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Similarities and differences in performance between two WGS-based NIPT tests – 10 years of experience of the Genomed SA laboratory

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Introduction

Non-invasive prenatal testing (NIPT) becomes a routine method of prenatal screening. It is characterised by no miscarriage risk, accuracy (decreased number of confirmatory testing) and early timing (10w of pregnancy). Numerous testing approaches, methodologies, ranges, report options are being applied worldwide.

In Poland NIPT started to be offered in 2013. The first Genomed NIPT laboratory (performing NIFTY based on a BGI license) was opened in 2015. In 2018 the company switched to the Illumina VeriSeq™ v1 NIPT, offered under its own brand SANCO. In 2020, the test was expanded into VeriSeq™ v2 **genome-wide prenatal screening** for chromosomal abnormalities.

The objective of this study was to compare data on the performance of two large series of different NIPTs provided by the Polish pan-country laboratory.

The tests differed in the applied chemistry, NGS sequencers, bioinformatic algorithms and range of analysis.

Genomed *is a member of*

Global NIPT Consortium

Study group

Altogether 41 064 reports, issued between 2014 and 2023, were analysed. Data have been extracted from a test-dedicated database, order forms, final reports, follow-up sheets and personal communications. Two NGS-based NIPT technologies were applied: BGI (15850 samples) and Illumina (VeriSeq v1 - 5191 samples and v2 – 20020 samples).

Test ranges

Basic NIPT has been recommended for singleton and twin pregnancies to screen for trisomies 21, 18 and 13 plus sex chromosomes aneuploidy (SCA) - the range corresponding to VeriSeq v1. The extended version of the test (Veriseq v2) is performed as the whole-genome test that screens for all autosomal aneuploidies, common SCA, fetal sex and all deletions/duplications ≥7Mb. The basic NIFTY range covered the v1 range, but the test also enabled screening for several microdeletion syndromes and selected rare trisomies (T9, T16, T22). The frequency of aneuploidy detection within the common range of these two tests did not differ significantly, with some exceptions that subsequently were attributed to false positives.

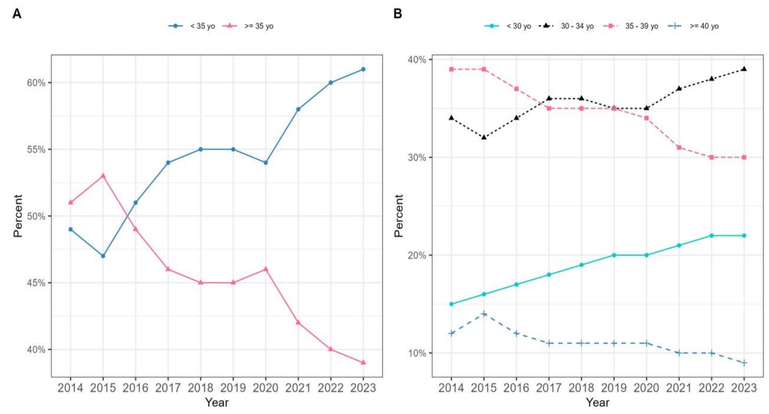

Fig 1. Proportion of accepted samples by age group over time: (**A**) two groups - under 35 and ≥35 yo (**B**) sub-division into four age groups to underline the trend in <30 yo population.

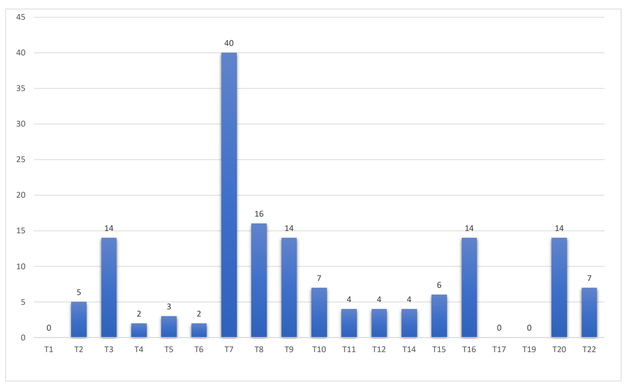

Fig.2. Type and frequency of different rare autosomal aneuploidies (RAA) detected by genome-wide NIPT.

Trends

Advanced Maternal Age and related reasons for NIPT testing have quickly begun to change towards preventive first-tier tests (**Fig.1**).

After the genome-wide test introduction, majority of patients opted for expanded test version, enriching positive results in RAAs (**Fig.2**) and CNVs.

Differences in performance

Despite a slightly younger population tested with **VeriSeq** v2, frequencies of the main aberrations remained stable **(Tab.1)**. None of the NIFTY CNVs has been confirmed to be fetal by diagnostic testing, compared to nearly 55% of those indicated by VeriSeq (less than 20% feedback in both groups). The percentage of SCA has decreased twofold, resulting in a lower false positive rate.

The switch from the BGI to the Illumina test allowed to:

- reduce the turn-around time by half (5.5 vs 2.5 days);
- decrease the percentage of both false negative (from 0.044 to 0.028%) and no-call (0.44% to 0.20%) cases.

Table 1. Outcomes of two tests performed by the Genomed SA laboratory

Feature (% if not specified otherwise)		BGI	Illumina	
			v1	v2
Common range	T21	1.58	1.86	1.54
	T18	0.42	0.33	0.40
	T13	0.23	0.19	0.21
	SCA	0.98#	0.29	0.45
	T9, T16, T22	0.12	NA	0.14
Other RAAs (excluding T7)		0.06	NA	0.25
CNVs		0.18	NA	0.56
Feedback on CNVs		17.24	NA	19.64
True positive CNV		0	NA	54.55
False negative T21		0.044	0.028	
Turn-around time (days)		5.5	2.5	
No-call rate		0.44	0.14	0.20

50% of FP samples re-tested with Illumina turned out to be negative

Conclusion

The Illumina technology, based on PCR-free, low-coverage WGS, with genome-wide reporting and dynamic fetal fraction incorporation in metrics, enables superior performance in the turn-around time, no-call rate as well as false positive and false negative ratios.

Conflict of interests

Nothing to disclose – all the data were generated and/or collected using the Genomed SA resources

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