GENOMICA
Next Generation Genetics

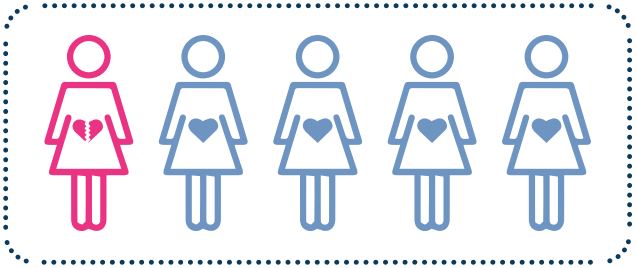
NGS-Based Product Of Conception Karyotyping

POCADVANCE TISSUE
NGS-BASED POC KARYOTYPING

www.pocadvance.it

POCADVANCE TISSUE

ABOUT MISCARRIAGE



1 out of **5**

Pregnancies terminated due to miscarriage

Miscarriage is the most common complication during the early stages of pregnancy and occurs in about **15-25%** of clinically diagnosed pregnancies, most of which in the first trimester of gestation.
There are many known causes and risk factors for spontaneous abortion but about 60% of cases originate from chromosomal abnormalities[1-2].
Diagnosing a chromosomal abnormality as a cause of miscarriage **provides important information for predicting the risk of recurrence** and helps identify familial chromosomal rearrangements that can predispose couples to recurrent miscarriages or the birth of babies with congenital abnormalities and / or intellectual disabilities. In 2016, the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medi- cine recommended the search for chromosomal abnormalities on the placenta, amniotic fluid and the **product of conception** (POC) **in cases of intrauterine fetal death** and **perinatal mortality[3]**.

1. D'ippolito et al., 2017
2. JA Rosenfeld et al., 2015
3. Committee Opinion No. 581, 2016

POCADVANCE TISSUE

THE FETAL KARYOTYPE BY USING TRADITIONAL CYTOGENETIC TECHNIQUES

The cytogenetic investigation (or karyotype) on the product of conception has traditionally been performed by culturing the fetal cells present in the fetal tissue and subsequent microscopic analysis of the chromosomes in metaphase.
Traditional karyotyping from product of conception tissue is characterized by technical difficulties and diagnostic limitations:

- **Extended turnaround time:** Cell cultures require 15-20 days for reporting of results, which are necessary for the development
of colonies of fetal cells.
- **Risk of culture growth failure:** Sometimes it is possible that the fetal cells placed in culture do not grow adequately, resulting in the inability to achieve a diagnosis. This problem is very common; it occurs in about 50% of POC tissue cultures. The high frequency of culture failure depends on the fact that to perform a karyotype analysis with traditional techniques it is necessary to have living cells, capable of dividing once placed in culture. This is not always possible in the case of analysis on POC tissue, which contains almost all non-living cells.
- **Risk of contamination with maternal cells:** the POC tissue is obtained by revision of the uterine cavity, so in this sample there
are also maternal cells, which could grow in cell culture, in competition with fetal cells. Therefore, when a traditional cytogenetic karyotype from abortive tissue is performed and the result is "normal female karyotype", it is not possible to rule out of
having examined maternal cells instead of fetal cells, which in culture are indistinguishable.
- **Resolution limits:** with the cytogenetic karyotype both aneuploidies, i.e. the alterations in the number of chromosomes, responsible for the most frequent syndromes, and the structural alterations of a certain entity are clearly highlighted. Inother words, structural anomalies larger than 10-15 Mb with a bandwidth resolution of 350-400 bands can be highlightedwith this test. Therefore, the diagnosis of pathologies deriving from submicroscopic chromosomal alterations (microdeletions ormicroduplications) is missed.
- **Possibility of "in vitro" artefacts:** most often referable to pseudomosaicisms. This can happen in 2-3% of cell cultures.

POCADVANCE TISSUE

POCADVANCE TISSUE is an advanced molecular test that, using the latest generation of fully automated sequencing technologies (**Next Generation Sequencing - NGS**), allows to determine the fetal karyotype from the POC tissue with high efficiency, accuracy and resolution.

POCADVANCE TISSUE is able to provide information on the possible causes of a miscarriage with the aim of helping the couple in family planning.

BENEFITS

Cell culture is not required

- Exclusion of the risk of achieving no results due to lack of cell growth;
- Significant reduction in turnaround time **(5-7 days)**, instead of the 15-20 days required with "classical" cyto- genetic techniques.
- Exclusion of the risk deriving from the growth in culture of **maternal cells instead of fetal ones**

High reliability of results

Assessment of fetal origin: Determination of the DNA profile of the sample extracted from the abortive tissue and subsequent comparison with the maternal one to verify the **fetal origin** of the DNA undergoing to molecular karyotype analysis.

Greater resolution and accuracy compared to traditional karyotyping

Much higher resolution: 6Mb instead of 10-15 Mb for the traditional karyotyping.

POCADVANCE TISSUE

A GROUNDBREAKING TECHNOLOGY THAT MAKES THE DIFFERENCE

Fetal and maternal (buccal swab) sample collection

Separation of fetal from maternal tissue

DNA extraction

Determination of the DNA profile of the POC sample and comparison with the maternal profile

Next Generation Sequencing (NGS)

Fetal DNA testing followed by bioinformatic analysis

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TEST RESULTS

Chromosomal abnormality detected: this result shows that the test detected a chromosomal abnormality in the fetus.

Chromosomal abnormality not detected: this result shows the test has not detected any chromosomal abnormality. This result is suggestive of euploidy (normal fetal karyotype)

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This test is unable to detect balanced chromosomal rearrangements (reciprocal translocations, inversions), chromosomal mosaicisms (i.e. the presence of two cell lines with different karyotype) with a poorly represented cell line (less than 10%), microdeletion/ microduplication syndromes, structural chromosomal anomalies with a size below 6Mb, point mutations, methylation defects, polyploidies.

POCADVANCE TISSUE

INDICATION FOR TESTING

✓ SUGGESTED

* Women who have had a miscarriage

✓ STRONGLY RECOMMENDED

** Women who have had recurrent miscarriages

*** Women who have had miscarriages following IVF treatments

THE TESTING PROCESS

1. **Request the test kit**
2. **Collect the sample**
3. **Ship the sample to Genomica Lab**
4. **Receive results**

The transportation kit contains the tubes suitable for shipping the POC sample. It is recommended to place the sample in the supplied tube and fill it with saline solution.
The sample must be stored at +4°C until shipping.

GENOMICA
Next Generation Genetics

Advanced molecular diagnostics solutions using state-of-the art technologies

GENOMICA is recognized as one of the most advanced molecular diagnostics laboratory in Europe, both for the state-of-the-art instruments and technologies, as well as for its high quality standards.

With a **comprehensive portfolio of over 10.000 genetic tests,** GENOMICA is able to satisfy increasingly specialised requests in the field of molecular genetics, providing physicians and their patients with innovative and highly specialised diagnostic solutions for any clinical need.

Over **100.000** genetic tests/year

Fast TAT

Laboratories with **groundbreaking technologies** and high quality standards

Test performed in Italy
(Rome or Milan)

Dedicated R&D team

International **Partnerships**

Personalized genetic counseling with genetic counselors experts in discussing genetic test results and familial risks

Professionals with 20+ years expe- rience in the field of genetics and prenatal molecular diagnostics

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