

Women's Health

APRIL 2021 | A NEWSLETTER FOR MEDICAL PROFESSIONALS

Counseling patients with positive NIPT results can be complicated.

Mosaicism Ratio, an NIPT reporting metric, provides personalized information for patients with positive NIPT results, offering valuable insights when you need them most.

Refine each patient's risk for aneuploidy using personalized data specific to their NIPT results.

The final result is the most important aspect of a non-invasive prenatal test (NIPT), and while most NIPT laboratories work hard to deliver the best possible results, experience, sequencing technology, and capability varies from lab to lab, along with result reliability and the risk for false positive results.

After nearly a decade of experience with NIPT, we have observed the tendency for NIPT samples with 'mosaic' data to have lower positive predictive values (PPV).¹ MaterniT® 21 PLUS with Mosaicism Ratio helps to refine your patient's risk for aneuploidy using personalized data specific to their results, supplementing the current PPV calculation using maternal age and gestational age.

Now there is a way to identify which NIPT results are more likely to be true positive results, offering providers greater reliability and confidence as they counsel their patients.

What is Mosaicism Ratio?

- A metric calculated in the event of a positive NIPT result for trisomy 21, 18, or 13

- Requires two data points:

- **Affected fraction** –

the percentage of cell-free DNA that is impacted by aneuploidy

- **Fetal fraction** –

the percentage of cell-free DNA contributed by the pregnancy

$$\text{Mosaicism Ratio} = \frac{\text{Affected fraction}}{\text{Fetal fraction}}$$

How is Mosaicism Ratio interpreted?

Groups	Likelihood of POSITIVE result being a TRUE POSITIVE
High mosaic	Positive NIPT result is more likely to be a true positive, associated with a higher PPV (see report below)
Low mosaic	Positive NIPT result is more likely to be a false positive, associated with a lower PPV (see report below)
Non-mosaic	Positive NIPT result that is very likely to be a true positive, associated with the highest PPV. No 'mosaic' language will display on the report.

Test Result	Positive Trisomy 13
Lab Director Comments This specimen showed an increased representation of chromosome 13, suggestive of high mosaic trisomy 13, which may affect the reported PPV (Rafalko et al, 2020). In placental testing, trisomy 13 is a common finding that is often confined to the placenta (CPM), Grafi et al, 2014. However, true fetal involvement is associated with phenotypic abnormality. Genetic counseling, confirmatory diagnostic testing, and clinical correlation are recommended.	

Test Result	Positive Trisomy 18
Lab Director Comments This specimen showed an increased representation of chromosome 18, suggestive of low mosaic trisomy 18, which may affect the reported PPV (Rafalko et al, 2020). In placental testing, trisomy 18 is a common finding that is often confined to the placenta (CPM), Grafi et al, 2014. However, true fetal involvement is associated with phenotypic abnormality. Genetic counseling, confirmatory diagnostic testing, and clinical correlation are recommended.	

Positive Predictive Value (PPV) by trisomy and Mosaicism Ratio group¹

In general, as Mosaicism Ratio increases, so does the positive predictive value (PPV) of the result. The PPV associated with an individual patient result depends on the trisomy involved and the Mosaicism Ratio associated with the results (i.e. non-mosaic, high mosaic, or low mosaic).



Mosaicism Ratio Group (MR value)	Trisomy 21	Trisomy 18	Trisomy 13
Non-mosaic (0.7 and above)	98.4% [95% CI: 96.6-99.3%]	96.3% [95% CI: 91.2-98.6%]	93.9% [95% CI: 82.1-98.4%]
High mosaic (0.5-0.69)	90.0% [95% CI: 66.9-98.2%]	85.7% [95% CI: 70.8-94.1%]	66.7% [95% CI: 46.0-82.8%]
Low mosaic (0.2-0.49)	28.6% [95% CI: 5.1-69.7%]	63.2% [95% CI: 38.6-82.8%]	7.9% [95% CI: 2.1-22.5%]

What are the potential causes of a low Mosaicism Ratio?

Though it may be difficult to pinpoint the exact cause of a low Mosaicism Ratio in any particular case, in general a depressed Mosaicism Ratio may be the result of placental mosaicism, prior co-twin demise, or other biological phenomenon.

Conclusion

- Mosaicism Ratio allows clinicians to provide customized counseling for patients with positive results for trisomy 21, 18, and 13 in singleton pregnancies
- MaterniT 21 PLUS with Mosaicism Ratio identifies when a positive result is more likely to be a true positive
- The lower the Mosaicism Ratio, the greater the chance for a discordant result from diagnostic testing
- Regardless of Mosaicism Ratio, diagnostic testing and genetic counseling are recommended for all positive NIPT results according to ACOG, Practice Bulletin 226²
- Mosaicism Ratio is validated in a recently released peer reviewed publication, and discussed in detail on the webinar: Test. Better. Enhanced NIPT Reporting for Patients with Positive Results, presented by Thomas Westover, MD, FACOG and Jill Rafalko, MS, CGC, LGC

[Download study and view the webinar recording here](#)

April Health Awareness Calendar

- World Autism Awareness Day (April 2)
- World Health Day (April 7)
- Medical Laboratory Professionals Week (week of April 20th)
- National Infertility Awareness Week (April 21-27)
- World Immunization Week (April 22-28)
- Parkinson's Awareness Month



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References

1. Rafalko et al. Impact of Mosaicism Ratio on positive predictive value of cfDNA screening. *Prenatal Diagnosis*, 2020.
2. American College of Obstetricians and Gynecologists. Screening for Fetal Chromosomal Abnormalities. Practice bulletin no. 226. *Obstet Gynecol.* 2020;136(4):859-867