fraction Amplification (FFA) increases FF as compared to standard NIPS.

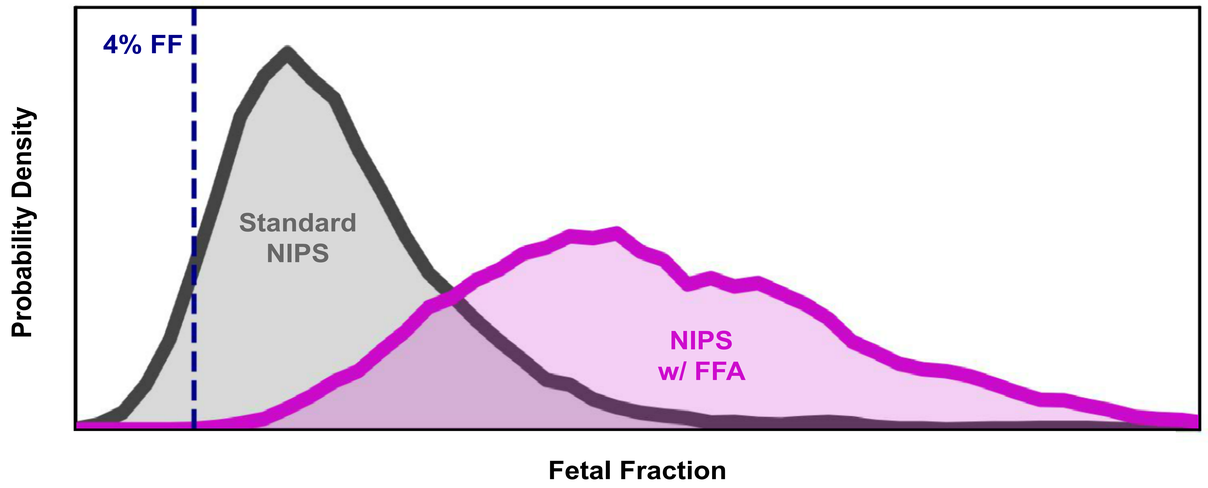
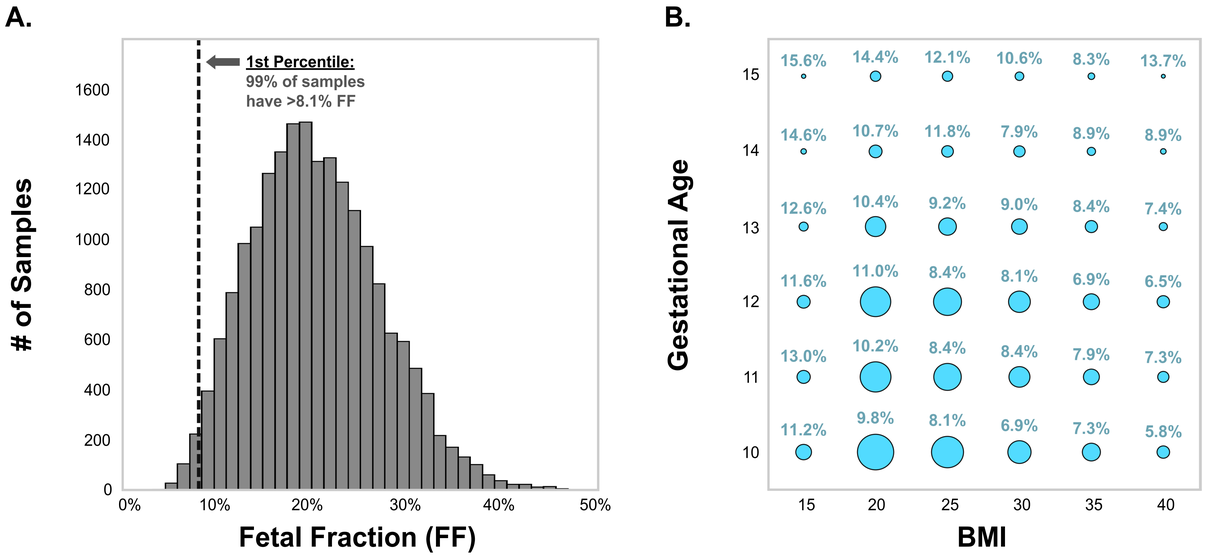


Figure 2. FFA performance in >19,000 clinical samples.

(A) Fetal fraction distribution across >19,000 clinical samples. (B) FF was assessed looking at the 1st percentile FF for a variety of combinations of BMI and gestational age. The dot size corresponds to the number of women with the indicated BMI and gestational age.



CONCLUSION

- A commercial NIPS using FFA for all samples provides confident results regardless of a patient's risk factors for low FF. FFA provides ample FF, preventing unnecessary test failures in NIPS.

REFERENCES: 1. Welker, N. C. et al. High-throughput fetal fraction amplification increases analytical performance of noninvasive prenatal screening. *Genet. Med.* (2020) doi:10.1038/s41436-020-01009-5