

Clinical Laboratory Experience in Fetal Aneuploidy Detection: A Comparative Analysis of NGS-based and dPCR-based NIPT Methods

Veronika Korenika*1, Samanta Strojeva1, Sandra Martinsone1, Dmitrijs Perminovs1, Mikus Gavars1
1 E. Gulbis Laboratory, Riga, Latvia

E. Gulbja Laboratorija

Background

Non-invasive prenatal testing (NIPT) utilizes cell-free fetal DNA (cfDNA) from maternal blood to screen for fetal aneuploidies. Currently, the most widely used technologies for detecting common trisomies include next-generation sequencing (NGS) and microarray-based methods (1). More recently, digital PCR (dPCR) has been introduced in clinical trials as an alternative approach (4). While NGS-based NIPT offers higher sensitivity and accuracy, allowing for the detection of a wider array of aneuploidies, it is also more costly and time-intensive (2). In contrast, dPCR-based NIPT is less expensive and faster, making it feasible to conduct within local clinical laboratories, thereby avoiding the need to send samples to central labs (1, 3). Studies have shown that both dPCR and NGS-based NIPT exhibit assay sensitivities of 100% and specificities ranging from 95% to 100% (1, 3, 5).

Objectives

- To compare the performance of NGS and dPCR in the detection of fetal aneuploidies involving chromosomes 13, 18, 21, and X.
- To evaluate the sensitivity, specificity, and overall efficiency of NGS and dPCR in NIPT.
- To assess the feasibility of dPCR as a cost-effective and efficient alternative to NGS-based NIPT in clinical practice.

Aim

The aim of this study is to determine whether dPCR can serve as a viable and cost-effective alternative to NGS for detecting common fetal aneuploidies, providing accurate and reliable results that can be implemented in local clinical laboratories.

Methods

Sample collection
(110 samples, average gestational age: 14 weeks (± 4.4 SD))

Cell-free plasma DNA extraction
(QIAGEN)

NIPT method – dPCR
(Atila BioSystems)

NIPT method – NGS
(Sistemas Genómicos)

Chromosome Analysis
(13, 18, 21, and sex chromosomes)

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Figure 1. Study design for method evaluation.

Results

Comparative analysis showed no difference in sex determination between the two methods. On average, dPCR-based NIPT exhibited a reduced fetal fraction estimation by 3.7 percentage points or 29% ($p < 0.001$) for male fetuses and 3.7 percentage points or 34% ($p < 0.001$) for female fetuses (Figure 2.).

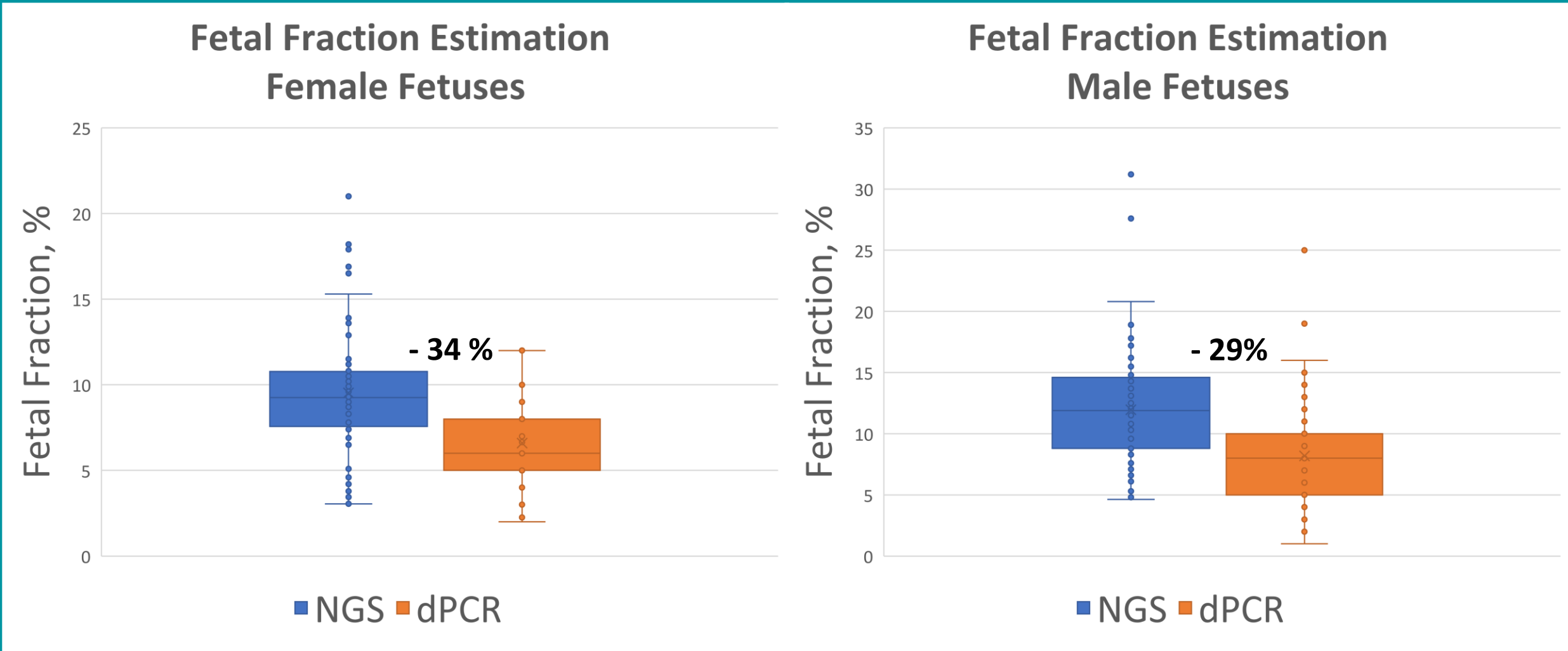


Figure 2. Fetal fraction estimation differences for male and female fetuses using dPCR and NGS methods.

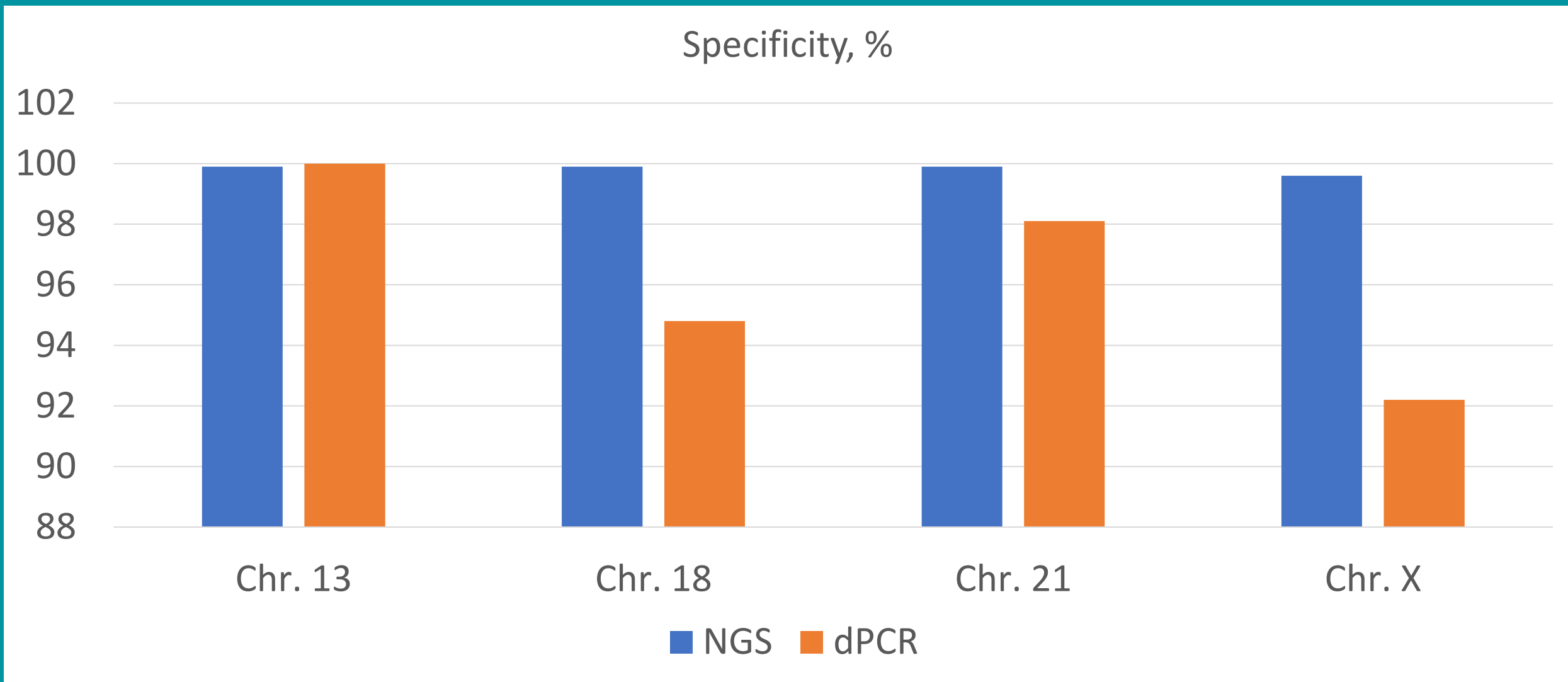


Figure 3. Specificity of dPCR and NGS NIPT.

Specificity for dPCR NIPT (chromosomes 21, 18, 13, X) was 98.1%, 94.8%, 100%, and 92.2%, respectively, with a sensitivity of 100%. NGS-based NIPT demonstrated higher specificity ($>99\%$) (Figure 3.).

In a detailed case study involving a confirmed vanishing twin, NGS-based NIPT indicated no aneuploidy and suggested a male fetus. Conversely, dPCR NIPT detected a fetal fraction of 6.2%, with a Y chromosome count of 1.8%.

Conclusion

dPCR-based NIPT provides a rapid (24-48 hour turnaround) and cost-effective alternative for screening fetal aneuploidies, particularly in chromosomes 13, 18, 21, and X. While NGS-based NIPT remains the more comprehensive and sensitive method, dPCR's simplicity and affordability make it a practical option for local clinical laboratories. The integration of both methods could enhance the accuracy and efficiency of prenatal screening, ensuring better clinical outcomes. This dual approach could lead to a more accessible and reliable NIPT, improving prenatal care on a broader scale.

References

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