ivfconferenceggrc

Georgia`s leading medical magazine

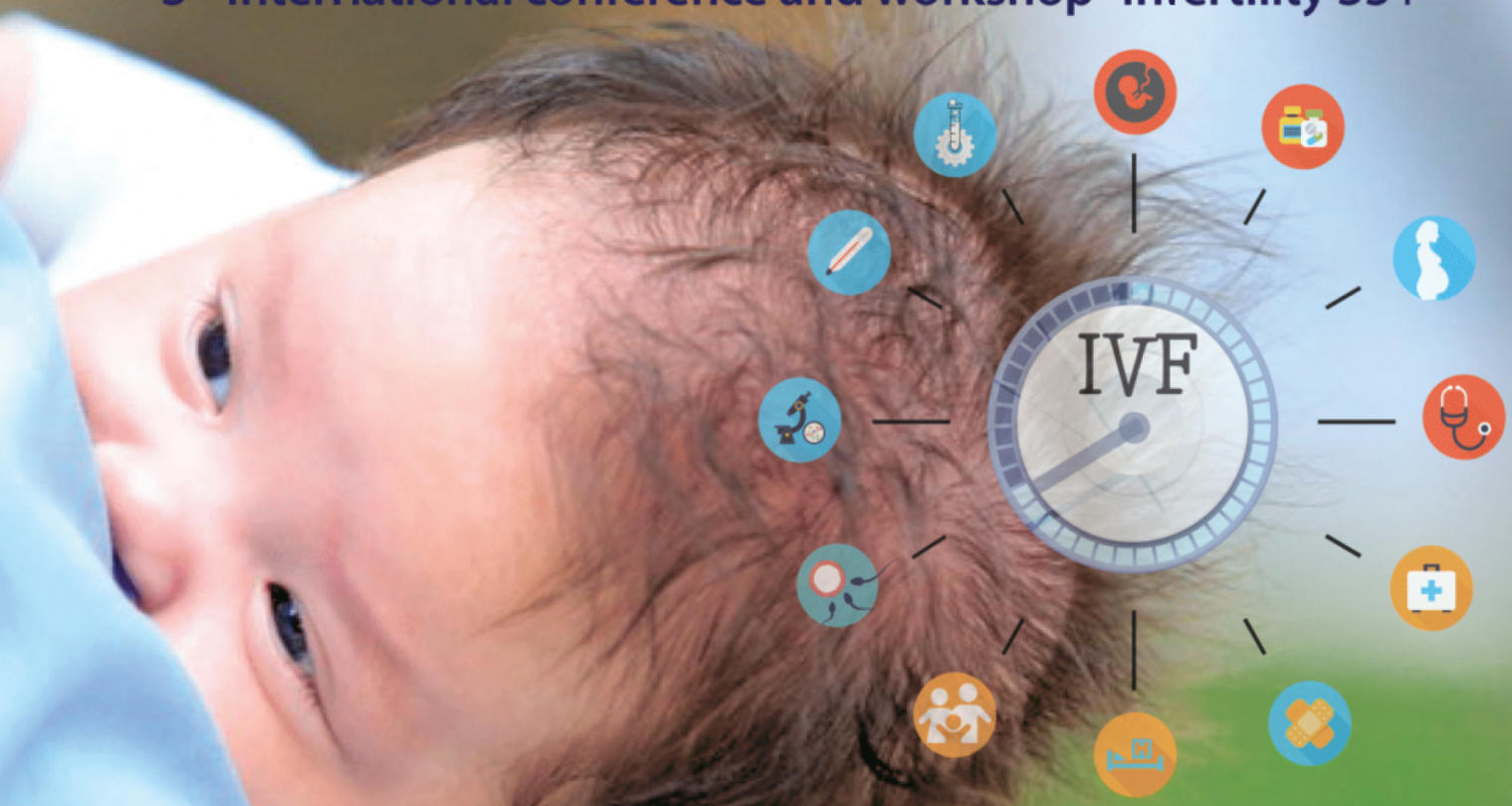
TBILISI, GEORGIA

# MEDICAL TIMES

18-19 September 2022 - Special Edition

MAGAZINE №1

## 3rd International conference and workshop "Infertility 35+"




**Archil Khomasuridze MD, PhD, Professor**
President of the Georgian Association of Reproductology, Conference chairman

**Victor Gomel MD, FRCSC**
**Professor Emaritus / Emerita**
Division of Reproductive Endocrinology & Infertility
The University of British Columbia

**„Long-term Experience Sharing on Regenerative Applications in terms of Ovarian Rejuvenation and IVF"**
**Josie Muscat, MD, ARDMS**
Chairman of Saint James Hospital Groups in Malta

**"Preimplantation Genetic Testing (PGT) for late genetic diseases"**
**Alexander Simon, MD Professor**
IVF Specialist,
Hadassah Medical Center, Israel

**"Fertility Sparing in Cervical Cancer"**
**Rene Laky, MD**
Deputy Head Gynecology Division,
Medical University of Graz, Austria

**"URINARY TRACT ENDOMETRIOSIS"**
**Revaz Bochorishvili - Ph.D., MD, Profesor**
Director of the International Center for Endoscopic Surgery, France

www.ivfggrc.com/conference

# MEDICAL TIMES

## 3rd International Conference and Workshop “Infertility 35+”

## №1

Tbilisi, Georgia
2022

*ISSN* **2720-8508**
*ISBN* **977-2720-8-5000-5**

**SUPPORTING COMPANIES FOR THE 3RD INTERNATIONAL MEDICAL CONFERENCE "INFERTILITY 35+"**

# CONTENTS

# CONTENTS

# CONTENTS

Georgian-German Reproductive Center (GGRC) is organizing the 3rd International Scientific Conference “Infertility 35+” in Tbilisi at Biltmore Tbilisi Hotel and on the Zoom platform on September 18 -19, 2022. The participants will have the opportunity to listen to the presidents of reproductive associations of different countries and doctors of the world’s leading clinics from the USA, Canada, Austria, Latvia, Estonia, Israel, Germany, Turkey, Kazakhstan, Ukraine, France, Russia, Armenia, and Azerbaijan.

- “News in assisted reproductive technologies and methods”;
- “Importance of genetic studies in reproductive medicine”;
- “Pregnancy management during diabetes”;
- “Receiving biological material of oncology patients”;
- “Rising Infertility Statistics and Studies”;
- “Isolation of stem cells and PRP procedure” etc.

The conference participants will learn the details of the workshop, which will be held in the minor operating block and embryology laboratory of GGRC.- Topic “Isolation of stem cells and PRP procedure" – GGRC laboratory is the only one with FDI and ISO certificates. Georgia's Ministry of Labor, Health and Social Protection supports the conference. According to the decision of the N14 session of the Professional Development Council on June 24, 2022, the conference format program – “Infertility 35+" (Acr. N C0359) was awarded 1 type 9 UPG points for “Reproductive Medicine," “Obstetrics and Gynecology”, “Urology”, “Clinical Oncology”, for doctors certified in “endocrinology" and “oncosurgery”. The registered participants of the conference will be given appropriate certificates."

„GEORGIAN – GERMAN REPRODUCTIVE CENTER“

- 51 g. V. Barnovi st., 0179 Tbilisi
- (+995) 544 44 83 43
- 032 283 34 43; 032 2 509 509
- WWW.IVFGGRC.COM

# ARTIFICIAL ABORTION – THE GEORGIAN STORY

***KHOMASURIDZE ARCHIL**, MD, PhD, Prof.*
*Georgian Association of Reproductive Health, Tbilisi, Georgia*

## SUMMARY

This chapter provides a comprehensive overview of the current state of abortion and contraception in Georgia, highlighting the unique characteristics that set them apart from other regions. The second section explores the principles of eliminating restrictive policies on abortion and contraception. The final and main topic presents the author's profound thoughts and philosophy on abortion and life issues, inviting the reader to engage in thoughtful discussion.

**Keywords:** Artificial abortion, Contraception, Reproductive health

## INTRODUCTION

The reader may wonder: Why the Georgian Story?

1. Maybe because Georgia is the first and the only country in the world where Reproductology, the science about both women's and men's reproductive health, has widely been recognized as the officially independent medical discipline, starting since 1997, not just the part of obstetrics and gynecology.
2. Georgia possesses a nonofficial record in the fast spreading of modern contraception. In any case, according to the research of the Zhordania Institute of Reproductology (the oldest clinic of this type in the world, established in 1958) in Georgia, in 1987, when the population averaged 5.5 million, the artificial abortion total rate was 300,000, two-thirds of which was illegal, approximately 2-4 abortions per woman. In this period, Georgia was a part of the Soviet Union, which was the first in the world abortion statistics, and Georgia was one of the leaders among the Soviet republics. Furthermore, the usage of modern contraception was 0 (zero), which means that contraception, as the regulatory method

of reproductive function, did not exist in our country. By the year 2010, the prevalence of modern contraception exceeded 70%. We consider this jump from 0 to 70 per cent a unique fact, and we rely on the Zhordania Institute's studies but not the CDC's data, which we consider unreliable since the survey was carried out with serious omissions: men were not included in the research.

3. We take great pride in our country being the one in the Christian world where complete understanding has been achieved between the Church and reproductive specialists, a successful collaboration that can serve as a model for other regions. For instance, no significant issues were encountered during In Vitro Fertilization (IVF) development and implementation. All those mentioned above result from permanent and frequent consultations between the Georgian Orthodox Church and the Zhordania Institute of Reproductology. Our experience will benefit Christian countries struggling to develop and use the main principles of reproductive health.

Regarding the contemporary dynamics of abortion and contraception, our experience points out that the abortion rate is 10,000, and the use of contraception reaches up to 90%. It may be said that the unpleasant phenomenon of abortion is defeated in Georgia. The same is shown in the statistical analysis of recent years (Unfortunately, only until 2010. After this, no research has been conducted due to the government's unstable political situation and inattention) and in the results of interested specialists' permanent surveillance in the Zhordania Institute. To be more exact, artificial abortion has not been eliminated. Disappointingly, the abortion rate is 10 to 12 thousand per year[3], which is relatively high for a country with a population of 3.7 million. It must be noticed that illegal abortions are eliminated. The rest of the registered abortion rate has steadily positive dynamics, which means it is reducing. Here, it must be noted that the main reason for this achievement in our country is the comprehensive implementation of contemporary contraceptives by the Zhordania Institute, a reassuring sign of progress. It may not be ignored that local media representatives were helpful in this process and are still helping us. We appreciate the Ministry of Health, Labor, and Social Affairs of Georgia's noninterference in our oversight areas.

The position of our Church is critical as well, which believes that abortion is a big sin and must be eliminated. This opinion is wholly shared, with the added belief that abortion is detrimental to a woman's health and should be abolished. As for contraception, the Georgian Christian Orthodox Church also considers it a sin but "less sin than abortion." This kind of assessment is, at this time, acceptable for us, the reproductologists, especially, because it does not make an accent on abortion and its administrative prohibition or reduce the usage of contraception, which, of course, is the result of our explanations, based on the facts of the world experience.

## METHODS

Data were sourced from the Zhordania Institute of Reproductology, the oldest clinic of its type in the world, and other relevant Georgian health statistics. The analysis covers periods when reliable data were available, particularly up to 2010, as subsequent data collection was hindered by political instability.

The study focuses on the historical and current prevalence of artificial abortions and contraception use in Georgia. It includes qualitative assessments based on consultations between reproductive specialists and the Georgian Orthodox Church.

Quantitative data were gathered from national statistics and Zhordania Institute records. Qualitative data were collected through interviews and consultations with key stakeholders, including healthcare providers and church representatives.

## RESULTS

### Historical Context and Current Statistics

In 1987, Georgia, then part of the Soviet Union, had an artificial abortion rate of 300,000 annually, with two-thirds being illegal. Modern contraception was non-existent at that time. By 2010, the prevalence of contemporary contraception had increased to over 70%, leading to a significant reduction in abortion rates. As of the latest reliable data, the abortion rate is approximately 10,000 to 12,000 per year, with illegal abortions primarily eliminated.

### Role of Contraception and Church-State Collaboration

The successful reduction in abortion rates is attributed to the widespread adoption of modern contraceptives and effective collaboration between reproductive health specialists and the Georgian Orthodox Church. The Church, while considering both abortion and contraception as sins, has worked with health specialists to prioritize contraception as a lesser evil compared to abortion.

### Impact of Policies on Abortion Rates

Evidence from Georgia and other post-Soviet countries indicates that restrictive abortion laws do not reduce the number of abortions but increase the incidence of unsafe, illegal procedures. The introduction of contemporary contraceptives and public education has been crucial in reducing abortion rates in Georgia.

## DISCUSSION

### Abortion as a Public Health Issue

Today, there is no doubt in competent specialists that in the sphere mentioned above, any prohibition does not bring any result and does not change the abortion rate but increases the number of illegal and nonmedical artificial abortions only. The latter leads to an increase in maternal mortality and morbidity rates, as evidenced by the bitter experiences of post-Soviet countries, Romania, Ireland, Poland, and others. Evidence shows that restricting access to abortions does not reduce their number.1 Countries with highly restrictive abortion laws have a significantly higher proportion of unsafe abortions compared to those with more liberal laws.2 Besides, paradoxical is the fact that the administrative prohibition of abortion causes the rise of so-called Gynecological Tourism. The women, for the need and reason of abortion, travel to other countries where the procedure is permitted. In addition, the world study showed that in countries where abortion was restricted, the proportion of unintended pregnancies ending in abortion had increased. However, it decreased in countries where abortion is broadly legal.[1] It is believed that abortion should not

be prohibited but rather eliminated through the introduction of modern contraceptives, comprehensive public information, and adequate education. Until abortion remains the reality of our lives, talking about its prohibition is detrimental. It is necessary to speak about the harm it brings to a woman's health. At the same time, a temporary introduction of modern alternatives to artificial abortion is required. In Georgia, such a temporary alternative has become the so-called Mini-Abortion (Vacuum Aspiration Procedure), which is much more harmless for the woman's health compared to traditional surgical abortion. It had served its purpose, but by 2000, it was decided that Mini-Abortion had become outdated. Consequently, Medical Abortion was introduced, as it is less harmful to women, more cost-effective, and does not require hospitalization.

Our consideration of any abortion is negative, and it must be eliminated, not by prohibition and forcefulness, but only through explanation, interpretation, promotion of relevant knowledge, and education. We are sure that if there is anyone who hates abortion, that is us, the doctors of the field of Reproductology, in the first place. The reasonable position of the Georgian Association of Reproductive Health is that in recent years, the attitude of our country towards abortion and family planning has been fair and proper and should be continued as long as the results are evident.

### Ethical and Philosophical Considerations

We are often asked: is abortion a murder? The response is delivered with firm determination: Yes, abortion is murder because human life begins from its conception. This kind of answer is conducive to the second, natural question: Should the killing doctors who carry out abortions be punished? Our definite answer is: "No" if the doctor does the procedure altruistically, only when he is sure the patient has the vital, medical, and social contraindications for pregnancy. Additionally, the doctor must thoroughly explain everything to the patient to persuade her to maintain the pregnancy.

All this does not relieve the doctor from murder responsibility!

Due to the unfair situation, and after extensive consideration, a philosophy of antenatal life was developed with the hope that, along with the elimination of abortion, the practical necessity for this philosophy will eventually disappear. We are probably not comforting ourselves or imposing our opinions on anybody.

Nevertheless, let us introduce our thoughts on the readers' theoretical and practical assessment.

As already mentioned, we accept the suggestion that all types of artificial abortion are thought to be the facts of life termination and murder. However, it must also be noted that, in our opinion, life is of two types: antenatal and postnatal. Postnatal life begins after delivery, and it belongs to the newborn. Artificial interruption of this life is the greatest crime and is judged accordingly. Antenatal life differs qualitatively from postnatal life because it belongs to the fetus and the mother. As the fetus is not capable of deciding for God, the responsibility for the sin must be placed on the mother and not on the doctor, who is forced into having an abortion. Is it necessary to judge the mother for the crime, or is it not a separate issue? We think that artificial abortion is the mother's sin but not a crime, and only God can judge its level.

Presumably, everybody agrees that there are many such facts in our lives, the fair definition of which exceeds our thinking ability. The rank-and-file cannot analyze such facts but put their trust in God's will. One of them is the still-existing abortion. We have repeatedly clarified that the abovementioned theory is the product of our subjective thinking, which we are not imposing on anybody.

Readers and colleagues are encouraged to consider the fairness and objectivity of this theory.

## CONCLUSION

1. Abortion should be eliminated but not prohibited or restricted.
2. Informing the population of modern contraception and its education in this connection must be made essential.
3. Abortion is indeed murder, but in this particular situation, it is a sin rather than a crime.
4. Considering our theory about dividing life into "Antenatal" and "Postnatal" types, all the sins of abortion should be placed on the mother, but not on the doctor.

Declarations of interests: We declare no competing interests.

### Acknowledgements

We alone are responsible for the views expressed in this article, and they do not necessarily represent the views, decisions, or policies of the institutions with which they are affiliated.

## REFERENCES

1. Bearak J, Popinchalk A, Ganatra B, et al. Unintended Pregnancy and Abortion by Income, Region, and the Legal Status of Abortion: Estimates from a Comprehensive Model for 1990-2019. Lancet Glob Health. 2020;8(9). doi:10.1016/S2214-109X(20)30315-6.
2. Ganatra B, Gerdts C, Rossier C, et al. Erratum: Global, Regional, and Subregional Classification of Abortions by Safety, 2010–14: Estimates from a Bayesian Hierarchical Model. Lancet. 2017; 390(10110):2372-2381. doi:10.1016/S0140-6736(17)31794-4.
3. National Statistics Office of Georgia. Healthcare. https://www.geostat.ge/en/modules/categories/54/healthcare.

# PREIMPLANTATION GENETIC TESTING (PGT) FOR LATE-ONSET GENETIC DISEASES

***SIMON ALEX**, Prof.*
*IVF Unit; Hadassah Medical Center, Jerusalem, Israel*

## SUMMARY

Preimplantation genetic testing (PGT) for late-onset genetic diseases raises moral and ethical arguments regarding its application. Although some healthcare providers find it justifiable, others dispute it. The genetic variant of Creutzfeldt–Jakob disease (CJD), which is one of the known late-onset diseases, can be prevented through PGT. Approximately 15% of CJD cases are inherited disorders associated with PRNP gene mutations. This is an autosomal dominant late-onset neurodegenerative disorder with nearly 100% penetrance and is prevalent among Jews of Libyan descent due to a common PRNP E200K founder mutation. Many young patients at risk for CJD prefer not to know their genetic status but still do not want to pass on the mutation, if it exists, to their offspring. PGT or prenatal diagnosis through direct mutation analysis forces them to learn their carrier status. A solution to this problem is referred to as “testing by exclusion”. This method tests the embryos to ensure they do not carry any allele of the relevant gene from the affected grandparent. This procedure is designed to prevent the birth of at-risk offspring to individuals who choose not to perform a predictive test.

**Keywords:** Preimplantation, genetic, testing, late-onset, diseases, Creutzfeldt–Jakob, PRNP.

# CHROMOSOMAL ANOMALIES IN COUPLES WITH RECURRENT PREGNANCY LOSS

***KRISTESASHVILI JENARO**, MD, PhD*
*Medical Faculty of Medicine, I. Javakhishvili Tbilisi State University;*
*Center for Reproductive Medicine "Universe", Tbilisi, Georgia*
***SIGUA NINO**, PhD*
*Georgian Centre of Prenatal Diagnostics, Tbilisi, Georgia*

## SUMMARY

This study explores the landscape of chromosomal anomalies in couples with recurrent pregnancy loss (RPL) who have not previously delivered abnormal fetuses. From 2014 to 2021, we analyzed 122 couples who had experienced more than two first-trimester miscarriages. After excluding common causes of RPL, we conducted a cytogenetic analysis using G-banding. The results revealed chromosomal anomalies in 8.2% of cases, including balanced reciprocal translocations in 4 men and two women, Robertsonian translocations in 2 men, and subfertility in 3 men. Additionally, one woman had a pericentric inversion of chromosome 9, and another had a mosaic karyotype 46, XX/47, XXX. The introduction of genetic counseling led to two successful pregnancies with normal karyotypes. These findings underscore the potential of karyotyping to identify genetic causes and inform reproductive planning, empowering couples to make informed decisions about their future pregnancies.

**Keywords:** Recurrent pregnancy loss, chromosomal anomalies, balanced translocation, Robertsonian translocation, cytogenetic analysis, genetic counseling, karyotyping

## INTRODUCTION

Genetic factors are the most frequent causes of spontaneous abortions (SA). Numerical chromosomal anomalies, such as aneuploidy or polyploidy, are detected in 50-80% of first-trimester miscarriages. The detection rate depends on the investigation methods used (e.g., FISH, CGH microarray), the composition of the groups studied (such as women of advanced age), and the specifics of family or obstetric history.[1,2] Most chromosomal abnormalities that cause miscarriage have random character. First-trimester SA expresses most (90%). However, these abnormalities might be associated with RPL.[3,4] According to different data, the frequency of chromosomal ab-

normalities in couples with RPL is 2-6%. [1,5,6] Translocation in one of the partners is a common and confirmed cause of recurrent miscarriage[7,8]. Prevalence of balanced translocations is higher in females than in males and higher in couples with a family history of stillborn or abnormal liveborn and, according to some authors, in subfertile men.[1,3,9,10]

Based on a meta-analysis of 79 studies, Tharapel A.T. et al. revealed that among couples with RPL, the structure of identified chromosomal abnormalities is as follows: either partner of couples with RPL has balanced reciprocal translocation in 50%, Robertsonian translocation in 24%, sex chromosome mosaicism in 12%, and in other cases, inversions and different sporadic chromosomal abnormalities were observed.[11]

The presence of a balanced chromosomal rearrangement in one partner can result in an unbalanced translocation in offspring. Phenotypic consequences (abort uses or abnormal liveborn) depend on the specific duplicated or deficient chromosomal segments. [1,2,5]

Translocations do not correlate with the age of mothers and the number of previous miscarriages. [1,6,12]

The theoretical risk of transmission of balanced translocations to offspring in unbalanced form is considerably higher than the empirical risk, which might be explained by the lethality of many segregant products.[1,5,6,8]

Different chromosomal aneuploidies may be expressed in translocation cases due to interchromosomal effects.[1,13] In first-trimester abortions, recurrent aneuploidy occurs more often than expected by chance, which might be tied to the mother's age and also to germ cell mosaicism.[1]

According to the last period data, in cases of structural abnormalities of chromosomes, IVF accompanied by PGD decreases the risk of spontaneous abortions but also decreases the chance of live birth compared to spontaneous pregnancy. In spontaneous pregnancies, considering concomitant factors, the live birth chance is up to 70%.[2,5,12]

There are no standard views on the necessity of karyotyping concepts or whether the karyotyping of couples with RPL (RCOG, ASRM, ECHRE protocols) is economically justified.[14,15]

Some experts recommend karyotyping couples with RPL if there is no information on the Karyotype of conceptuses.[15, 16]

Detection of frequency and types of chromosomal anomalies in couples with I trimester RPL without the history of delivery with the abnormal fetus.

## METHODS

One hundred twenty-two couples with > 2 first trimester miscarriages were involved in a prospective observational study in 2014-21 based on the Center for Reproductive Medicine "Universe" and the Georgian Centre of Prenatal Diagnostics.

The mean age of women was 30,3+2, and the mean age of men – was 32.1+3.

In all cases, family history and obstetric anamnesis were collected and analyzed.

Common causes of RPL—anatomic (congenital and/or acquired), hormonal (luteal insufficiency, diabetes, thyroid dysfunction, PCOS, hyperprolactinemia, etc.), and immunological (APS)—were excluded for all couples;

All couples have undergone cytogenetic investigation. The Karyotype was detected in peripheral blood lymphocyte cultures (G-banding).

*Ethical considerations:* Written informed consent was obtained from all participants before their inclusion in the study.

## RESULTS

Personal or family history of pregnancy and delivery of a fetus with congenital anomalies or child with mental retardation was not detected in any of the cases;

The Karyotype of previous concepts was not investigated in any of the cases;

The mean number of previous miscarriages in the standard group of RPL was 3,15, and in the couples with chromosomal anomalies – 2,9; Chromosomal anomalies in one partner were revealed in 10 cases (8.2%) (Table 1) Balanced reciprocal translocations were detected in 4 men and two women (Fig. 1), Robertsonian translocation – in 2 men, and three from 6 men with translocations (2 Robertsonian and one reciprocal) were subfertile (oligozoospermia); The total frequency of balanced translocations was 6,6%[8]; One woman had a pericentric inversion of chromosome 9, and one woman – had mosaic karyotype 46, XX/47, XXX.

***Table 1.*** ***Type of Chromosomal Anomalies and Reproductive disorders in couples with RPL***

| N | Karyotype | Numbers of first trimester miscarriages | Other reproductive disorders |
|---|---|---|---|
| 1 | 46, XX, t (2;13) (p14;q32) | 2 | |
| 2 | 46, XX, t (5;16) (p12;q22) | 2 | |
| 3 | 46, XY, t (2;9) (p22;p24) | 2 | |
| 4 | 46, XY, t (18;21) (q22;q21) | 3 | |
| 5 | 46, XY, t (10;18) (q11,2; q2,1) | 3 | subfertility (olygozoospermia) |
| 6 | 46, XY, t (6;22) (p21.3;q13.3) | 4 | |
| 7 | 45, XY, rob (13;15) (q10;q10) | 4 | subfertility (olygozoospermia) |
| 8 | 45, XY, rob (13;14) (q10;q10) | 3 | subfertility (olygozoospermia) |
| 9 | 46, XX, inv (9) (p11;q12) | 3 | |
| 10 | 46, XX / 47XXX (18/32) | 3 | |

***Figure 1.***

***Couple with 2 SA Woman 21y old, Karyotype 46, XX, t (2;13) (p14;q32)***

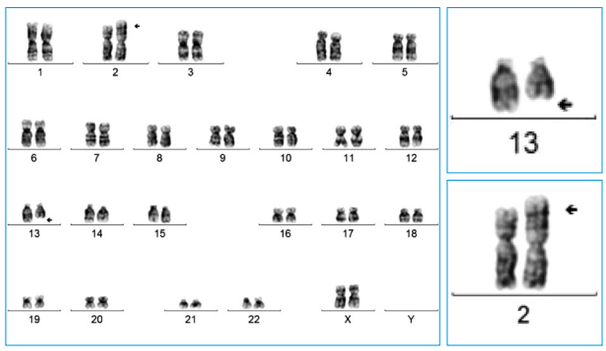
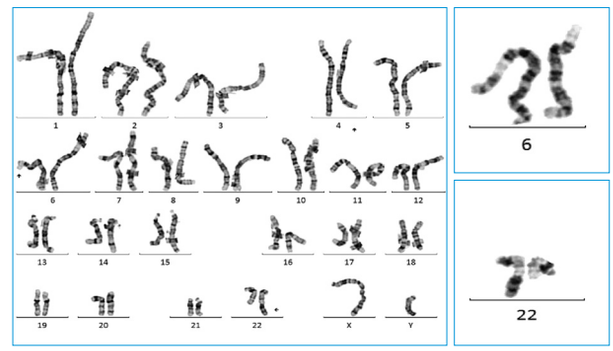



***Figure 2.***

***Couple with 4 SA Male partner 30 y old, Karyotype 46, XY, t (6;22) ( p21.3;q13.3)***



Pericentric inversion of chromosome 9 was revealed in 1 woman with a history of 3 previous I trimester spontaneous abortions, karyotype – 46, XX, inv$^{9}$(p11; q12); Pericentric inversion of chromosome 9 is considered as a variant of normal Karyotype with incidence 1-3% of the general population.[17] This inversion does not correlate with abnormal phenotypes, but in the literature exist, conflicting views regarding the association of this variant with such clinical conditions as infertility, RPL, and stillbirth.[17,18,19]

A mosaic karyotype 46, XX/47, XXX (37/63) was found in 1 woman with a history of 3 previous I-trimester spontaneous abortions. It is important to note that sex chromosome polysomy is a scary condition, occurring in only 0.05% of spontaneous abortuses, and it is not incompatible with life.[1]

## DISCUSSION

The causative relationship of pericentric inversion of chromosome 9 and X chromosome polysomy with RPL needs further investigation. Genetic counseling was conducted for all couples with detected chromosomal anomalies, informing them of their risks and reproductive opportunities, including IVF with PGD, spontaneous pregnancy with or without CVS or amniocentesis, gamete donation, and child adoption.

Following genetic counseling, two women achieved spontaneous pregnancies. One 24-year-old woman, whose 26-year-old husband had a reciprocal translocation 46, XY,t$^{6;22}$(p21.3;q13.3) and a history of four previous first-trimester spontaneous abortions, became pregnant and received intensive prenatal care and psychological support. Noninvasive prenatal genetic screening results were expected, and the pregnancy ended with the timely physiological delivery of a phenotypically usual girl with a karyotype of 46, XX. Another 39-year-old woman with a history of two previous first-trimester spontaneous abortions, who had a reciprocal translocation 46, XX-,t$^{5;16}$(p12;q22), also achieved spontaneous pregnancy. At 18 weeks, fetal balanced translocation (similar to the maternal) was detected by amniocentesis. The pregnancy was maintained and ended with the physiological delivery of a phenotypically normal fetus.

Revealing the natural causes of RPL by karyotyping couples might benefit these couples and the experts managing their cases. Our results indicate that karyotyping couples with RPL without a history of delivering abnormal fetuses is reasonable, as chromosomal anomalies among them are not rare.[8,2] Balanced chromosomal rearrangement in one partner can result in an unbalanced translocation in offspring, and phenotypic consequences (abortions or abnormal live births) depend on the specific duplicated or deficient chromosomal segments.[1,2] These chromosomal disorders can often be clinically revealed mainly by spontaneous abortions.[3,13]

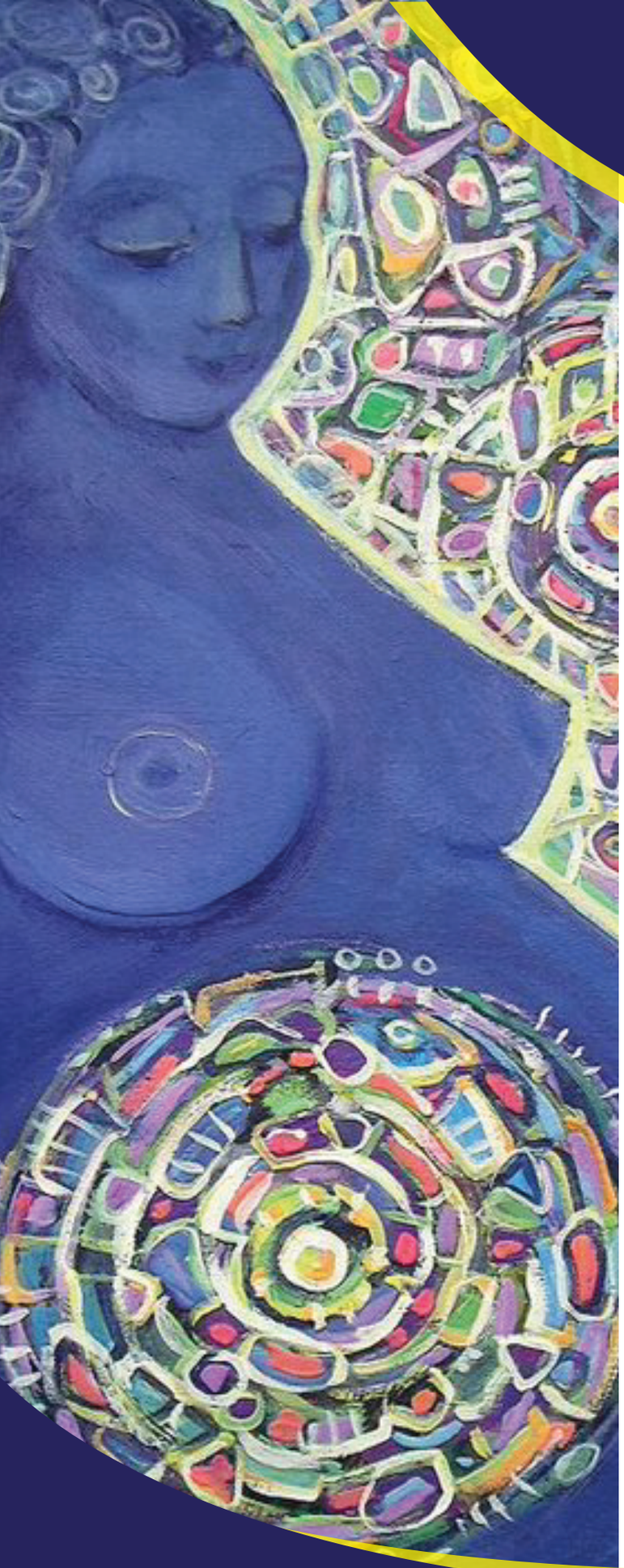
## CONCLUSION

In couples with RPL and without a history of delivery with the abnormal fetus, when the chromosomal status of previous miscarriages is unknown, considerable frequency of balanced structural chromosomal anomalies (with prevalence in male partners- 6/2) indicates on the reasonability of karyotyping of such couples, especially when the male partner is subfertile.

## REFERENCES

1. Simpson JL, Elias S, Martin AO. Genetics of spontaneous abortions. In: Recurrent Pregnancy Loss: Causes, Controversies and Treatment. CRC Press; 2015: 29-42.

2. Rabinowitz M, Ryan A, Gemelos G, Hill M, Baner J, Cinnioglu C, Banjevic M, et al. Origins and rates of aneuploidy in human blastomeres. *Fertil Steril.* 2012; 97(2): 395-401.
3. Elhady GM, Kholeif S, Nazmy N. Chromosomal aberrations in 224 couples with recurrent pregnancy loss. *J Hum Reprod Sci.* 2020; 13(4): 340-348.
4. Suzumori N, Sugiura-Ogasawara M. Genetic factors as a cause of miscarriage. *Curr Med Chem.* 2010; 17(29): 3431-3437.
5. Li S, Chen M, Zheng PS. Analysis of parental abnormal chromosomal Karyotype and subsequent live births in Chinese couples with recurrent pregnancy loss. *Sci Rep.* 2021; 11: 20298.
6. Ashalatha PR, Priya N, Manju M, Shyja. Recurrent pregnancy loss – chromosomal anomalies in couples. *Int J Biomed Res.* 2021; 12(2): e5576.
7. Simpson JL, Elias S, Martin AO. Parental chromosomal rearrangement associated with repetitive spontaneous abortion. *Fertil Steril.* 1981; 36(5): 584-590.
8. Goddijn M, Joosten JHK, Knegt AC, van der Veen F, Franssen MTT, et al. Clinical relevance of diagnosing structural chromosomal abnormalities in couples with repeated miscarriage. *Hum Reprod.* 2004; 19: 1013-1017.
9. Simpson JL, Elias S, Martin AO. Translocations are infrequent among couples having repeated spontaneous abortions but no other abnormal pregnancies. *Fertil Steril.* 1989; 51(5): 811-814.
10. Rajangan S, Tilak P, Aruna N, Devi R, et al. Karyotyping and counseling in bad obstetric history and infertility. I*ran J Reprod Med.* 2007; 5(1): 7-12.
11. Tharapel AT, Tharapel SA, Bannerman RN. RPL and parental chromosome abnormalities: a review. *Br J Obstet Gynaecol.* 1985; 92(9): 899-914.
12. Kochhar PK, Ghosh P. Reproductive outcomes of couples with recurrent miscarriage and balanced chromosomal abnormalities. *J Obstet Gynaecol Res.* 2013; 39: 113-120.
13. Alibakhshi R, Nejati P, Hamani S, MirAhadi N, Jalilian N. Cytogenetic analysis of 570 couples with recurrent pregnancy loss: reporting 11 years of experience. *J Hum Reprod Sci.* 2020; 13(3): 216-220.
14. Carp H. Should fetal karyotyping be performed in RPL? Yes. In: RPL Causes, Controversies and Treatment. CRC Press; 2015: 43-49.
15. Borochowitz Z. Should fetal karyotyping be performed in RPL? No. In: RPL Causes, Controversies and Treatment. CRC Press; 2015: 49-55.
16. Kuttech WH, Raymond WK, Brezina PR. A new algorithm for evaluation and treatment of RPL. In: RPL Causes, Controversies and Treatment. CRC Press; 2015: 389-400.
17. Mierla D, Stoian V. Association of pericentric inversion of chromosome 9 and infertility in Romanian population. *Maedica* (Buchar). 2012; 7(1): 25-29.
18. Simpson J, Bombard A. Spontaneous abortion. In: Edmunds KB, ed. Spontaneous Abortion. Oxford: Blackwell; 1987: 51-76.
19. Nonaka T, Takahashi M, Nonaka C, Enomoto T, Takakuwa K. The analysis of chromosomal abnormalities in patients with recurrent pregnancy loss, focusing on the prognosis of patients with inversion of chromosomes. *Reprod Med Biol.* 2019; 18: 296-301.



# GGRC

**GGRC Ambulatory Service integrates "one-stop" clinics and "day surgery" operations as an alternative to traditional outpatient consultations and inpatient surgery. Our commitment is to advance reproductive healthcare for both women and men, instilling hope and confidence in our prospective patients.**
**Our services encompass:**

- **Treatment for infertility**
- **Screening and management of gynecological disorders**
- **Care for endometriosis**
- **Management of congenital reproductive system disorders**
- **Treatment of sexually transmitted diseases**
- **Diagnosis and treatment of cervical pathology**
- **Colposcopy**
- **Microscopic and computer-assisted analysis of testicular fluid**
- **Pregnancy monitoring**
- **Sono hysterography**
- **Endocrine gynecology**
- **Aesthetic endocrinology (addressing conditions like hirsutism, acne/seborrhea, and weight concerns)**
- **Neuroendocrinology (focused on climacteric and premenstrual syndromes)**
- **Placement of intrauterine devices (IUDs)**

**AT GGRC AMBULATORY SERVICE, OUR PRIMARY GOAL IS TO OFFER A COMPREHENSIVE ARRAY OF REPRODUCTIVE HEALTHCARE OPTIONS. THESE INCLUDE CONSERVATIVE, SURGICAL, AND ASSISTED REPRODUCTIVE TECHNIQUES, SUCH AS INTRAUTERINE INSEMINATION (IUI) AND IN VITRO FERTILIZATION (IVF), AS WELL AS INNOVATIVE THERAPIES LIKE STEM CELL AND PRP THERAPY.**


+995 32 2 509 509
+995 544 44 83 43
Tbilisi, 51g V. Barnovi str.

ggrcreproduction www.ivfggrc.com info@ivfggrc.com

*New Word in*
*Reproductive Medicine*

GGRC has established partnerships with leading specialists from Germany, Israel, Turkey, Russia, Belarus, and Ukraine. Georgian patients can consult with these specialists online. The clinic utilizes modern treatment methods and follows the guidelines of European clinics. In addition to collaborating with foreign companies in the medical tourism sector, GGRC's unique surrogacy-donation program sets it apart. This program connects Georgian surrogate mothers with foreign childless couples, providing a ray of hope. The clinic's corporate social responsibility includes the charity fund "For You," which supports Georgian childless couples through a co-financing program for in vitro fertilization. Notably, GGRC is the first and only reproductive clinic in Georgia to have obtained the ISO standard, holds a license from the American Laboratory Quality Standard FDA, and is accredited by the Israeli Ministry of Health

*Together for new life!*

# SUPERCHARGED MECHANICAL STROMAL-CELL TRANSFER (MEST)

***COPCU H. ERAY**, MD*
*Izmir, Turkey*

## SUMMARY

PRP and fat-derived stromal cell applications are the most commonly used regenerative medicine methods. PRP has a broad spectrum of indications. Due to their advantages, mechanical methods have recently become very popular in fat-derived stromal cell applications. Combining these two methods has produced more successful results, providing reassurance about the effectiveness of the MEST method. This combination combines two products obtained separately before they are administered to the patient. In this study, fat tissue and blood samples obtained from eight volunteers were mixed with PPP, a new idea not previously reported in the literature, and stromal cells were obtained mechanically with sharp blades (adinizing). Later, the obtained PRP was added to the final product and became "supercharged." The results were tested by the dual fluoroscopy method for cell number and viability, and the results obtained were analyzed statistically. By adding the plasma to the oil before stromal cells were obtained and cutting with sharp blades by mechanical separation, twice the volume and 4.7 times more cells were obtained compared with that obtained in the saline group ($P < 0.001$). We believe that the reason for this is the "binding" effect of the proteins in the plasma. This approach provided a higher cell count using PPP, a "waste product," and increased potential efficiency by adding PRP. However, the clinical results of this innovative method should be evaluated with advanced clinical studies. (Plast Reconstr Surg Glob Open 2021; 9: e3552; doi: 10.1097/GOX.0000000000003552; Published online May 10, 2021)

**Keywords:** PRP, fat-derived stromal cells, regenerative medicine, MEST method, PPP, cell viability, mechanical separation

## INTRODUCTION

In many medical disciplines, regenerative medicine has recently been a fast-growing and popular trend. Using fat-derived stromal cells and blood-derived platelet-rich plasma (PRP) is one of the

most common applications.[1] Stromal cells are obtained mechanically rather than enzymatically, not only because of legal restrictions but also because such procedures are more accessible and are capable of obtaining more cells efficiently and economically.[2] Obtaining stromal cells from adipose tissue by enzymatic method has been described elsewhere in detail.[3] To date, many devices have been applied in different ways. However, consensus has yet to be reached on the definition of the final product or even the preparation protocols in mechanical ways.[4] Copcu and Oztan, in their study published in 2020 on using sharp-knife systems, obtained a high number of stromal cells mechanically without creating blunt-force pressure.[2] The name they gave to the procedure of cutting fat tissue with a sharp knife was “adinizing” and represents the first time indication-based protocols were established for the final product, its desired physical structure (solid, liquid, emulsified), and the required number of cells. Unlike enzymatic methods, they suggested that the term total stromal-cell (TOST) should be applied to the final product instead of stromal vascular fraction (SVF).[4] PRP, on the other hand, has a much longer history than stromal cells, and many methods are used successfully regarding the effects of growth factors on wound healing and regeneration.[5] In this study, as an innovative alternative to the saline solution used in the indication-based protocols, the process of cutting with sharp blades (adinizing) was performed by combining platelet-poor plasma (PPP) and condensed fat. Thus, by using plasma stromal as a “binder” for cells, the aim was to obtain more cells and greater volume.

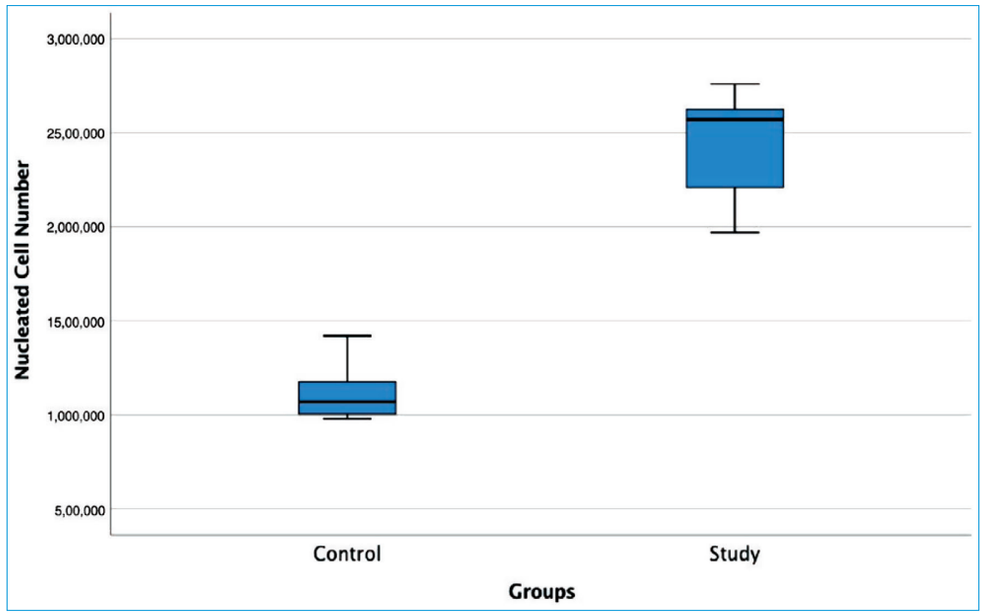
## METHODS

This study was conducted according to the standards of good medical practice (ICH-E6) and the principles of the Declaration of Helsinki. All patients were provided detailed information preoperatively, and they gave written consent for all surgical procedures, anesthesia, intraoperative video recording, and photography. In addition, a written consent form was obtained from the patients stating that they willingly donated their adipose tissue for laboratory analysis. This study used a patented CE marking and ISO 13485-certified blade system, and rules of minimal manipulation were followed. No enzymes and similar chemicals were used, and the structure of the fat tissue was not altered. A TriCell PRP kit (Rev-Med Inc, Korea) was used to obtain PPP. Twenty-seven cm3 of venous blood was mixed with 3 cm3 citrates. It was first centrifuged at 3200 rpm for 4 minutes, then at 3300 rpm for 3 minutes, and after the second centrifuge, the PPP in the second chamber of the kit was automatically obtained. Under local anesthesia, 15 cm3 of adipose tissue was harvested from the abdominal area with a 3-mm-diameter 4-hole cannula and then centrifuged at 500 G for 2 minutes, and condensed fat was obtained by discarding tumescent fluid and blood elements.

An estimated 5 cm3 condensed fat was mixed with 5 cm3 PPP in the study group, and 5 cm3 saline in the control group, and then the adinizing process was performed with 2400-µm, 1200-µm, and 600- µm diameter ultra-sharp blades, respectively (Adinizer, BSL-rest, Korea) with 25 back-and-forth movements between the two injectors. Finally, stromal cells were obtained by centrifugation at 1200 G for 5 minutes. The final product, total stromal cells (TOST), was received mainly in liquid form. (See Video [online], MEST preparation.) Total viable nucleated cell recovery and the viability percentage were determined using a LunaStem Automated Fluorescence Cell Counter device (Logos Biosystems, South Korea) with acridine orange/propidium iodide stain in each delivery method before and after the process. After the process was completed, PRP was added to TOST.

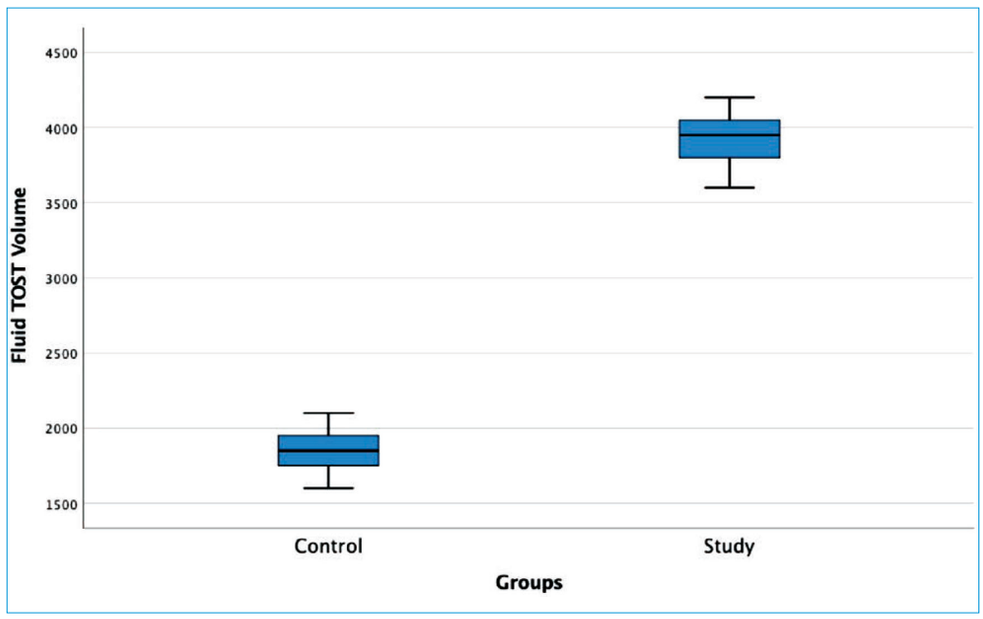
Thus, stromal cells were obtained mechanically from adipose tissue using PPP simultaneously, and a much stronger effect was expected by adding PRP obtained from blood to TOST.

***Figure 1.*** ***Comparison of nucleated cells in milliliters.***



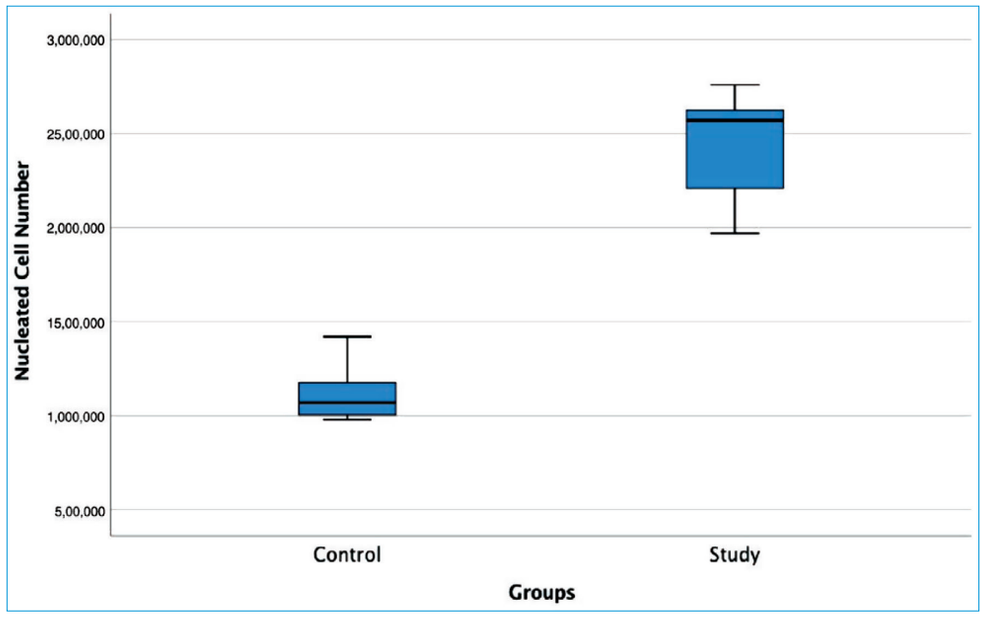

*While an average of 1.11 x 106 ± 1.46 × 105 nucleated cells were obtained in the control group, this number was 2.44 x 106 ± 2.99 × 105 in the study group. The 2.2-fold difference between them was statistically significant (<0.001).*

***Figure 2.*** ***Comparison of volumes of total stromal cells (TOST ).***




*While an average of 1.85 ± 0.16 mL TOST was obtained after the procedure in the control group, this volume was 3.92 ± 0.19 mL in the study group. The 2.1-fold difference between them was statistically significant (<0.001).*

***Figure 3.*** ***Comparison of total nucleated cells in 10 mL condensed fat.***




*When 10 cm3 of condensed fat tissue was taken as reference in the control group, an average of 4.11 × 106 ± 6.78 × 105 stromal cells were obtained after all procedures, while this number was 19.16 x 106 ± 2.58 × 105 in the study group. The 4.7-fold difference between them was statistically significant (<0.001).*

## RESULTS

Supercharged mechanical stromal cell transfer (MEST) was tested in 8 cases, and results are presented in Figures 1-4. Figure 5 presents components of whole blood and agonized fat after centrifugation.

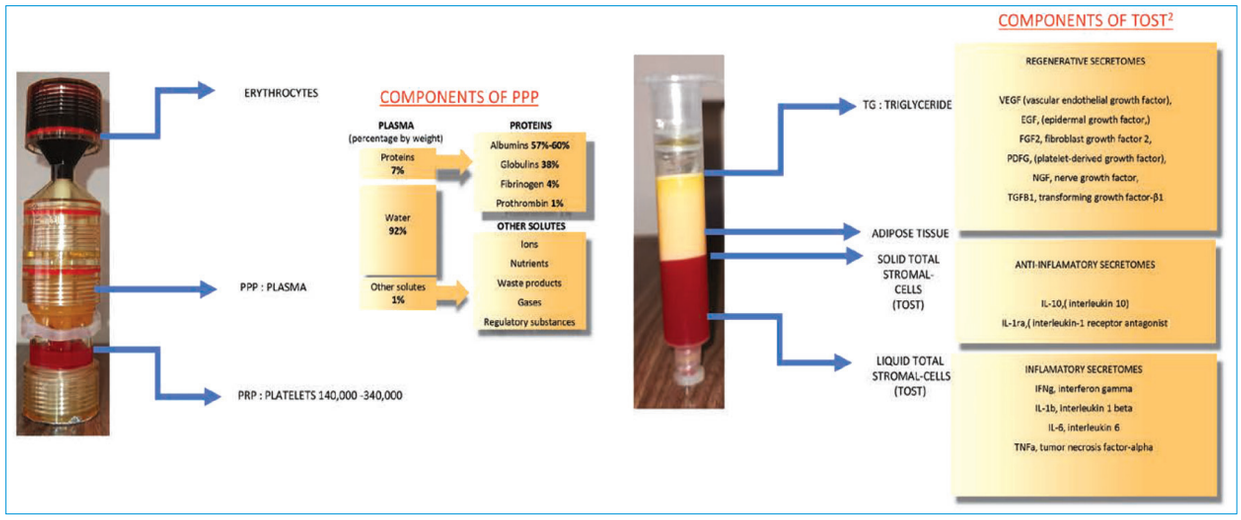
***Figure 4.*** ***Comparison of results of control and study group.***

| | Control group | Study group | P |
|---|---|---|---|
| **Nucliated Cell Number in ml.** | 1,11 x $10^6$ ± 1,46 x $10^5$ | 2,44 x $10^6$ ± 2,99 x $10^5$ | <0.001 |
| **Fluid TOST Volume ml.** | 1,85 ± 0,16 | 3,92 ± 0,19 | <0.001 |
| **Total Nucliated Cell Number in 10 cc Adipose Tissue** | 4,11 x $10^6$ ± 6,78 x $10^5$ | 19,16 x $10^6$ ± 2,58 x $10^5$ | <0.001 |
| **Viability (%)** | 92,25 ± 3,19 | 92,13 ± 1,56 | 0.922 |
| **Average Nucleated Cell Size (µm)** | 9 ± 2 | 8 ± 3 | 0.896 |

*(The data analysis was done using IBM SPSS Statistics for Windows (version 21.0; IBM Corp., Armonk, NY). The descriptive statistics were given as mean ± SD. The normal distribution of the numerical variables was determined using the Shapiro-Wilk normality test. If the data complied*

*with a normal distribution, the statistical differences between the groups were evaluated using the 1-way analysis of variance and post hoc tests. Mann-Whitney U tests were used if the data did not comply with a normal distribution. A P value of <0.05 was considered to be statistically significant.) The study group found 2.2 times more nucleated cells in 1 mL (<0.001). As a result of the process, TOST was obtained at 2.1 times higher volume (<0.001). When 10 cm3 of condensed adipose tissue was taken as a reference, a total of 4.7 times more stromal cells was obtained (<0.001). There was no statistically significant difference in viability and average cell size in the study and control groups (0.922, 0.896).*

***Figure 5.*** ***Components of whole blood and adinized condensed adipose tissue after centrifugation.***




## DISCUSSION

When PRP is obtained in conventional applications, the plasma part (called PPP) is discarded, and the PRP part is applied in a broad spectrum due to the growth factors it contains.[5] The clinical application of PRP by combining it with stromal cells obtained from adipose tissue both enzymatically and mechanically is a concept that has been introduced previously.[1,5-7] Stevens et al. described this approach as plate let-rich stroma and reported that it would yield more successful results in androgenic alopecia and osteoarthritis than PRP alone or SVF alone.[1,6] Similarly, Butt et al. obtained stromal cells from adipose tissue mechanically. They emphasized that its combination with PRP provided results far superior to the sole use of PRP.[7] Our study differs from all stromal cell PRP combinations in the literature.[1,5-7] In our research, for the first time, we obtained stromal cells from adipose tissue by mixing 50% of the condensed adipose tissue with PPP before the procedure, mechanically using sharp blades. In the technique described previously by Copcu,[2] indication-based protocols were defined to obtain a higher number of stromal cells in liquid form (conventionally, they are in solid or emulsified fatty consistency) by mechanical stromal cell recovery processes. In this approach, when the adipose tissue was mixed with saline at a rate of 50% before adinizing, more cells and total stromal cells were obtained in liquid form. This may be due to polarity and density. Adipocytes have no positive and negative charged points – the charge

distribution is equal, indicating that they are nonpolar. Nonpolar molecules do not dissolve well in polar structures like water; they tend to repel each other and remain separated, even when shaken vigorously.[8]

However, mesenchymal stromal cells respond to superficial electric charges, unlike adipocytes.[9] The back-and-forth movements described above release the stromal cells when the adipose tissue passes through the metal blades between the two injectors. However, the kinetic energy generated at this time affects the polarity of the cells. In pre-adinizing dilution, this electrical polarity affects the relationship between saline and stromal cells and helps separate stromal cells more successfully. Zimmerlin also described the intra-tracheal route of stromal cells combined with fibrin as a glue.[10] In the innovative approach we are presenting in this study, plasma is used instead of saline. The content of plasma is 7% protein and 4% fibrinogen. Thanks to these structures in the plasma acting as a binder for stromal cells, it is possible to obtain both twice the volume and 4.7 times more stromal cells.

## CONCLUSION

At the same time, adding the obtained PRP to this final product will allow the application of "supercharged" cells in a much stronger sense, as described in many studies in the literature. However, advanced clinical studies are required to prove this hypothesis.

## REFERENCES


1. Stevens H.P., Donners S., de Bruijn J. Introducing platelet-rich stroma: platelet-rich plasma (PRP) and stromal vascular fraction (SVF) combined to treat androgenetic alopecia. *Aesthet Surg J.* 2018; 38: 811–822.
2. Copcu H.E., Oztan S. New mechanical fat separation technique: ARAT and MEST. *Aesthetic Surg J Open Forum.* ojaa035.
3. Raposio E., Bertozzi N. Isolation of ready-to-use adipose-derived stem cell (ASC) pellet for clinical applications and a comparative overview of alternate methods for ASC isolation. *Curr Protoc Stem Cell Biol.* 2017; 41: 1F.17.1–1F.17.12.
4. Copcu H.E., Oztan S. Not stromal vascular fraction (SVF) or nanofat, but total stromal-cells (TOST): A new definition. Systemic review of mechanical stromal cell extraction techniques. *Tissue Eng Regen Med*. 2021; 18: 25–36.
5. Alves R., Grimalt R. A review of platelet-rich plasma: History, biology, mechanism of action, and classification. *Skin Appendage Disord.* 2018; 4: 18–24.
6. Stevens H.P., van Boxtel J., van Dijck R., et al. Platelet-rich STROMA, the combination of PRP and tSVF, and its potential effect on knee osteoarthritis. *Appl Sci.* 2020; 10: 4691.
7. Butt G., Hussain I., Ahmad F.J., et al. Stromal vascular fraction enriched platelet-rich plasma therapy reverses the effects of androgenetic alopecia. *J Cosmet Dermatol.* 2020; 19: 1078–1085.
8. Boston University School of Public Health. Basic Cell Biology. Available at http: //sphweb.bumc.bu.edu/otlt/MPH Modules / PH/PH709_BasicCellBiology/PH709_BasicCellBIology4.html. Accessed April 20, 2021.

9. Khlusov I.A., Dekhtyar Y., Sharkeev Y.P., et al. Nanoscale electrical potential and roughness of a calcium phosphate surface promote the osteogenic phenotype of stromal cells. *Materials* (Basel). 2018; 11: 978.
10. Zimmerlin L., Rubin J.P., Pfeifer M.E., et al. Human adipose stromal vascular cell delivery in a fibrin spray. *Cytotherapy*. 2013; 15: 102–108.

# CURRENT ADVANCES IN CARRIER SCREENING AND AN INNOVATIVE APPLICATION: CARRIER CHECK

***AKTUNA SÜLEYMAN**, Prof.*
*Mikrogen Genetic Diagnosing Laboratory Yüksek İhtisas University Faculty of Medicine Department of Medical Genetics, Ankara, Turkey*

## SUMMARY

More than 1800 inherited RDs are estimated to vary frequently across geographic areas due to population genetic diversity, environmental or societal factors, or survival rates.[1] In Europe, 12 RDs account for 90% of all cases;[2] according to Mikrogen's own PGT-M data of ~2500 patients from Turkey and Middle Eastern countries, the overall rate of these same 12 diseases remains at 35%. Due to high consanguinity rates, rare heterozygous conditions manifest as homozygous, resulting in offspring affected by rare or novel syndromes. Europe is becoming increasingly heterogeneous, with growing proportions of individuals reporting mixed ancestry, increasing numbers of mixed-ethnicity couples, and migration waves.[3] Currently, there are 3.6 million registered Syrian refugees in Turkey,[4] and 320.000 refugees from other nationalities (Iraqi, Afgan, others) are also registered.[5] The Turkish Statistical Institute states that 30% of Syrian refugees are of reproductive age, and in the last four years, 518.730 refugee newborns were recorded.[6] In 2019, 27 million people migrated to Europe, 21% from Middle Eastern countries[7]. Due to continuous migration, high reproductive rates, and consanguinity of Syrian refugees, the fight against rare diseases has gained a new dimension for Europe as a public health priority.[8] Unknown genetic variants of common RDs and novel syndromes are being introduced into the genetic makeup of Europe and are expected to increase in frequency in the short term. Preconception screening is a crucial component of preventing future generations from RDs.

This points to the need for a screening test covering the most prevalent diseases without compromising test sensitivity and detecting diverse variants from European and Middle Eastern genetic pools to respond to the diversity of geography, becoming increasingly multi-ethnic and multi-cultural. Most preconception screening tests report only Class I and II variants, which are pathogenic (99% certainty) or likely pathogenic (90% certainty), respectively, to stay safe. Howev-

er, carrier status information of an RD can be carried on a novel variant, even if the susceptibility gene is well studied and the variant's pathogenicity still needs to be clarified. Thus, detecting and interpreting Class III variants of uncertain significance (VUS), which can also be detected in unlikely genome regions, like intronic and deep intronic regions, requires additional analysis and interpretation attention. Certain areas of the genome are challenging to cover both by wet-lab and in-silico techniques. Regions containing pseudogenes (i.e., CYP21A2), chromosomal mutations (i.e., deletions, duplications), or CNVs require special attention due to potential overcalls (false positives) or loss of detection precision when using an NGS-based test. Conventionally, these problems are overcome by performing additional tests such as MLPA, which brings additional costs. Population-based databases provide information on the variant frequencies for RDs, but specific ethnic populations, age groups, and genders remain under-represented. Therefore, how many of the >1000 known AR conditions should be included in an ECS panel is still debatable.[10] Carrier Check's concise gene and target content will be selected using a comparative and integrative gene selection method, scanning various sources of existing ECS tests and in-house registry data. ECS panels include a collection of causative genes with differing technical difficulties in detecting genetic variants residing in both coding and non-coding regions. Gene panel design should take a comprehensive perspective on the properties of included genes, facilitating gene-capture tool selection, sequencing depth determination, and dedicated data analysis.[2] An integrated and iterative workflow for assay and analysis pipeline development will follow. Detecting variants in complex regions in the genome requires multiple workflows and assays. For technically challenging variant types, novel solutions will be developed and tailored to the assay based on Genoox's proprietary machine-learning-based bioinformatic tools, both by algorithm design and model training. The methods will be thoroughly validated in this project using orthogonal methods. Variant classification is only sometimes solid information; the classification of a variant can change depending on the accumulated data. Moreover, the classification of a variant can differ among different databases, and the reporting decision of a VUS can be problematic. To tackle this problem, Carrier Check will be integrated with Genoox's cloud-based public interpretation tool.

**Keywords:** Inherited RDs, preconception screening, genetic variants, consanguinity, multi-ethnic populations, class III variants, genoox bioinformatics

# KEY ASPECTS OF PREIMPLANTATION GENETIC TESTING (PGT)

***BALTACI VOLKAN**, Prof.*
*Mikrogen Genetic Diagnosing Laboratory Yüksek İhtisas University Faculty of Medicine Department of Medical Genetics, Ankara, Turkey*

## SUMMARY

Preimplantation Genetic Testing (PGT) encompasses three types: Preimplantation Genetic Testing for Monogenic Disorders (PGT-M), Preimplantation Genetic Testing for Aneuploidy (PGT-A), and Preimplantation Genetic Testing for Structural Rearrangements (PGT-SR). These PGT approaches have unique crucial points that can alter the test's confidence, applicability, and efficiency. PGT-M for genetic diseases that can be diagnosed has been applied for many years. Simultaneous monogenic disease testing and euploid embryo selection (combined PGT) have become possible with the development of Whole Genome Amplification (WGA) technologies. With the widespread use of whole exome and genome sequencing technologies, the range of single-gene diseases referred to PGT-M has expanded. This has resulted in a significant increase in the number of setup studies conducted for rare diseases. Trophectoderm biopsy is widely performed for PGT-A, yet the efficiency of PGT-A results in different IVF centers shows substantial variability. Most PGT-A samples are outsourced, a process commonly referred to as 'transport PGT, 'where the samples are sent to other centers for testing. This is often done in conjunction with the reported findings claiming that the potential discrepancies in the efficiency of Whole Genome Amplification (WGA) quality parameters of biopsy cells obtained from different centers might originate from the diversity in the techniques of biopsy practitioners. PGT-SR for detecting chromosomal rearrangements using Next Generation Sequencing (NGS) has been applied with a resolution of ≥ 5-20 Mb, the declared detection limit of commercially available kits. However, some patients still carry chromosomal rearrangements below the detection limit. Therefore, the utilization of a customized analysis approach is required for the effective use of this technology in the detection of a broad range of chromosomal imbalances.

**Keywords:** PGT, monogenic disorders, aneuploidy, structural rearrangements, whole genome amplification, trophectoderm biopsy, next-generation sequencing.

# NEW CHALLENGES OF ANEUPLOID EMBRYO TESTING BY NON-INVASIVE CFDNA

***KORNILOV NIKOLAY**, MD*
*Medical Director of NGC Clinics: St. Petersburg, Moscow, Ufa, Vladivostok, Vladikavkaz, Kirov*

## SUMMARY

The high incidence of chromosomal aneuploidy in human gametes and embryos is a major cause of in vitro fertilization (IVF) failure and miscarriage. To improve live birth rates with single embryo transfer, the use of preimplantation genetic testing for aneuploidy (PGT-A) has significantly increased. PGT encompasses methods that allow embryos to be tested for inherited conditions or screened for chromosomal abnormalities. However, PGT relies heavily on invasive trophectoderm (TE) biopsy, which can hinder clinical outcomes and pose unknown health risks in the long-term development of the embryos. Additionally, embryo biopsy requires specialized equipment and extensive expertise, making it difficult to standardize and challenging to meet the demand in every IVF-eSET treatment. Therefore, an effective non-invasive chromosome screening approach is highly demanded to prioritize embryo transfer in clinical IVF-eSET practice.

In recent years, an increasing number of studies have evaluated the feasibility of SCM-based niPGT-A approaches, with some encouraging results. The success rate of cfDNA amplification and detection is high, ranging from 73% to 100%. In a clinical context, Rubio et al. compared the outcomes of two groups of patients: one with both TE biopsy and SCM results showing euploidy and the other with TE biopsy-negative and SCM results showing aneuploidy. The transplant success rate for patients with both euploid TE and SCM results was more than double (52.9% vs. 16.7%) that of the latter group. Zero miscarriages were observed (0/9) when both the TE and SCM results indicated euploid embryos.

Moreover, a single-center clinical trial conducted in 2019 using niPGT-A on patient groups with either repeated implantation failures (≥3) or repeated miscarriages (≥3) showed a clinical pregnancy rate of 58% (29/50) and a spontaneous miscarriage rate of ~10% (3/29), resulting in the successful delivery of 27 babies. While the scale of these studies and clinical trials was small, cfDNA-based

niPGT-A demonstrated that it could reduce miscarriage rates and improve sustained pregnancy rates.

The current report focuses on the consistency of aneuploidy detection between cell-free DNA (cfDNA) and embryos. However, comparing consistency requires consideration of many factors, such as the definition of consistency, sampling methods, and analysis techniques. We aimed to compare the advancements and limitations of non-invasive PGT (niPGT)-A.

In our NGC clinic in St. Petersburg, more than 70,000 trophectoderm biopsies and 40,000 NGS tests have been performed in our NGC genetic lab. Since 2018, we have started testing cfDNA from spent media. Initially, we validated our approach by comparing sequencing results from 5-10 trophectoderm cells of a blastocyst and cfDNA from the same embryo. To date, 550 cfDNA examinations have been performed in our practice for embryo selection in IVF cycles. Non-invasive testing has required different interpretation approaches, particularly concerning mosaic results.

This report will present more details on the limitations and peculiarities of both laboratory and clinical practices related to niPGT-A.

**Keywords:** Chromosomal aneuploidy, preimplantation genetic testing, trophectoderm biopsy, non-invasive PGT-A, Cell-free DNA, embryo selection, IVF outcomes.

# DETERMINATION OF DNA DAMAGE FROM SPERM PREPARATION METHODS IN ICSI CYCLES AND MITIGATION WITH SPERM CHIP METHOD

***BIROL AYDIN, GUDKOVA DARIA, DOROFEYEVA ULIANA, STRELKO GALINA, ULANOVA VERONIKA, MALIUTA OLGA, PISCHANA TETIANA, KOROBKO MAKSYM, KOTLIAROVA OLENA, LYZUHOB OKSANA***

## SUMMARY

Male factor infertility, responsible for nearly 50% of infertility cases, often involves DNA damage in sperm that standard semen analysis cannot detect. This study evaluates the effectiveness of sperm chip technology in improving outcomes in ICSI cycles using donor oocytes. We retrospectively analyzed fertilization and blastocyst formation rates for two groups from 2018-2019: a control group with standard sperm DNA fragmentation and a study group with >30% fragmentation. Results showed that sperm chip technology significantly improved fertilization (90.4% vs. 83.3%), blastulation (68.3% vs. 57.5%), and pregnancy rates (70.4% vs. 59.3%) compared to density gradient centrifugation. Our findings suggest that microfluidic sperm chips enhance embryo development and clinical pregnancy rates, offering a promising approach for treating male infertility even with donor oocytes.

**Keywords:** Male factor infertility, Sperm DNA fragmentation, sperm chip technology, ICSI cycles, donor oocytes, embryo development, pregnancy rates

## INTRODUCTION

Almost 50% of infertility cases may be associated with male factors. However, standard semen analysis does not provide information about the genetic constitution of the sperm, which is essential for normal embryo development. A high level of DNA damage and aneuploidy in sperm cells can cause male infertility that conventional examinations cannot detect. Therefore, sperm chips based on microfluidic channel mechanics appear to be a promising tool for selecting physiologically competent sperm for fertilization, thus increasing the efficiency of male infertility treatment. But does this method benefit oocyte donation programs, or can young and healthy oocytes compensate for sperm abnormalities by themselves?

## METHODS

To assess the influence of sperm DNA fragmentation on the development of embryos created from donor oocytes, fertilization and blastocyst formation rates were retrospectively estimated for two groups of cases from 2018 to 2019. The control group (n=40) included couples with average DNA fragmentation assay results, while patients whose sperm DNA fragmentation rate initially exceeded 30% were assigned to the study group (n=40). To investigate sperm chip efficacy, we compared the results of oocyte donation cycles where fertilization was done with sperm with a high DNA fragmentation index. In the control group (n=50), sperm processing was done using the density gradient centrifugation method, while in the study group (n=50), sperm chip technology was used for sperm preparation. DNA fragmentation of raw and washed sperm was tested with the Halo sperm kit (Halotech). “Fertile” sorting chips were used for sperm processing. Fertilization was performed using the ICSI method. Fertilization, good blastocyst (AA, BA/AB, and BB grades), and ongoing pregnancy rates were calculated for each cohort.

## RESULTS

Investigation of sperm DNA fragmentation impact on donor oocytes ICSI results showed that in the study group, the fertilization rate of donor cells was 77.2%. In contrast, in the group with standard sperm DNA fragmentation, it reached 84.7% (NS, $p>0.05$). The most significant difference was in the blastulation rate after fertilization with sperm with different DNA fragmentation indices. In the group with a high degree of sperm DNA fragmentation, only 37.4% of zygotes formed blastocysts, while in the control cohort, the blastocyst rate was 51.2%. This difference underscores the impact of the research. While assessing sperm sorting chip efficacy, we noted 83.3% fertilization, 57.5% blastocyst formation, and, after the transfer of two embryos, 59.3% pregnancy rates in the control group (mean male age – 33.7±4.2 years). In the study group (mean male age – 34.6±3.7), where sperm chip technology was used as the sperm preparation method, 90.4% fertilization, 68.3% blastulation, and 70.4% pregnancy rates (pic.2) were achieved, with a statistically significant difference in blastocyst rate and PR ($p<0.05$).

Thus, the use of microfluidic sorting chips for sperm processing significantly increased the probability of obtaining blastocysts for transfer and freezing and increased the chance of more clinical pregnancies for couples with male infertility factors.

## CONCLUSION

Since severe sperm DNA fragmentation negatively affects the embryologic step of IVF, careful sperm selection for fertilization may be a crucial step toward a positive cycle result. As microfluidic sperm chips have shown to enhance treatment effectiveness in terms of embryo development and clinical pregnancy rate, their potential to increase the efficacy of infertility treatment, even in cases of oocyte donation, is a reason for optimism.

TBILISI MEDIC

# ALL MEDICAL EQUIPMENT IN ONE SPACE!


Tbilisi Medic, a #1 Golden Brand company of 2021 is a long-time supporter of the medical field, importing and selling a large variety of medical products, equipment, specialized furniture, consumables, surgical tools and patient care supplies all across Georgia.

Tbilisi Medic strives to provide all of its customers with maximum possible comfort by offering services such as:

- PAYMENT BY INSTALMENTS
- DELIVERY
- ONLINE PURCHASE
- TECHNICAL SUPPORT

The company is the official and exclusive dealer and representative of the following brands in Georgia: global brands Johnson & Johnson, Bausch and Lomb, American brands Ortho-clinical Diagnostic and ASP, Japanese brand Nidek, Chinese brands Mindray and SonoScape, Turkish brand Turmed and others.

In addition to being the distributor, Tbilisi Medic also offers exclusive engineering services that allow it to provide timely and efficient technical assistance to its clients.

As of today, Tbilisi Medic has two offices in Tbilisi, the capital, and is represented by subsidiaries (Batumi Medic and Kutaisi Medic) in the regions. By cooperating with American, European and Asian brands, ensuring uninterrupted supply of high-tech goods and timely services, Tbilisi Medic facilitates and supports development of the medical field in Georgia.


**TBILISI:**
Saburtalo - 18a Iona Vakeli
588 885 217
Lubliana st. №28a (Dighomi)
032 2375177

**KUTAISI:**
str. Gamsakhurdia 22
577 124 231

**BATUMI:**
str. Bagrationi 196T.
577 12 20 29

## WHEREVER YOU MAY BE, JUST WISH TO CARE!

# HUMAN ERROR MEASUREMENT AND HUMAN ERROR REDUCTION WITH ELECTRONIC WITNESSING SYSTEM (EWS)

***AYDIN BIROL, GUDKOVA DARIA, DOROFEYEVA ULYANA, STRELKO GALINA, ULANOVA VERONIKA, MALIUTA OLGA, PISCHANA TETIANA, KOROBKO MAKSYM, KOTLIAROVA OLENA, OKSANA LYZUHOB***

## SUMMARY

This study evaluates the effectiveness of an Electronic Witnessing System (EWS) using RFID chips in reducing human errors during in vitro fertilization (IVF) processes. Analyzing data from 15,000 IVF cycles recorded between 2016 and 2020 across 36 clinics, we assessed error warnings at various stages, including oocyte pick-up, denudation, ICSI, dish change, embryo transfer, and sperm preparation. The EWS, employing electronic chips, wristbands, and barcode systems, secured biological materials throughout all laboratory procedures, reducing errors to minimal levels. While no error warnings were received during the cryopreservation phase, overall, 169 error warnings were recorded, highlighting areas needing improvement. The study concludes that EWS ensures biological material safety and reduces human errors. It is recommended for regular use in IVF, genetic, and biochemistry laboratories to enhance procedural accuracy and material integrity.

**Keywords:** Electronic witnessing system, RFID chips, IVF processes, error reduction, oocyte pick-up, embryo transfer, biological material safety

## INTRODUCTION

Human error in routine in vitro fertilization (IVF) can be measured with an Electronic Witnessing System (EWS). Using our RFID chip EWS, human error can be significantly reduced. Existing studies demonstrate that the EWS works effectively in all stages of IVF applications; however, improvements are needed in cryopreservation and software. The EWS should secure all stages of the IVF process, from when the patient enters the clinic to completing all laboratory procedures. Our study is designed to ensure the safety of biological material with EWS. It aims to reveal statistical data on a system that can be actively used in all laboratory processes. We also evaluated the

cryopreservation process and the performance of all IVF personnel with the system, highlighting the importance and effectiveness of the EWS in reducing human errors.

## METHODS

15,000 IVF cycles from 2016-2020 were recorded using the IVFID Electronic Witnessing System. Error warnings from 36 IVF clinics were analyzed, and error distributions were determined at each stage of IVF. Regular IVF patients, including egg donation and surrogacy groups, were registered. Errors at various IVF stages were identified by analyzing records of possible errors for each patient group. RFID electronic chips, electronic wristbands, and barcode systems were utilized at every stage for patient groups, securing biological materials throughout the entire laboratory process. The system recorded data via electronic chips through software and calculated it statistically. Human errors in the embryology and andrology laboratories were documented. Additionally, the system was supported with personal witnessing patient software, reducing the error rate to zero.

## RESULTS

Our study evaluated 15,000 IVF cycles, analyzing human error data from 36 different clinics. Error warnings were received in 169 out of 15,000 IVF cycles at various stages. Specifically, error warnings were received 14 times during the oocyte pick-up phase, 17 times during the denudation phase, 26 times during the ICSI phase, eight times during the dish change phase, 68 times during the embryo transfer phase (17 during the fresh embryo transfer phase and 51 during the thaw embryo transfer phase), and 36 times during the sperm preparation phase. When evaluating error distribution across different clinics, 23 out of 36 clinics reported error warnings at various stages. The RFID electronic chip system prevented human errors, providing visual and auditory warnings to the embryologist during procedures. No error warnings were reported during the cryo phase with the vitrification straw chip system. Individual embryologist performance revealed error warnings from 32 different embryologists.

## CONCLUSION

The purpose of EWS is to reduce human error and ensure the safety of biological materials. The system's use is essential at every stage in Embryology/Andrology Laboratories. While the system can alert specific human errors, 100% biological material safety cannot be guaranteed. Human factors will always exist, necessitating support from individual witnesses. Regular use of EWSs in IVF laboratories is crucial to prevent human error-based interferences with biological materials, and their use should be routine. Additionally, EWSs can be actively utilized in genetic laboratories during the IVF process and in biochemistry laboratories.

# METABOLIC ENDOTOXEMIA AND MALE INFERTILITY

***KHELAIA ALEKSANDER**, Prof.*
*National Center of Urology, Tbilisi, GeorgiaGeorgian German Reproduction Center, Tbilisi, Georgia*
*Georgian Urological Association, Tbilisi, GeorgiaCo-chair of the Andrological Section, Tbilisi, Georgia*
*European University, Tbilisi, Georgia*

## SUMMARY

Infertility affects 10-15% of couples of reproductive age. Metabolic syndrome (MetS), especially in younger populations, is a risk factor for fertility disorders. Obesity and high-fat diets disrupt gut mucosal barriers, leading to endotoxemia and systemic inflammation, which negatively impact male fertility. This review examines the relationship between MetS, gut microbiota dysbiosis, and male infertility. Studies show that high-fat diets increase gut permeability and endotoxin levels, impairing spermatogenesis and sperm motility. Probiotics and prebiotics have shown promise in improving gut barrier function, reducing endotoxemia, and enhancing sperm quality. Weight loss and dietary modifications also improve semen quality and reproductive hormones. There is a need for evidence-based preconception nutritional guidance for men. Further research is necessary to explore how diet impacts male reproductive function and to develop effective treatments for idiopathic male infertility using microbiota-targeted therapies.

**Keywords:** Infertility, metabolic syndrome, gut microbiota, male fertility, endotoxemia, probiotics, dietary modifications.

## INTRODUCTION

Infertility is a global health problem affecting 10–15% of couples of reproductive age. Lifestyle factors can impact male fertility through alterations in endocrine profiles, spermatogenesis, and sperm function. Identifying contributing factors to infertility may offer more straightforward and/or more effective therapeutic options than current treatments. The increasing worldwide prevalence of metabolic syndrome (MetS), especially in younger populations, is a risk factor for fertility disorders. Obesity and a high-fat or high-calorie diet can cause a breakdown in the gut mucosal barrier, leading to the passage of gut bacteria membrane remnants into the systemic circulation

and initiating chronic systemic inflammation. This inflammation, particularly in adipose tissue, is implicated in diet and obesity-related insulin resistance.[1] However, a direct correlation between MetS and male infertility remains unclear.

## METHOD

Gómez-Elías et al.[2] induced a metabolic syndrome-like condition in (C57BL/6xBALB/c) F1 male mice by feeding them a high-fat diet (HFD, 30% fat) for 19 weeks, while controls received a normal-fat diet (NFD, 6% fat). Ning Ding et al.[3] investigated if HFD-induced gut microbiota dysbiosis could influence spermatogenesis and sperm motility. Fecal microbes from HFD-fed or regular diet (ND)--fed male mice were transplanted to mice maintained on ND. Sperm count and motility were analysed. The study explored how diet impacts male reproductive function and developed evidence-based preconception nutritional guidance for men. Dardmeh et al. investigated the effect of probiotics (Lactobacillus rhamnosus) on sperm kinematic parameters, testicular weight, lipid profiles, and reproductive hormones in male mice. Maretti and Cavallini conducted a placebo-controlled study on the impact of prebiotic/probiotic therapy on testosterone levels and sperm quality in infertile men.

## RESULTS

HFD-fed mice exhibited increased body weight, hypercholesterolemia, hyperglycemia, and glucose intolerance, with more gonadal fat, lower epididymal weight, and decreased epididymal sperm count. Sperm analysis showed significant differences between HFD- and NFD-fed mice in sperm count, viability, morphology, and motility. Transplantation of HFD gut microbes into ND-maintained mice significantly decreased spermatogenesis and sperm motility and increased proinflammatory cytokines in the epididymis.[3] Obesity and high-fat diets result in changes to gut bacteria and increased intestinal permeability, leading to metabolic endotoxemia. Kelton Tremellen postulated that bacterial lipopolysaccharide (LPS) from the gut lumen into circulation is a critical inflammatory trigger underlying male hypogonadism.[4] Linn B. Hakonsen et al. observed that weight loss improved semen quality.[5] Karma L. Pearce et al. found that metabolic endotoxemia and its associated oxidative stress may drive sperm DNA damage in obese men.[6] Dardmeh et al.[7] showed probiotics could eliminate obesity's adverse effects on semen quality. Everard et al.[8] found prebiotic treatment improved gut barrier function and metabolic parameters. Valcarce et al.[9] demonstrated probiotics improved sperm quality in asthenozoospermic men. Maretti and Cavallini[10] reported a significant improvement in testosterone levels and sperm quality with prebiotic/probiotic therapy.

## DISCUSSION

Obesity and a high-fat/high-calorie diet cause changes in gut bacteria and intestinal permeability, leading to metabolic endotoxemia and systemic inflammation, negatively affecting male fertility. High-fat diets are more efficient in transporting bacterial endotoxin from the gut lumen into circulation. The relationship between diet composition and obesity involves interactions between dietary macronutrients. There is a clear need to explore further how diet impacts male reproductive function to develop evidence-based preconception nutritional guidance. Probiotics and pre-

biotics can improve gut barrier function, reduce metabolic endotoxemia, and positively impact sperm quality and reproductive hormones.

## CONCLUSION

Obesity and high-fat/high-calorie diets contribute to metabolic endotoxemia and systemic inflammation, negatively affecting male fertility. Lifestyle changes, including weight loss and dietary modifications, can improve semen quality and reproductive hormones. Probiotics and prebiotics offer potential therapeutic options for improving male fertility by enhancing gut barrier function and reducing metabolic endotoxemia. Further research is needed to develop evidence-based nutritional guidance for men to improve reproductive outcomes.

## REFERENCES


1. Mehta NN, McGillicuddy FC, Anderson PD, Hinkle CC, Shah R, Pruscino L, Grivennikov SI, Ley K, Mosser DM, Miller LS, Toliver-Kinsky T, de Souza LS, Ferreira RA, Sierra JC, Balter A, Mandell L, Schlaepfer DD, Tabas I, Stoffel M, Reilly MP. Experimental endotoxemia induces adipose inflammation and insulin resistance in humans. *Diabetes*. 2010; 59(1): 172-81. doi:10.2337/db09-0367
2. Gómez-Elías MD, Rodríguez-González GL, Ávila-González CC, Lara-Padilla E, Rivas-Arancibia S, Granados-Badillo A, López-Meza JE, Jiménez-Estrada M, Ortiz-Lazareno PC, Pérez-Camarillo S. Association between high-fat diet feeding and male fertility in high reproductive performance mice. *Sci Rep.* 2019; 9: 18546. doi:10.1038/s41598-019-54799-3
3. Ding N, Zhang X, Zhang XD, Zhang C, Jin J, Ma YH, Dong JY, Zhang YL, Wang YX, Ma ML, Guo YX, Huang CJ, Wei Y, Wang LH, Jin DM, Yang QL. Impairment of spermatogenesis and sperm motility by the high-fat diet-induced dysbiosis of gut microbes. *Gut*. 2020; 69(9): 1608-1619. doi:10.1136/gutjnl-2019-319127
4. Tremellen K, Pearce K. Dysbiosis of Gut Microbiota (DOGMA) – a novel theory for developing Polycystic Ovarian Syndrome. *Basic Clin Androl.* 2016; 26: 7. doi:10.1186/s12610-016-0032-1
5. Hakonsen LB, Thulstrup AM, Aggerholm AS, Olsen J, Bonde JP, Andersen CY, Bungum M, Ernst EH, Hansen ML, Gernow A, Ramlau-Hansen CH. Does weight loss improve semen quality and reproductive hormones? Results from a cohort of severely obese men. *Reprod Health.* 2011; 8: 24. doi:10.1186/1742-4755-8-24
6. Pearce KL, Tremellen K, Lopez-Villalobos N, Kang HJ, MacDonald C, Sheedy JR. Obesity-related metabolic endotoxemia is associated with oxidative stress and impaired sperm DNA integrity. *Basic Clin Androl.* 2019; 29: 6. doi:10.1186/s12610-019-0087-y
7. Dardmeh F, Alipour H, Gazerani P, Vaegter HB, Alipour B, Nielsen HI. Lactobacillus rhamnosus PB01 (DSM 14870) supplementation affects markers of sperm kinematic parameters in a diet-induced obesity mice model. *PLoS One.* 2017; 12(10) doi:10.1371/journal.pone.0185964
8. Everard A, Belzer C, Geurts L, Ouwerkerk JP, Druart C, Bindels LB, Guiot Y, Derrien M, Muccioli GG, Delzenne NM, de Vos WM, Cani PD. Cross-talk between Akkermansia muciniphila

and intestinal epithelium controls diet-induced obesity. *Proc Natl Acad Sci U S A*. 2013; 110(22): 9066-9071. doi:10.1073/pnas.1219451110

9. Valcarce DG, Herráez MP, Robles V. Probiotic administration improves sperm quality in asthenozoospermic human donors. *Benef Microbes.* 2017; 8(2): 193-206. doi:10.3920/BM2016.0142
10. Maretti C, Cavallini G. The association of a probiotic with a prebiotic (Flortec, Bracco) to improve the quality/quantity of spermatozoa in infertile patients with idiopathic oligoasthenoteratospermia: a pilot study. *Andrology*. 2017; 5(3): 439-444. doi:10.1111/andr.12340

# PREVENTION OF HPV RECURRENCE WITH HPV VACCINATION AFTER LASER VAPORIZATION AND CONIZATION IN REPRODUCTIVE-AGE PATIENTS WITH HSIL (PRELIMINARY STUDY)

***JUGELI MADONA**, MD, PhD*
*Caraps Medline, Department of Office Gynecology, Tbilisi, Georgia*
***MUSERIDZE NINO**, MD, PhD*
*Georgian German Reproduction Center, Tbilisi, Georgia*
***TEVDORASHVILI GEORGE**, MD, PhD*
*Tbilisi State Medical University, Department of Obstetrics and Gynecology, Tbilisi, Georgia*
***ANDGULADZE MARIAMI**, MD*
*Medical Center "LASER", Department of Obstetrics and Gynecology, Tbilisi, Georgia*

## SUMMARY

This study evaluates whether Gardasil vaccination can prevent the recurrence of Human Papilloma Virus (HPV) in patients treated for high-grade intraepithelial lesions (HSIL-CIN2) via laser surgery. The study included 145 patients with HSIL-CIN2 confirmed through Pap smear, colposcopy, biopsy, and immunohistochemistry (P16+). All patients underwent CO2 laser conization and vaporization. Post-surgery, 53 patients received Gardasil vaccination (control group), while 92 did not (study group). Follow-up involved Pap smears, colposcopy, and PCR detection of HPV types 6, 11, 16, 18, and 31 every three months for one year. The vaccinated group showed a statistically significant reduction in HPV-induced lesions at 6, 9, and 12 months compared to the unvaccinated group ($p < 0.05$). Preliminary findings indicate that Gardasil vaccination post-laser surgery may reduce HPV recurrence in patients with HSIL-CIN2, suggesting its efficacy as a preventive measure.

**Keywords:** HPV recurrence, high-grade intraepithelial lesions (HSIL-CIN2), laser surgery, vaccination, preventive measure, pap smear

## INTRODUCTION

Based on our preliminary data, we can suppose that vaccination by "Gardasil" after laser surgery of intraepithelial lesion may prevent recurrence in patients with HPV. Prevention of Human Papilloma Virus (HPV) recurrence by "Gardasil" after surgical treatment of patients with high-grade intraepithelial lesion HSIL-CIN2 and HPV infection.

## METHODS

145 patients with HSIL-CIN 2 were investigated (Pap smear, colposcopy, biopsy, immunohistochemistry P16+).

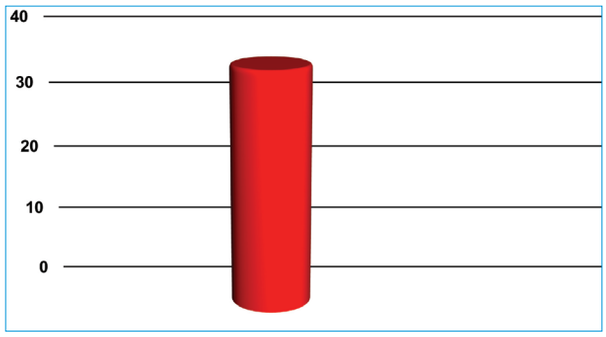
## RESULTS

All investigated patients (n=145) with HSIL-CIN 2 were treated by Co2 Laser conization and vaporization. They were suggested vaccination by "Gardasil." The leading control group includes 53 patients who agreed to vaccination. They were treated by "Gardasil" after surgical procedures and before sexual activity. The study group includes 92 unvaccinated patients. There were control PAP smears, colposcopy, and PCR detection of HPV (Type – 6,11, 16, 18, 31) infection after surgical treatment with three-month intervals over one year. HPV-induced lesion was statistically significant at 6, 9, and 12 months ($p < 0.05$).

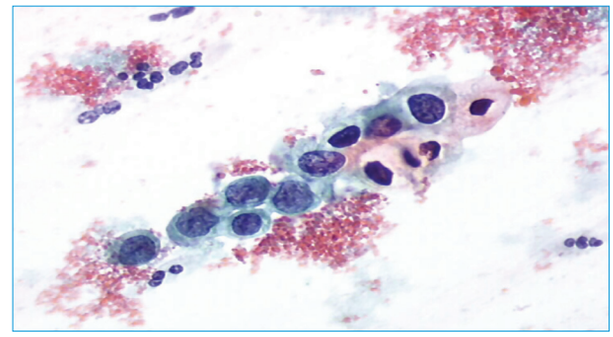
Conclusions Based on our preliminary data, we can suppose that vaccination by "Gardasil" after laser surgery of intraepithelial lesion may prevent recurrence in patients with HPV.

In the study group, cases of HPV-induced lesions were found.

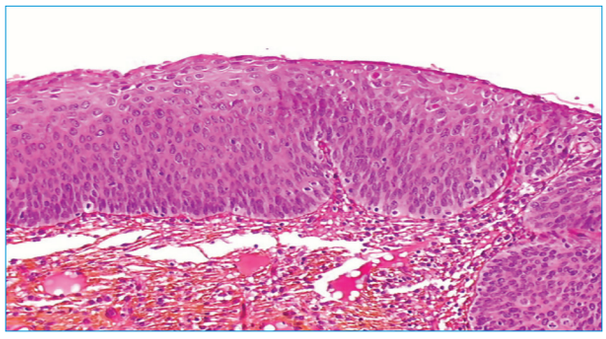
| Diagnostic Methods | Study Group Without Vaccination n - 92 | Control Group After Vaccination n=53 | Time After Conization and Vaporization months |
|---|---|---|---|
| Colposcopy | Adequate, acetowhite epithelium (2.7%) | Normal Colposcopy | 3 months |
| | Adequate, acetowhite epithelium, flat condyloma (5.9%) | Normal Colposcopy | 6 months |
| | Adequate, acetowhite epithelium, fine punctation (9,7%) | SCJ Visible | 9 months |
| | Adequate, fine punctation and mosaic (16,7%) | SCJ Visible | 12 months |
| Pap smear | NILM | NILM | 3 months |
| | LSIL - CIN 1 (HPV) | NILM | 6 months |
| | LSIL - CIN 1 (HPV) | Squamous Metaplasia | 9 months |
| | LSIL - CIN 1 (HPV) | Squamous Metaplasia | 12 months |
| PCR | HPV - Negative | HPV - Negative | 3 months |
| | HPV - Positive | HPV - Negative | 6 months |
| | HPV - Positive | HPV - Negative | 9 months |
| | HPV - Positive | HPV - Negative | 12 months |



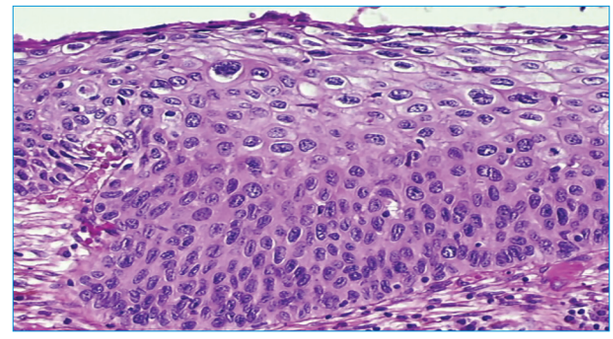

witout Gardasil after Gardasil



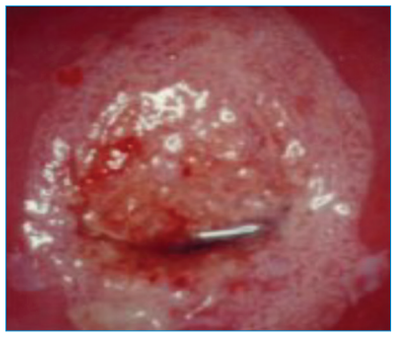
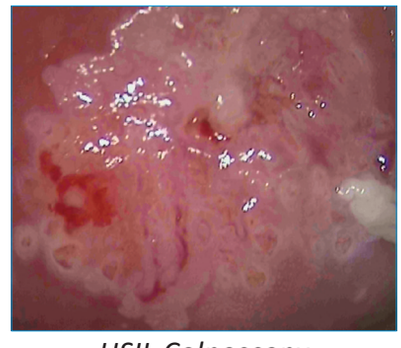
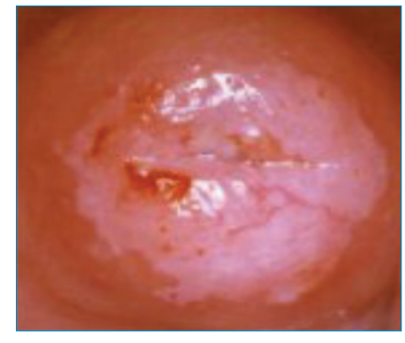
Pap smear HSIL, CIN+



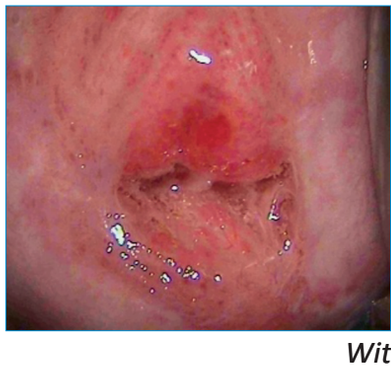
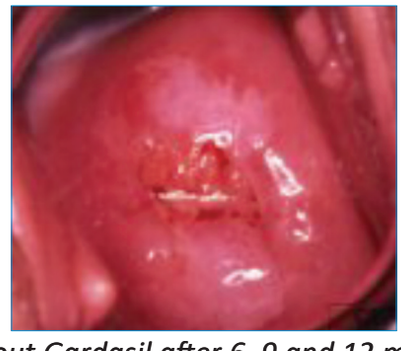
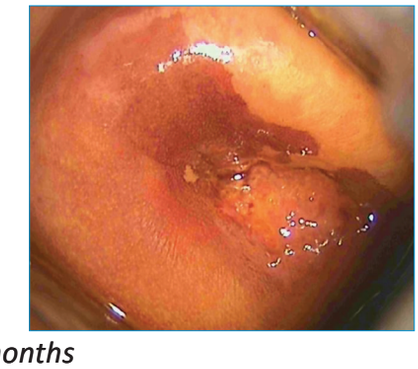
Biopsy, Histology HSIL+



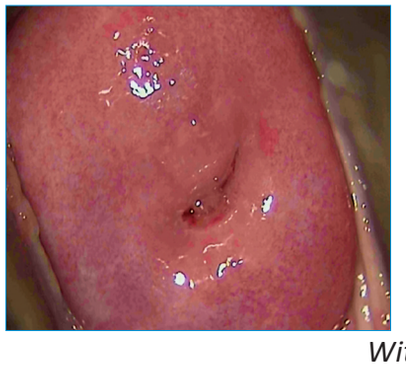
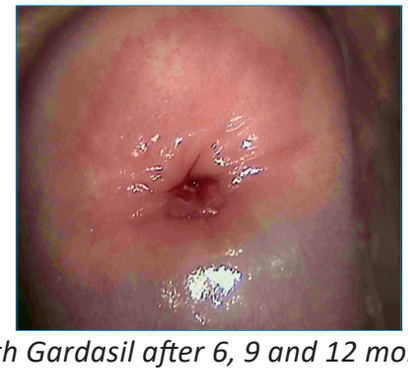
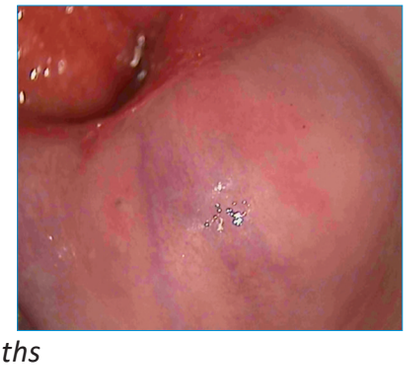
Immunohistochemistry P16+

HSIL Colposcopy

Without Gardasil after 6, 9 and 12 months

With Gardasil after 6, 9 and 12 months

## REFERENCES


1. Jugeli M, Tkeshelashvili B, Zakharaia L. Basics of Colposcopic Diagnosis and Management of Cervical, Vaginal and Vulvar Diseases. Tbilisi: 2014.
2. Prendiville W, Sankaranarayanan R. Colposcopy and Treatment of Cervical Precancer. IARC Technical Publication No. 45. *International Agency for Research on Cancer;* 2017.
3. WHO Guideline for Screening and Treatment of Cervical Pre-cancer Lesions for Cervical Cancer Prevention. 2nd ed. World Health Organization; July 2021.
4. Cox JT, Palefsky JM. Human Papillomavirus Vaccination. *UpToDate*. February 2022.


ABM
ThermoFisher
SCIENTIFIC

# About Company

„ABM LTD" is one of the rapidly growing and reliable companies on the Georgian market since 2011. The principal activity of the company is the implementation of advanced laboratory equipment, furniture, accessories, reagents, and consumables for research and diagnostic purposes, in the laboratory field.

The company offers customers a reliable partnership in IVF field, professional support and timely delivery of products. By cooperating with us, our clients can solve complex tasks efficiently with minimal costs. On the local market, ABM represents a worldwide well-known brand such as Thermo Fisher Scientific & Astec


# Our Brands

A long-term and stable relationship with manufacturing companies allows us to offer our customers a wide range of products.

For already 6 years, ABM has been representing Thermo Fisher Scientific in Georgia - a leading American company in the world that provides laboratory equipment, research, and diagnostic test systems.

Thermo Fisher Scientific, in turn, combines several different brands, including:

- Thermo Scientific
- Nunc
- Applied Biosystems
- Invitrogen
- Fisher Scientific
- BRAHMS
- Ion Torrent
- One Lambda
- Unity Lab Services
- Acros Organics

# FERTILITY SPARING IN CERVICAL CANCER

***LAKY RENE**, MD*
*Deputy Head Gynecology Division, Medical University of Graz, Austria*

## SUMMARY

Cervical cancer, ranked as the fourth most common cancer in women worldwide, disproportionately affects younger women compared to other malignancies. Around 42% of cervical cancer diagnoses occur in women aged ≤45 years. Given the increasing trend towards delayed childbearing, many of these patients express a desire to preserve fertility upon diagnosis. This lecture aims to provide an overview of current fertility-sparing treatment options for invasive cervical cancer, offering insights that may influence clinical practice and improve patient outcomes.

**Keywords:** Cervical cancer, fertility preservation, invasive cervical cancer, younger women, fertility-sparing treatment, delayed childbearing, clinical practice

# PRESERVATION OF FERTILITY IN ONCOLOGICAL PATIENTS OF REPRODUCTIVE AGE

***OSEPAISHVILI MAKA**, MD, PhD*
*Clinic of Reproduction and Genetics "Next Generation Clinic" Saint Petersburg, Russia*
***Lavrinovich O. E.***
*N. N. Petrov National Medical Research Center of Oncology, Saint Petersburg, Russia*

## SUMMARY

This study introduces Oncoreproduction, a new discipline addressing fertility preservation in reproductive-age cancer patients. In 2020, 2,191,040 new cancer cases were diagnosed in patients under 45, highlighting the need for fertility preservation due to gonadotoxic oncological treatments. We propose an interdisciplinary approach, including timely fertility consultations, expert histological assessments, and immediate access to advanced cryopreservation technologies. From March 2021, over 400 patients aged 18-45 were consulted at N.N. Petrov NMRC of Oncology in collaboration with Next Generation Clinic, resulting in 107 cancer patients having biological material cryopreserved. The average age of patients using assisted reproductive technologies was 28.4 years. Critical practices include quick referral to fertility specialists, comprehensive patient education, and robust interdisciplinary coordination. Our findings underscore the importance of informing patients about fertility preservation to enhance treatment adherence and post-recovery quality of life, with 26.7% of consulted patients utilizing modern assisted reproductive technologies to preserve biological material.

**Keywords:** Fertility preservation, cancer patients, cryopreservation, assisted reproductive technologies, interdisciplinary approach, patient education, oncological treatments

## INTRODUCTION

Peace consensus for a new discipline of the future – Oncoreproduction.

Malignant neoplasms in patients of reproductive age are an important medical and social issue worldwide. In 2020, 2,191,040 new cancer cases were diagnosed in patients under the age of 45, accounting for 11% of all cancer cases (Globacan). Advancements in diagnosis and treatment methods have improved recurrence-free and overall survival rates. For many reproductive-age

cancer patients, the possibility of delayed childbearing and having biologically natural children post-recovery is significant. Oncological treatments can have gonadotoxic effects due to chemotherapy, radiation treatment, and surgical castration, requiring long-term follow-up. Fertility issues should be discussed with young patients before specialized therapy, assuming a favourable prognosis.[1] This enhances treatment adherence and post-oncology rehabilitation.

## METHODS

Based on our experience, fertility preservation consultations should be aligned with a specific treatment strategy. This is established after assessing the oncological process through expert histological examination, including immunohistochemical tests to identify steroid hormone expression and hereditary cancer mutations. This helps form an opinion on the possibility of organ-preserving treatment, the gonadotoxicity of planned therapy, and disease prognosis.

## RESULTS

Based on the results, individualized measures to preserve reproductive potential and options for post-recovery pregnancy can be proposed. Patients' decisions should be based on competent information. We developed an interdisciplinary algorithm for timely care for this patient group. Key components include:

- Compliance with the timeframe between preliminary oncological diagnosis and fertility specialist consultation – no more than 1-2 days.
- Conclusion of a multidisciplinary oncological case conference in a specialized institution to choose a method for reproductive technology preservation.
- Immediate provision of advanced technologies for obtaining and cryopreserving biological material, including IVM, OTO-IVM, and ovarian tissue cryopreservation.
- Competent and timely legal information for patients, especially regarding embryo use.
- Secure transportation of biological material, complying with all standards.
- Training of medical personnel working with oncological patients (clinic administrators, nurses, biologists, laboratory assistants, anesthesiologists, etc.).

Since March 2021, after signing a memorandum on professional cooperation with the Next Generation Clinic (Saint Petersburg), over 400 patients aged 18 to 45 have been consulted about fertility preservation at N.N. Petrov NMRC of Oncology (Saint Petersburg); 85% were women and 15% men. The nosological forms of oncological diseases included 31% with malignant reproductive system tumors, 26% with mammary gland tumors, 15% with hemoblastoses, 10.2% with bone and soft tissue tumors, 8.7% with germ cell tumors, and 9.1% with other organ tumors, including brain tumors. As a result of close cooperation with Next Generation Clinic fertility specialists, 107 cancer patients had their biological material cryopreserved. Sixty-five ovarian stimulations for cryopreserving oocytes and embryos were performed under the Delayed Motherhood program, considering immunohistochemical pathomorphological test results, accounting for 20% of all consulted women. The average age of patients using assisted reproductive technology methods was 28.4 years (range 19-42 years). Seven intraoperative specimens of the ovarian cortical layer

were taken for OTO-IVM. Oocytes of 4 patients were cryopreserved, and three patients were referred for IVM due to uncertain ovarian stimulation risks.

## DISCUSSION

Over 40 men with testicular germ cell tumors and hematological malignancies used semen cryopreservation services before starting chemotherapy, representing about 80% of all consulted male patients. The average age was 28.4 years. More than 40 patients were consulted regarding the expiration of the follow-up period on safety issues and pregnancy methods; some were referred by obstetricians-gynecologists for pregnancy prolongation. 26.7% of all consulted patients used modern assisted reproductive technologies (ART) to preserve biological material, aligning with international fertility preservation measures.

## CONCLUSION

Oncologists should inform patients about organ-preserving treatment possibilities and fertility implementation strategies, requiring a multidisciplinary approach (oncologists, surgeons, pathologists, reproductive specialists, embryologists). Patients fully informed about infertility risks due to cancer treatment and preservation measures are less worried about aggressive treatment and have higher cure potential. Potential iatrogenic fertility loss and the loss of a possible child profoundly impact young women, sometimes causing more stress than the cancer diagnosis itself.[2]

## REFERENCES

1. Lambertini M, Del Mastro L, Pescio MC, et al. Cancer and fertility preservation: international recommendations from an expert meeting. *BMC Med.* 2016; 14: 1. doi:10.1186/s12916-015-0545-7.
2. Letourneau JM, Ebbel EE, Katz PP, et al. Pretreatment fertility counselling and fertility preservation improve the quality of life in reproductive-age women with cancer. *Cancer.* 2012; 118(6): 1710-1717. doi:10.1002/cncr.26459.
3. Lambertini M, Peccatori FA, Demeestere I, et al. Fertility preservation and post-treatment pregnancies in post-pubertal cancer patients: ESMO Clinical Practice Guidelines. *Ann Oncol.* 2020; 31: 1664-1678. doi:10.1016/j.annonc.2020.09.006.
4. Anderson RA, Amant F, Braat D, et al. ESHRE Guideline: Female Fertility Preservation. *Hum Reprod Open.* 2020; 2020. doi:10.1093/hropen/hoaa052.
5. Oktay K, Harvey BE, Partridge AH, et al. Fertility preservation in patients with cancer: ASCO clinical practice guideline update. *J Clin Oncol.* 2018; 36(19): 1994-2001. doi:10.1200/JCO.2018.78.1914.

# TWENTY-SIX-YEAR RESULTS OF THE ISRAELI-GEORGIAN PROGRAM DIABETES IN PREGNANCY

***KURASHVILI RAMAZ**, MD, PhD, Prof.*
***ASATIANI NATALIA, SHELESTOVA ELENE***
*National Center for Diabetes Research, Tbilisi, Georgia*

## SUMMARY

This study evaluates the effectiveness of the Israeli-Georgian Program Diabetes in Pregnancy over 26 years. A total of 526 women were enrolled, including 407 with preexisting diabetes (T1DM) and 119 with gestational diabetes mellitus (GDM). Participants were divided into four groups based on preconception care and gestation enrollment period. The results showed significant HbA1c reduction across all groups by term. Group 1, which received preconception care, exhibited lower rates of spontaneous abortions, pre-eclampsia, preterm deliveries, and macrosomia compared to other groups. Perinatal mortality was also lower in Group 1 compared to Groups 2 and 3. The study concludes that preconception diabetes control significantly reduces adverse pregnancy outcomes, demonstrating the feasibility and promise of effective pregnancy management in diabetes, even in low-to-middle-income countries.

**Keywords:** Diabetes in pregnancy, preconception care, HbA1c reduction, spontaneous abortions, pre-eclampsia, perinatal mortality, pregnancy outcomes

## INTRODUCTION

The number of people with diabetes globally reached 537 million in 2022; since 2019, this number has increased by 16%; 90% of all cases are type 2 diabetes. In 2021, Type 2 diabetes was diagnosed in 1,200,000 children and adolescents. It is estimated that 21.1 million (16.7%) of live births to women in 2021 had some form of hyperglycemia in pregnancy. Of these, 80.3% were due to gestational diabetes mellitus. In comparison, 10.6% were the result of diabetes detected prior to pregnancy, and 9.1% due to diabetes (including type 1 and type 2) first detected in pregnancy (IDF Atlas, 10th ed., IDF, 2021). Proper treatment and use of high-quality insulin are pivotal in managing diabetes in pregnancy. For several decades, people with diabetes, mainly pregnant

women, have been using high-quality insulin preparations (Novo Nordisk and Sanoifi). The Israeli-Georgian Program Diabetes in Pregnancy was initiated at the Georgian Diabetes Center (now National Center for Diabetes Research) in 1996 to provide care for women with diabetes. The Program has become possible due to the Twinning between the Georgian Union of Diabetes and Endocrine Association and the Israeli Diabetes Association.

The present work assesses treatment efficacy in women with Preexisting Diabetes (T1DM) and GDM. Clinical data of the study population:

## METHODS

In total, 407 Women with Preexisting Diabetes/T1DM and 119 Women with GDM were enrolled in the study. They were divided into four groups (Gr): Gr.1 – 223 patients who received preconception care; Gr.2 – 118 patients enrolled in the Program at gestation age < 10 weeks; Gr.3 – 66 patients enrolled in the Program at gestation age > 10 (11 – 21) weeks and Gr.4 – 119 patients with GDM.

***Table 1:*** ***Distribution of Participants with Diabetes (Preexisting and Gestational) by Group***

| | Gr.1 (N=223) | Gr.2 (N=118) | Gr.3 (N=66) | Gr.4 (N=119) |
|---|---|---|---|---|
| **Age (years)** | 22.9 ± 4.6 | 23.5 ± 5.1 | 23.2 ± 4.1 | 25.9 ± 5.3 |
| **Diabetes duration (years)** | 10.9 ± 7.2 | 11.7± 6.4 | 9.8 ± 6.9 | - |
| **Preconception care** | Yes | no | no | no |
| **Pre-pregnancy BMI (kg/m2)** | 21.6 ± 3.6 | 22.4 ± 2.4 | 23.3 ± 1.9 | 24.8 ± 4.9 |
| **HbA1c (%) before treatment** | 8.12 ± 0.5 | 8.17 ± 0.6 | 8.09 ± 1.6 | 6.7 ± 0.9 |
| **Preproliferative retinopathy (%)** | 8.96 | 13.5 | 13.63 | - |
| **Microalbuminuria (%)** | 6.27 | 11.86 | 16.6 | 10.08 |

All women were followed up throughout preconception care and pregnancies. The following parameters were controlled: 1) BG: fasting – 60-90 mg/dl, postprandial 1-hr < 140mg/dl, postprandial 2-hr < 120mg/dl, before a meal – 75-105 mg/dl; HbA1c < 6.5 %; Correction of intensive insulin therapy based on the SBGM; Avoid of severe hypoglycemia episodes. 2) Blood pressure control. 3) Ultrasound examination, cardio monitoring of a fetus. 4) Obstetrical/ gynecologic follow-up. 5) Folic acid supplement (5 mg/d). Strict metabolic control was achieved during preconception care and maintained throughout pregnancies. Screening for GDM revealed the condition in 119 pregnant women (75-g OGTT was performed at 24-28 weeks of gestation).

## RESULTS

At entry HbA1c(%) levels for Gr.1, 2, 3, and Gr.4 were 8.12 (0.05), 9.08 (0.6), 8.09 (1.6), 6.7(0.9), respectively; By the end of preconception care HbA1c levels in Gr.1 – 6.0(0.65)% were statistically lower in Gr.2 and 3 (P=0.000). By term, HbA1c levels statistically decreased in all the groups (P=0.024, P=0.000, P=0.000, respectively). The rate of spontaneous abortions was lower in Gr.1 (2.24%) than in Gr.2 (8.4%) P=0.000. In Gr.1 patients, the percent of pre-eclampsia (0.44%) was lower than in Gr.2(8.4%) and Gr.3 (10.6%) (P1-2 =0.0005; P1-3 = 0.0002). No statistical difference between Gr.1 and Gr.4 was revealed. In

Gr.1 patients, the percentage of preterm deliveries was lower than in Gr.2 and Gr.3 (P1-2 =0.0014; P1-3 = 0.0001). No statistical difference between Gr.1 and Gr.4 was revealed. In Gr.1, patients' percentage of macrosomia was lower than in Gr.2 and Gr.3 (P1-2 =0.0074; P1-3 = 0.0101); and in Gr. 1 and 4 (10.47 – 11.7%) – no statistical difference was observed. Perinatal mortality was observed in Gr.1 – 1.79%, in Gr.2 – 4.23% in Gr.3 – 7.5%, and in Gr.4 -1.68% (P1-2 =0.0944; P1-3 = 0.0129; P1-4 =0.7265).

***Table 2.*** ***Clinical Data in Women with Preexisting diabetes mellitus and gestational diabetes mellitus.***

| | Gr.1= 223 | Gr.2= 118 | Gr.3= 66 | Gr.4=119 GDM |
|---|---|---|---|---|
| Preeclampsia | 1 (0.44%) | 8 (6.7%) | 7 (10.6%) | 1 (0.84%) |
| No of deliveries<br>Vaginal (%)<br>Cesarean section (%) | <br>40.9<br>52.9 | <br>31.4<br>64.4 | <br>23.7<br>77.2 | <br>49.6<br>48.7 |
| Gestational weeks of delivery | 36 - 40 | 35 - 39 | 32 - 39 | 35 - 39 |
| Preterm delivery <37 weeks | 10 (4.8%) | 14 (11.8%) | 9 (13.6%) | 8 (6.7%) |
| Preterm delivery <34 weeks | - | 2 (1.6%) | 6 (9.9%) | 3 (2.5%) |
| Birth weight (g) | 3655±505.4 | 3469 ±491.1 | 3487±642.3 | 3495 ± 493.5 |
| Spontaneous abortions (%) | 1.7 | 7.62 | - | - |

***Table 3.*** ***Clinical Data in Women with Preexisting diabetes mellitus and gestational diabetes mellitus.***

| | Gr.1= 223 | Gr.2= 118 | Gr.3= 66 | Gr.4=119 GDM |
|---|---|---|---|---|
| Macrosomia | 59 (26.4%) | 33 (27.9%) | 19 (28.7%) | 29 (24.3%) |
| Neonatal hypoglycemia | 12 (5.3%) | 15 (12.7%) | 10 (15.1%) | 12 (10.08%) |
| Respiratory distress syndrome | 3 (1.7%) | 6 (5.08%) | 8 (12.1%) | 5 (4.2%) |
| Major congenital malformations | - | - | 3 (4.5%) | 1 (0.8%) |
| Stillbirths | 3 (1.34%) | 3 (2.54%) | 6 (9.9%) | 1 (0.84%) |
| Neonatal death | 0 | 2 (1.69%) | 2 (3.03%) | 1 (0.84%) |
| Perinatal mortality per 1000 births | 13.4 | 42.3 | - | - |

## CONCLUSION

1) If in patients with Preexisting DM, diabetes control was achieved before conception, the risk of spontaneous abortions was significantly lower than in patients in whom treatment was initiated already after conception.
2) In patients with Preexisting Diabetes and GDM, reasonable glycemic control during pregnancy significantly reduces the risk of pre-eclampsia, preterm delivery, and perinatal deaths.
3) This Program shows that a proper approach to pregnancy management in diabetes can be successfully implemented even in low-to-middle-income countries.

# INCIDENTS AND MISTAKES IN IVF

***ELIEZER GIRSH**, PhD, **BARNAN RAFAEL**, MD*
*Refael Care Medical Center, Rishon LeTZion, Israel*

## SUMMARY

This review examines notable incidents and mistakes in in vitro fertilization (IVF) from 1998 to 2009, highlighting the complex and high-stakes nature of the procedure. Critical cases include embryo mix-ups leading to children of different racial backgrounds and wrongful embryo transfers. Factors contributing to these errors include fatigue, high workload, poor communication, and inadequate supervision. Gender-based differences in brain structure and function further complicate message perception and decision-making. Distracting workplace conversations and a toxic work environment also increase the risk of errors. Implementing artificial intelligence for decision-making, fostering a positive work environment, and standardizing procedures are crucial to mitigate these risks. Regular training, audits, and inspections are recommended to ensure adherence to best practices and continuous improvement in IVF laboratories. Despite the rarity of such errors, understanding and addressing their causes is essential to improving IVF practices.
**Keywords:** IVF errors, embryo mix-ups, wrongful embryo transfers, decision-making, workplace environment, artificial intelligence, standardization

## INTRODUCTION

The era of in vitro fertilization (IVF), as part of medicine, had been started when Louise Joy Brown came to be due to an IVF procedure attempt on July 25, 1978. Robert Edwards and Patrick Steptoe were the first pioneers in IVF, who succeeded in this new field of medicine and opened the way for developing a new subject – clinical embryology. Twenty years later, in 1998, the sensational news was reported in the front-page article: “A black-skinned child was born by a white woman.” Yeah, curiously, weren’t mistakes in IVF during these twenty years, or maybe the unnoticed errors? The misconducts in IVF were not exposed to the public.

## METHOD

In 1999, a white woman from New York gave birth to twin boys: white and black. This woman had been treated in one of the IVF clinics in Manhattan and had been undergoing embryo transfer simultaneously with a black woman. Coincidently, an embryo from the black woman ended up in the white woman, most likely due to the improperly flushed catheter. In the issue, only the white woman became pregnant. The exact incident occurred in July 2002 in the UK. A white woman delivered black twins due to a mix-up in the NHS fertility clinic. This IVF's carelessness is thought to be the first to be revealed in the UK. The possible reason for this uncommon situation could be the fertilization of a white woman's egg by a black man's spermatozoa. Moreover, now the ethical issue arises: Who are the natural parents of the twins?

## RESULTS

In 2004, a Californian woman had compensation of 1 million dollars because the wrong embryo transferred her to an IVF clinic, and this mistake was revealed ten months later after the delivery of a baby. In 2007, at an IVF clinic in Cardiff (UK), a thawed embryo that belonged to a 42-year-old lady was incidentally transferred to another woman. Cardiff IVF clinic admitted liability and paid the couple an undisclosed sum of money, reportedly about 25,000 £. In 2009, in the Israeli Porya IVF clinic, a woman had been implanted with thawed embryos that belonged to another couple due to a mix-up. The same case was reported in Ohio, USA, in the same year. Despite this misstep, the couple has decided to continue with this pregnancy. Right after delivery, the newborn gained his biological parents.

## DISCUSSION

The errors in IVF could be quickly revealed by newborns' different skin colors or physical features. However, without evidence, the IVF's carelessness is challenging to discover. It's important to note that misconduct in IVF procedures is rare, but it could happen in any IVF clinic worldwide. Understanding the reasons for human errors in IVF is crucial. While these errors are complex and challenging to prevent, knowledge of their causes can empower us to take steps to minimize their occurrence. The possible reasons could be fatigue, workload, variability in message perceptions due to behavioral impact, poor interpersonal communication, invalid supervision, and teamwork issues. Fatigue can be triggered by sleeplessness, preoccupation, multitasking, being oxygen-less in the workplace, and stress. Workload can be induced by workplace overload, multitasking, and anxiety. Variability in message perception could be individually based on gender-dependent structural and functional differences in the human brain. Interestingly, the male brain shows hemispheric asymmetry: the left hemisphere functionally looks different from the right hemisphere. Indeed, the two hemispheres of a female's brain are much more alike. In women, there is proportionately more grey matter and less white matter; vice versa for men. It has been shown that women and men have different perceptions of messages. They listen, read, and express emotions in different ways. The causative reason for this difference is that men are likelier to use less brain capacity than women who use both hemispheres for the same task. The different perceptions lead to different social behaviors, which could lead to poor interpersonal communication, misguidance, and ability to make the right decision. It was shown that the brain

is rational but needs to be more objective. For these reasons, artificial intelligence (AI), which does not depend on our perception of incoming information, would help us make sound judgments, correct conclusions, and better decisions. Another primary subject of missteps could be distracting conversations in the workplace, including phone talks, which can divert workers' attention from their tasks. "Coffee blah, blah, blah" keeps workers' attention away from their jobs, thereby increasing the risks of errors.

## CONCLUSION

Maintaining a 'positive' work environment in the workplace is crucial to prevent oversights. This includes fostering trust, cooperation, safety, and risk-taking support. There must be a shared understanding and cohesion in the working team. The toxic atmosphere may occur when there is no support for workers from management, no support between the workers themselves, lethargy, absenteeism, verbal and physical intimidation, increased complaints, changes in employee behavior, and a pervasive culture of fear. Lastly, to improve the quality of the IVF laboratory and eliminate the likelihood of failure, it is essential to standardize the methodology and the working processes. For this purpose, it is necessary to arm the standard operation procedures (SOPs) and quality control, provide periodic employee training, and conduct annual audits and inspections.

# MENSTRUAL DYSFUNCTION 35+. A NEW VISION, A NEW TAXONOMY

***GEGECHKORI MAKA**, MD, PhD*
*TSMU Professor Reproductive Clinic of Zurab Sabakhtarashvili, Tbilisi, Georgia*

## SUMMARY

The long-standing nomenclature/taxonomy implemented in clinical practice has evolved over the last five years to a patient/woman and quality of life orientation. This shift is of utmost importance as it updates diagnostic methods, clinical management practices, and surgical and conservative (drug) management. It particularly emphasizes the disorders and management features of the puberty period depending on the seriousness of the age stage. This new taxonomy is critical for managing late reproductive age (progesterone-deficient period), pre-, peri- and menopausal dysfunction, especially in the category of reproductive planning. For managing menstrual dysfunction in late reproductive age, it is essential to consider the physiological, metabolic, and somatic features of age. The work highlights the unique properties of progestagen – dydrogesterone; Peculiarities of management of menstrual dysfunction; The main characteristics of dydrogesterone – potent progestogenic activity, without anti gonadotropic, mineralocorticoid/anti mineralocorticoid, estrogenic, androgenic/antiandrogenic activities; not metabolized to estrone; does not affect the synthesis and metabolism of endogenous progesterone; Does not affect ovulation; It is also possible during metabolic problems and hypertension; oral and easily acceptable comfortable form; Has a pronounced ability to affect embryoprotective gravidarum immunomodulation. The paper focuses on recent works that highlight the role of dydrogesterone in the treatment of excessive/intentional menstruation[8] and various effective regimens in treating dysmenorrhea. [9, 10, 12,13,14,15,16] The benign profile of dydrogesterone and its safe use with other medications have been described.[11] Its role is vital in pre- and post-menopause.[17]

**Keywords:** Taxonomy, reproductive planning, dydrogesterone, menstrual dysfunction, menopause management, progestogenic activity, clinical management

## REFERENCES


1. Marret H, Fauconnier A, Chabbert-Buffet N, et al. Clinical practice guidelines on menorrhagia: management of abnormal uterine bleeding before menopause. *Eur J Obstet Gynecol Reprod Biol.* 2010; 152(2): 133-137.
2. Abnormal Uterine Bleeding in Pre-Menopausal Women. *SOGC Clinical Practice Guideline.* No. 292, May 2013.
3. The International Federation of Gynecology and Obstetrics (FIGO) 2011 (2018) *AUB Guideline Update. NICE Heavy Menstrual Bleeding Clinical Guideline.*
4. Munro GM, et al. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynecol Obstet.* 2018; 143: 393-408.
5. NICE Heavy Menstrual Bleeding Clinical Guideline -National Collaborating Centre for Women's and Children's Health. *Heavy Menstrual Bleeding Clinical Guideline 44.* London: RCOG Press for NICE; 2007.
6. ACOG committee opinion no. 557: Obstet Gynecol. 2013 James A, et al. *EJOG-RB.* 2011.
7. Heavy menstrual bleeding: assessment and management (NG88). NICE, 2018. Available at: https://nice.org.uk/guidance/ng88.
8. Tajjamal A, Zaman F. Severity bleeding is a predictor of quality of life in women with heavy menstrual bleeding under dydrogesterone treatment in a prospective, multicentre, observational study. *Gazz Med Ital.* 2015; 174(9): 391-398.
9. Schweppe KW. The place of dydrogesterone in the treatment of endometriosis and adenomyosis. *Maturitas*. 2009; 65(Suppl 1). https://doi.org/10.1016/j.maturitas.2009.11.011.
10. Taniguchi F, et al. The efficacy and safety of dydrogesterone for treatment of dysmenorrhea: an open-label multicenter clinical study. *J Obstet Gynaecol Res.* 2019; 45(1): 168-175.
11. Schindler AE. Progestational effects of dydrogesterone in vitro, in vivo, and on the human endometrium. *Maturitas*. 2011; 65
12. Schindler AE, et al. Reprint of classification and pharmacology of progestins. *Maturitas*. 2008; 61(1-2): 171-180.
13. Karakus S, Kiran G, Ciralik HE. Efficacy of micronised vaginal progesterone versus oral dydrogesterone in the treatment of irregular dysfunctional uterine bleeding: a pilot randomised controlled trial. *Aust N Z J Obstet Gynaecol.* 2009; 49(6): 685-688.
14. Dydrogesterone CCDS. 15 January 2016.
15. Podzolkova N, et al. Dydrogesterone treatment for menstrual-cycle regularization in routine clinical practice: a multicenter observational study. *Gynecol Endocrinol.* 2016; 32(3): 246-249.
16. Trivedi N, Chauhan N, Vaidya V. Effectiveness and safety of dydrogesterone in the regularization of the menstrual cycle: a post-marketing study. *Gynecol Endocrinol.* 2016; 32(8): 667-671.
17. Baber RJ, et al. 2016 IMS Recommendations on women's midlife health and menopause hormone therapy. *Climacteric*. 2016; 19(2): 109-150.

LL Group

# ONLY THE HIGHEST

LLGroup LTD is a pharmaceutical distributor company established in 2010 in Tbilisi. LLGroup LTD is a licensed distributor of medical pharmaceuticals, including prescription and OTC products and natural health products. From 2010, LLGroup actively imports and distributes products as follows:

## PHARMACEUTICAL PRODUCTS:

Injectable;

Suppositories;

Tablets/Capsules.

Food supplements.

LLGroup LTD has significant capabilities to provide end-to-end service to international partners looking to expand their business in Georgia.

Working groups are: **Gynecology, Reproductology, Urology, Andrology, Gastroenterology, and lately added - pediatric line.**

# QUALITY PRODUCTS!

LLGroup proudly holds the exclusive distributorship of Lenus Pharma products, including the first study-proven fertility pills, Profertil and Profertil Female. This exclusivity ensures that our partners and customers receive the best-in-class products.

PROFERTIL®

PROFERTIL® female

With all employees working together as a single team, the company strives to develop the pharmaceutical and healthcare industry by continuing to launch products that meet market needs and better serve its partners and customers.

## OUR COMPETITIVE ADVANTAGES ARE:

- Satisfied existing customers and strong reputation;
- Close business network in leading company shareholders and executive team;
- Highly qualified and motivated team.

## LLGROUP PRODUCTS CAN BE FOUND IN THE FOLLOWING PLACES:

### PHARMACY

Vazha-Pshavela ave. N7
Tbilisi, Georgia
T: 032 223 81 07
+995 599 900 347

### WEB-SITE

www.llgroup.ge
www.profertil.ge

### FACEBOOK

www.llgroup.ge
LLGroup - ელელგრუპი

# IMPORTANCE OF EXPANDED CARRIER SCREENING AMONG OOCYTE DONORS – QUESTIONS AND CONCERNS

***DOROFEYEVA, U., SHARHORODSKA, Y.[2] KOZYRA, O.,[1] AYDIN, B.,[3] KARIMOVA, H.,[1] MOKRA, K.,[1] STRELKO G.[4]***

*[1] OVOGENE, Ukraine*

*[2] IVF, Ukraine*

*[3] LVIV, Ukraine*

*[4] Institute of Hereditary Pathology NAMS Ukraine, Genetic, Lviv, Ukraine*

## SUMMARY

This study evaluates the utility of expanded carrier screening (ECS) for oocyte donors using next-generation sequencing (NGS). A cohort of 92 potential donors aged 18-30 underwent ECS after testing negative for common CFTR mutations. Results showed that 86% were carriers of at least one genetic condition, with prevalent conditions including hemochromatosis, cystic fibrosis, and biotinidase deficiency. The findings underscore the high prevalence of genetic conditions among donors, highlighting the need for comprehensive genetic screening and standardized guidelines. Implementing ECS can enhance the safety and quality of donor programs without significantly reducing the pool of eligible donors.

**Keywords:** expanded carrier screening, oocyte donors, next-generation sequencing, genetic conditions, hemochromatosis, cystic fibrosis, biotinidase deficiency

## INTRODUCTION

The regulation of genetic testing for oocyte donors varies widely across countries, with most lacking standardized guidelines. Expanded carrier screening (ECS) is becoming more prevalent as it can identify a broader range of genetic conditions that may affect offspring. This study aims to assess the utility of ECS using next-generation sequencing (NGS) in identifying carriers of genetic conditions among oocyte donors.

## METHODS

A cohort of 92 potential oocyte donors aged 18-30 who tested negative for the 11 most common CFTR mutations using a PCR panel underwent further screening with a commercial ECS panel covering 302 genes. The NGS data was analyzed to identify carriers of genetic conditions.

## RESULTS

Out of the 92 donors screened, 86% were found to be carriers of at least one genetic condition. Specifically, 38% (35/92) were carriers for one condition, 34% (31/92) for two conditions, 7% (6/92) for three conditions, and 7% (6/92) for four conditions. The most prevalent conditions identified included Hemochromatosis Type 1 (22%), Cystic Fibrosis (11%), Biotinidase Deficiency (7.6%), 21-hydroxylase-deficient Congenital Nonclassical Adrenal Hyperplasia (6.5%), Krabbe Disease (6.5%), Usher Syndrome (6.5%), Nonsyndromic Deafness (5.4%), and Smith-Lemli-Opitz Syndrome (5.4%).

## DISCUSSION

The findings underscore the high prevalence of genetic conditions among oocyte donors using an expanded screening panel. This highlights the importance of comprehensive genetic screening to ensure the safety and quality of donor programs. The study also emphasizes the need for standardized guidelines for genetic testing of oocyte donors to ensure consistent and thorough screening practices.

## CONCLUSION

Expanded carrier screening using NGS identified a significant proportion of oocyte donors as carriers of genetic conditions, supporting the need for explicit genetic testing requirements and guidelines. This practice will enhance the safety of future pregnancies and maintain the quality of donor programs without significantly reducing the pool of eligible donors.

# GLOBAL NEED IN OOCYTE DONATION - EGG BANKING

***DOROFEYEVA, U., SHARHORODSKA, Y.,[2] KOZYRA, O.,[1] AYDIN, B.,[3] KARIMOVA, H.,[1] MOKRA, K.,[1] STRELKO, G.[4]***

*[1] OVOGENE, Ukraine*

*[2] IVF, Ukraine*

*[3] LVIV, Ukraine*

*[4] Institute of Hereditary Pathology NAMS Ukraine, Genetic, Lviv, Ukraine*

## SUMMARY

Oocyte donation has become an essential part of assisted reproductive technology (ART), addressing infertility issues due to poor oocyte quality, low ovarian reserve, or heritable genetic diseases. Since the first donation in 1983, egg banking has advanced significantly. Key considerations in selecting an egg bank include legal registration, qualified leadership, high-quality equipment, traceability systems, robust documentation processes, and reliable reimbursement policies. The bank's location, particularly in post-Soviet regions, necessitates caution due to potential risks. Customer care, adherence to ethical standards, and incorporating new technologies like artificial intelligence for quality control are vital. These factors collectively ensure the safety, effectiveness, and ethical management of oocyte donation and banking services.

**Keywords:** Oocyte donation, egg banking, assisted reproductive technology, infertility, genetic disease, cryopreservation, quality control, artificial intelligence.

## INTRODUCTION

Third-party reproduction has become one of the widely used fertility treatments that involve the use of gametes or embryos. With the improvements in oocyte cryopreservation techniques, a new era of health tourism has been initiated. The first oocyte donation was performed in 1983 in Austria, and since then, it has become a part of routine ART treatments. Thousands of oocyte donations have been made worldwide, resulting in thousands of births. The main drive of oocyte donations is the inability of females to get pregnant using their gametes due to poor oocyte quality after several failed in vitro fertilization (IVF) attempts or low/absent ovarian reserve because of advanced maternal age or premature ovarian failure. Oocyte donation can also be offered to women with a heritable genetic disease to prevent the transmission of the disorder to the next

generation. However, preimplantation genetic diagnosis is usually preferred with no history of infertility. Least commonly, oocyte donations can be offered to same-sex male couples in adjunct to surrogacy.

## METHOD

To identify critical factors for selecting an egg bank, a comprehensive review of existing literature, guidelines from ESHRE and ASRM, and expert opinions were conducted. Factors examined include legal registration, leadership qualifications, equipment quality, traceability systems, documentation processes, reimbursement policies, geographical considerations, customer care standards, ethical practices, and the incorporation of new technologies.

## RESULTS

1. **Legal Entity**: Any egg bank must have a registration of the legal entity. Many agencies or companies that consider themselves an egg bank are not legal entities and cannot use biological material for trading purposes. They also cannot take responsibility for biological material storage and distribution. Most egg banks just present a good-looking website and nothing more. These kinds of companies or agencies do not accept any responsibility but shift the responsibility to medical clinics. When a clinic orders from such an egg bank, they surprisingly find out they need to pay not to the egg bank but to the supplier clinic. The main risk is you won't be given any support or assistance in case of any difficulties. When you try to reach them, they will show the clinic address since they do not hold themselves accountable because they are a non-legal entity, "Egg Bank." Their defense will be that they were promoting the trademark of the supplier clinic.
2. **Qualified Leadership**: A legal entity of an egg bank must have a medical director, a scientific director, and a lab director. This is the main criterion you can trust as a legal entity of an egg bank. Many banks mention they are under the supervision of a well-known star or are advertised as having big-name scientific advisors or consultants work for them. However, this is only a marketing trick, as those people are not official employees of that egg bank and do not have any in-house physical presence. These people do not perform daily routine work or take responsibility for biological material creation, storage, or distribution. You must know about the medical director's education, experience, and leadership capability in an egg bank. The same criterion applies to a lab director, who must have extensive and considerable experience in cryopreservation, storage, and movement of biomaterial. Many egg banks hire several doctors and embryologists while positioning themselves as a legal entity of an egg bank. All other employees work either part-time or remotely.
3. **Equipment Quality**: An egg bank's equipment is essential. According to ESHRE and ASRM's recommendations, equipment quality may affect the result by up to 70%. The equipment quality, the lab team that uses the equipment, and the laboratory environment are three key influencing factors according to ESHRE and ASRM recommendations. You must have a high-quality laboratory to create a high-standard egg bank. All equipment must have CE marks, annual service reports, and operations. Like cell phones that get updated over time, IVF equipment must also be upgraded as it will start to lose function and become outdat-

ed. Equipment quality will change the outcome even if you use low-quality sperm, egg, or embryo over time.

4. **Traceability**: Traceability is critical, also known as double witnessing or electronic witnessing. Most clinics don't consider investing in electronic witnessing or employing one more embryologist for double witnessing. If a clinic uses regular IVF cycles, the situation is simple, unlike with a double control and signature of both embryologists. However, double witnessing becomes risky and limited when an active egg bank does up to 100 egg pick-ups per month and has a storage of up to 10,000 eggs. Suppose an egg bank or clinic does not have an RFID electronic witness system or any computer software for tracking. In that case, there will always be a risk of mixed-up biological material. For a clinic or egg bank that does not use double witnessing or electronic witnessing, there will not be a possibility of finding or proving a mistake in the case of mixed-up biological material.
5. **Documentation Processes**: Document flow, donor database control, arrangement, storage of documentation, and editing rights of the documentation are essential processes for egg banking. Most egg banks work with simple Excel or Google Sheets, which are very limited and difficult to control. These systems are not trackable and may allow anyone to make fundamental changes regarding donor information and donor medical cards. Unfortunately, nobody will quickly notice any changes in case of a mistake. Especially in extraordinary situations, such as if a baby were born with a genetic anomaly, controlling the material and documentation system retrospectively will be impossible.
6. **Reimbursement**: Reimbursement is another critical factor. Many egg banks state they produce high-quality biomaterial. Suppose an egg bank provides a guarantee and a compensation system under ESHRE criteria (such as survival rate, fertilization, and blastocyst rate). In that case, this egg bank follows a strict algorithm. Usually, such egg banks even give a much higher percentage of survival rate or blastocyst rate than all published statistics.
7. **Location and Compliance**: The country and storage of the material are important considerations. Most partners understand that today, most banks operate in the post-Soviet market. Therefore, there are risks of falsification and non-compliance of the chosen donor's biological material and the risk of not being able to sue the bank. Corruption in the post-Soviet countries is a serious issue. When selecting a bank located in a post-Soviet country, one must clearly understand and assess all these risks that could seriously affect future reputation and the ability to receive compensation or a court decision or experience the birth of a child with genetic defects and pathologies. Therefore, the location of a bank should be carefully noted. Alternatively, if you have decided to use a bank in that location, the biological material must comply with predetermined and strict criteria. Many central world banks buy biological materials in post-Soviet countries. Still, the risk then falls on these bigger banks, and you don't have to worry because the latter bank is responsible for its reputation.
8. **Customer Care**: Customer care is a noteworthy process of an egg bank. High-quality egg banks will always follow these rules:
    - Customer should get a response within 24 hours.
    - Customer should get access to a catalog within 24 hours.

- Customer should receive a contract within 24 hours.
- Customer needs to get medical information within 24 hours.
- Customer needs to get communication with the team and chief embryologist.
- Customer needs to get communication with the chief doctor within 24 hours.

9. **Safety and Ethics**: Safety and ethics are essential to egg banks. The recruitment of egg donors, their compensations, the medical preparation of egg donors, and their standards should be considered in accordance with moral ethics and legal standards. Egg banks must adhere to safety and quality stimulation protocols with high-quality hormonal medications, the number of stimulations, and breaks between stimulations.
10. **New Technologies**: The new biological material quality control and selection method has become more computer-based. Many parts of different processes in the medical area are controlled and processed by artificial intelligence. Human eyes are limited, especially under a microscope. The future is for artificial intelligence since it offers sheer perfection in a morphology base. The system can simultaneously track a sample, a supplier, an embryologist, and the quality of the material, which is priceless for a high-quality egg bank. An electronic storage mapping system is another promising technology that allows you to automatically track the location and amount of biological material in storage by the computer system. This provides high-quality traceability and control mechanisms for egg banks.

## DISCUSSION

The review highlights the importance of several key factors in the selection and operation of egg banks. Legal and ethical considerations, leadership qualifications, and equipment quality are foundational to ensuring oocyte donation and banking safety and effectiveness. Traceability and documentation processes are critical to maintaining the integrity of biological materials. Due to varying legal and ethical standards, an egg bank's geographical location can significantly impact its reliability and trustworthiness. Integrating new technologies, such as AI, offers promising quality control and efficiency advancements.

## CONCLUSION

Oocyte donation is a vital component of ART, offering solutions to infertility and genetic disease prevention. Selecting a high-quality egg bank involves careful consideration of legal status, leadership, equipment, traceability, documentation, reimbursement policies, and ethical practices. Additionally, the geographical location and incorporation of new technologies are critical factors. By adhering to these criteria, healthcare professionals and patients can ensure safe, effective, and ethical management of oocyte donation and banking services.

kromos
genetics laboratory

kromos.ge

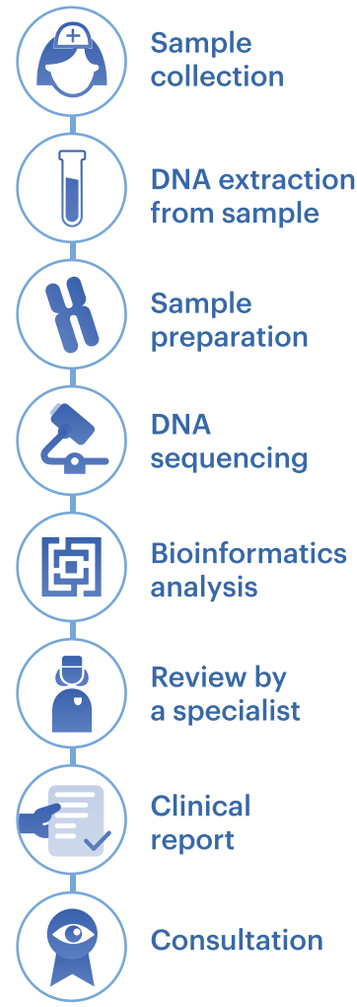
Beliashvili str. 76
+995 32 211 00 50
info@kromos.ge

kromos
genetics laboratory

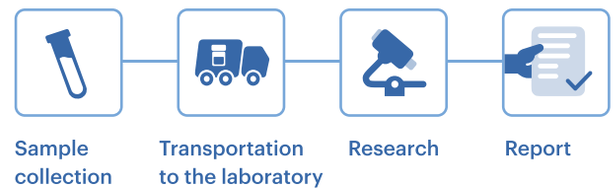
**Kromos** is the first genetics laboratory of Georgia, based in Tbilisi, performing a full cycle of all tests for reproductive health, rare disorders, and oncology. We provide medical diagnostic services, using such innovative technologies as **Next Generation Sequencing (NGS)**, **Sanger Sequencing** and **fragment analysis**. These technologies are widespreaded throughout the world in reproductive health, oncology and rare disease diagnostics.

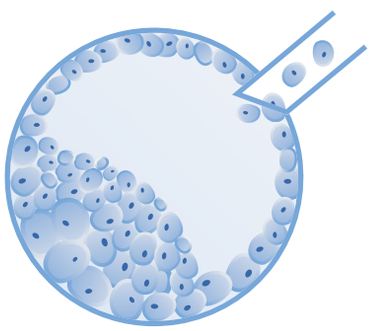
## Our mission is to improve people's life quality with the help of high-tech genetic solutions.

Our main goal is the implementation of modern diagnostic solutions in the Georgian healthcare system. The laboratory is equipped with modern technologies in accordance with standards. The team consists of professional geneticists, molecular biologists, bioinformaticians, IT developers who design genetic solutions and perform genetic tests for clinics and patients. This is a step towards the prevention of diseases, diagnosis and selection of adequate therapy, as well as, in general, improvement of the health condition of the population. Knowledge of genetic information and its use for medical purposes can improve the quality and duration of life.




Kromos genetics laboratory can perform diagnostic tests on site without sending all samples abroad, that's why we can provide more advantages in price and time frames without loss of test quality.



In reproductive health, using **Next Generation Sequencing (NGS)** technology, Kromos performs **Preimplantation Genetic Testing (PGT-A)** of embryos for chromosomal abnormalities (aneuploidy). This testing is used during in vitro fertilization (IVF) to detect extra/insufficient chromosomes or their parts in the embryo. PGT-A is a powerful tool for a doctor-embryologist and a patient that helps to make an appropriate decision about transfer of a specific embryo.

# ELECTROMYOGRAPHIC EVALUATION OF THE PELVIC MUSCLES ACTIVITY AFTER HIGH-INTENSITY FOCUSED ELECTROMAGNETIC PROCEDURE AND ELECTRICAL STIMULATION IN WOMEN WITH PELVIC FLOOR DYSFUNCTION

***SILANTYEVA ELENA**, MD, PhD, **ZARKOVIC DRAGANA**, MSc*
***SOLDATSKAIA RAMINA**, MD, **ASTAFEVA EVGENIIA**, MD, **ORAZOV MEKAN**, MD, PhD*

## SUMMARY

Electromyography (EMG) effectively measures pelvic floor muscle (PFM) activity, revealing differences in muscle function in women with pelvic floor dysfunction (PFD). This study compares the efficacy of high-intensity focused electromagnetic (HIFEM) therapy and traditional electrical stimulation in treating PFD. Surface EMG and subjective assessments (Pelvic Floor Impact Questionnaire, PFIQ) were used to evaluate PFM strength, endurance, and relaxation changes. Results showed that HIFEM significantly improved muscle activation, relaxation, and endurance compared to electrical stimulation. The PFIQ scores also indicated a more significant improvement with HIFEM, suggesting it is more effective than electrical stimulation for restoring PFM strength and alleviating PFD symptoms. These findings highlight HIFEM's superior efficacy in PFM rehabilitation, offering a promising alternative for postpartum women and those with urinary incontinence or sexual dysfunction.

**Keywords:** Electrical stimulation, electromyographye HIFEM procedure, pelvic floor dysfunction; pelvic floor muscles

## INTRODUCTION

Electromyography (EMG) is a method frequently used to examine the electrical activity of muscle tissue. Although this technology is relatively new, it is assumed to be reliable and objective while causing minimal or no discomfort to patients. Essentially, EMG uses the surface or intramuscular electrodes to record the intensity of signals propagating in the muscle fibers during the contraction because muscle tissue conducts electrical potentials similar to the nerves. The results of the measurements are expressed as a function of voltage over time. Except for single-fiber EMG, one

measured value represents a sum of all signals originating from the muscle tissue of a specific body area.[2-4]

Besides ultrasound,[5,6] magnetic resonance,[7] manometers,[8] dynamometers,[9] or simple palpation combined with observation,[10] surface EMG (sEMG) is one of the possible objective methods for monitoring resting level, strength, and endurance of the pelvic floor muscles (PFMs). The pelvic floor consists of 3 main compartments – anterior (bladder and urethra), middle (vagina and uterus), and posterior (rectum). Furthermore, there are morphologically complex multilayers of anatomical structures such as the pelvic diaphragm (composed of the levator ani and coccygeus muscles), urogenital diaphragm (consisting of connective tissue, perineum, bulbospongiosus, and ischiocavernosus muscles), and urethral/anal sphincters. These tissues are arranged in the pelvic area and have multiple attachments to the surrounding structures.[1] Under normal circumstances, the PFM prevents multiple disorders such as incontinence (urinary/fecal), sexual dysfunction, or pelvic organ prolapse accompanied by pain and discomfort. However, the atrophy and relaxation of PFMs may promote the manifestation of these health issues, collectively referred to as pelvic floor dysfunction (PFD),[10-12] occurring naturally with ageing or as a consequence of childbirth. Recording of sEMG in women who showed specific symptoms of PFD was reported previously by multiple authors. It has been found that EMG is a suitable method for the investigation of PFM functioning among healthy subjects and women with signs of urinary incontinence or PFM weakness.[13-21] Despite the various protocols and electrode configurations used, there is a clear relationship between the characteristics of the EMG signal and PFD. In comparison with the healthy and asymptomatic subjects, postmenopausal and even premenopausal women affected by some form of PFM impairment show distinctively lower EMG values. The intensity of maximum voluntary contraction (MVC) is reduced because the PFMs are weakened, and the endurance of contraction and muscle activity during rest are also affected.[13,14,18-20] Aside from sEMG, various subjective questionnaires (Pelvic Floor Disability Index, Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire, Pelvic Floor Impact Questionnaire, International Consultation on Incontinence Questionnaire Vaginal Symptoms or Pelvic Floor Bother Questionnaire) were also used to document strengthening and reeducation of the PFM which helped patients to improve their symptoms.[22,23] Besides regular exercise,[24] the function of the weakened PFM can be enhanced by noninvasive PFM stimulation. With well-established electrical stimulation,[25,26] high-intensity focused electromagnetic (HIFEM) technology has been more frequently used in recent years.[27-29] Both technologies deliver electric currents into the pelvic floor to depolarize membranes of motoneurons to elicit action potential and achieve brain-independent muscle contractions when the action potential of sufficient strength reaches the neuromuscular junction.[30] However, despite the direct flow of electric charge through the electrode-tissue surface, the HIFEM induces electrical currents selectively in the PFM by the mechanism of electromagnetic induction.[31] As the magnetic field passes any medium without energy attenuation, the induced contractions may be achieved at greater depths and intensities[32] to provide better outcomes. Based on the previous rationale, this study aims to investigate and compare treatment outcomes of the HIFEM procedure and electrical stimulation in women suffering from PFD. The expected changes in PFM activity would be examined by subjective (Questionnaire) and objective (sEMG) methods. The measured values will be compared with asymptomatic subjects.

## MATERIALS AND METHODS

### Patient's Recruitment Criteria

The inclusion criteria were specified as follows: women of age 18-45 years, who had a vaginal delivery, and who already stopped lactation. There were three patient groups. The symptomatic patients who reported PFD symptoms related to weakened PFM as lower urinary tract or bowel symptoms (incontinence) and/or sexual dysfunction (dyspareunia, vaginal laxity, decreased sensitivity during intimacy, inability to achieve orgasm – anorgasmia) were randomly (2:1) divided into the G1 group treated by HIFEM and G2 group which received electrical stimulation. The third group, G3, consisted of healthy postpartum patients to obtain sEMG values of the normal population. Exclusion criteria were the presence of any metal implants or devices, which include metal components, pregnancy, malignant tumor, history of surgical procedure in the pelvic region, presence of pelvic organ prolapse of stage II-IV as per the Pelvic Organ Prolapse Quantification classification, and all general contraindications for physiotherapy. Patients were asked to perform pregnancy tests before the first treatment and then retest regularly.

### Considerations

This study was approved by the local ethics committee of Hospital Lapino (MD medical group). It complied with ethical principles stated in the Declaration of Helsinki, Convention on Human Rights and Biomedicine, and International Ethical Guidelines for Health-related Research Involving Humans, and it completely excludes impairment of patients' interests and damage to health. All subjects were informed about the study's potential risks and possible benefits, and all participants provided written informed consent.

### Treatment Protocol

Both intervention groups received ten treatments in total addressing the stimulation of PFM. The G1 group was treated using a BTL EMSELLA (BTL Industries Inc, Boston, MA) device, which uses HIFEM technology for noninvasive PFM stimulation and reeducation based on the principle of electromagnetic induction. The device consists of a generator connected to the chair where the stimulation coil is located. The coil emits a focused magnetic field of intensities up to 2.5 Tesla, responsible for the induction of muscle contraction up to depths of 10 cm. Each therapy with the BTL EMSELLA device lasted 28 minutes and was administered under a skilled physician's supervision at the Lapino Hospital. Patients were seated in a chair, and the intensity of the stimulus was modulated on the scale of 0-100% (0-2.5 Tesla) by their feedback up to the maximum tolerable threshold when patients felt a strong muscle contraction but without pain or discomfort. All patients have achieved 100% intensity during the first or second procedure. Treatments with HIFEM were addressed 2-3 times per week for four weeks. The sessions were planned to suffice this interval per the patient/device availability. Two consecutive treatments were spaced at least 48 hours apart to prevent muscle fatigue. The G2 group performed home-based and self-administered procedures with a BioBravo (MTR Vertriebs, GMBH, Germany) electrical stimulation device:

1. The patients were comprehensively trained to safely and effectively use a BioBravo stimulator.

2. They were instructed to finish treatments at home by repeating therapy every other day. The stimulation protocol was identical for both groups because the settings of the BioBravo device were adjusted to reflect those used by the BTL EMSELLA device.
3. Group G3 did not receive any treatment.

### sEMG Measurements

The study's primary outcome was to perform sEMG measurements to determine the activation of the PFM in symptomatic and asymptomatic patients and to document the hypothesized changes caused by muscle strengthening. At first, by using a Myomed 632 myofeedback device (Enraf-Nonius B.V., Netherlands), the patients were instructed on how to correctly perform contractions of the PFM without (voluntary) involving the muscles of the anterior abdominal wall and gluteal or hip region. When performing contractions, patients were lying in the supine position. During the examination, they were requested to repeat three specified PFM activations, which consisted of the following: five short (quick flick) contractions at maximum intensity with an interval of 10 seconds, followed by sustained contractions and relaxation (both 10 seconds long, five repetitions) and finally the sustained contraction held as long as possible to determine PFM endurance.[33] The sEMG recordings were performed by the Myomed 632 device at the baseline (all groups) and after the patient's last treatment (only G1 and G2). To isolate the signal originating in the PFM, two types of superficial electrodes were used: the first was applied on the anterior abdominal area (served as reference), and the second (vaginal) electrode was mounted on the intravaginal probe. The neutral gel was always applied on the sensor introduced into the vagina. An experienced physiotherapist confirmed the correct placement of the intravaginal probe and PFM contractions. Concurrent registration of muscular electric potential by using the vaginal and skin electrodes allowed differentiating PFM contractions. During the sEMG examination, myofeedback (in the form of a graph) was displayed on the device's monitor and the external monitor unit connected to the device to enlarge the graphic output. The sEMG measurements were performed automatically by the Myomed device, following the pattern of PFM activations described above. These parameters were acquired for each patient during each visit: MVC, mean MVC, mean activity at rest/resting level (all in mV), and endurance of contraction (in seconds).

### Standardized Questionnaire

The secondary outcome was to assess subjective changes in the perception of PFD by the PFIQ-7. This standardized Questionnaire was used to determine the impact of PFD on the patient's quality of life, as it was shown to be psychometrically valid and reliable in previous research.[34] Patients from groups G1 and G2 were given the PFIQ-7 at baseline and after the last treatment. Based on their answers, the PFIQ mean scores (on a scale from 0 = no distress to 300 = maximal distress) were calculated and compared against baseline and between both groups.

### Safety

The safety of treatments, sEMG measurements, and possible adverse events (AEs) were monitored. Patients were also asked to report any signs of discomfort or pain during the therapies or caused by the positioning of the intravaginal electrode.

### Statistical Analysis

All variables were checked for normality using the Kolmogorov-Smirnov test. Descriptive statistics were estimated by the sample mean with a 95% confidence interval. The differences between groups were tested using an analysis of variance test followed by Least Significant Difference post hoc tests. Levene's variance homogeneity test was run before variance analysis to verify the equal variances in groups. A student's t-test tested paired variables. All statistical tests were 2-tailed. A whole statistical analysis was conducted with Statistica v.6 (StatSoft Inc, Tulsa, OK), and the significance level was set as default to 0.05 (5%). Initially, the minimum sample size was verified by using Statistica software. At least 19 subjects must have been included in the three tested groups to achieve a power of 80% with a = 5%.

## RESULTS

### Patient Group Characteristics

In total, 95 patients were recruited between 2018 and early 2019 following the specified criteria and the current state of patients in the clinic: G1 (n=50), G2 (n=25), and G3 (n=20). See Table 1 for detailed characteristics of patient groups. All recruited patients from the G1 and G2 groups finished a prescribed number of treatment sessions. Eight patients with zero PFIQ-7 score at the baseline (G1=5, G2=3) were excluded from the questionnaire evaluation. No AEs were observed regarding the delivered treatments or sEMG measurements. Subjects seldom reported only mild discomfort when recording sEMG using an intravaginal electrode.

***Table 1.*** ***Characteristics of patient groups at the time of recruitment (mean followed by 95% confidence interval)***

| Group | Age (years) | BMI (kg/m2) | Vaginal deliveries | PFD symptoms (% of patients) |
|---|---|---|---|---|
| G1 (n = 50) | 31.12 (1.52) | 23.27 (0.76) | 1.76 (0.22) | Urinary incontinence (74%); decreased sexual desire (36%); decreased sensitivity during intimacy (70%); dyspareunia (26%); hypo/anorgasmia (52%) |
| G2 (n = 25) | 31.96 (3.20) | 24.32 (3.70) | 1.56 (0.27) | Urinary incontinence (72%); decreased sexual desire (44%); decreased sensitivity during intimacy (44%); dyspareunia (24%); hypo/anorgasmia (40%) |
| G3 (n = 20) | 27.20 (2.02) | 22.40 (1.27) | 1.25 (0.21) | - |

BMI = body mass index; PFD = pelvic floor dysfunction.

### Quantification of the EMG Signal

The results of sEMG measurements are summarized in Table 2. In general, there are significant differences between the symptomatic groups in comparison with healthy patients. On the other hand, the changes in the measured values after the HIFEM or electrical stimulation were highly

statistically significant (P < .001) in comparison with the baseline, showing that stimulation of the PFM modifies the muscle (electrical) activity.

At baseline, the measured peak intensity of the MVC signal was significantly higher in healthy patients by approximately 22 mV on average than in the G1 or G2 group. At the same time, there was no change between the intervention groups. At the end of the study, the G1 group showed significantly higher EMG values than the G2 group (P < .001), reaching an average change of 10.58 mV (57.29%) and 1.44 mV (7.34%), respectively. Although the HIFEM treatment considerably increased the PFM activity, the G1 group still showed lower values than the control. Similar findings were observed in the case of average MVC. As expected, the average MVC magnitudes are lower in each group. A more profound increment was also observed in the G1 group (6.65 mV, 58.69%) compared with a modest increase in the G2 group (0.91 mV, 6.81%). There were also significant differences between the G1 and G2 groups after treatments (P < .05). Despite the observed improvement, asymptomatic subjects still showed greater EMG values.

Interestingly, the examination of muscle activity at rest revealed divergent tendencies. Initially, only the G1 group showed significantly different (higher) values from the control (P < .05), while after the last therapy, the G1 average resting level decreased at the level of G3 (2.08 mV and 1.90 mV, respectively). Conversely, the average resting level of the G2 group had risen from 2.42 mV to 3.94 mV. In conclusion, the G2 subjects manifested significantly higher EMG values than the control and G1 groups at the end of the study (P < .001). Regarding endurance, significant differences were observed between the symptomatic and the control groups at the baseline and after the treatments (see Table 2). The measurement of the G3 group showed that healthy patients could hold the contraction of the PFM on average for 62.25 seconds.

Furthermore, we observed a significant increase in the endurance of PFM contraction by 48.24% in the G1 group because the patients could hold a contraction by 13.44 s longer after their treatments, reaching 41.30 s in total. The G2 group improved by 36.26%, and PFM contraction was prolonged on average by 6.60 s.

***Table 2.*** ***Results of the sEMG measurements at the baseline and after the last therapy for both treated groups (G1 and G2) and control subjects (G3) are presented as mean followed by a 95% confidence interval in brackets***

| Measurement | Group | Baseline | After |
|---|---|---|---|
| Peak MVC (mV) | G1 (n=50) | 19.49 (2.31) | 30.06*** (3.75) |
| | G2 (n=25) | 19.56 (2.93) | 21.00 (2.82) |
| Average MVC (mV) | G1 (n=50) | 11.33 (1.54) | 17.99†,* (2.50) |
| | G2 (n=25) | 13.39 (2.46) | 14.30 (2.42) |
| Resting level (mV) | G1 (n=50) | 3.83†,* (0.82) | 2.08 (0.38) |
| | G2 (n=25) | 2.42 (0.45) | 3.94†,*** (0.60) |
| | G3 (n=20) | 1.90 (0.63) | - |
| Endurance (s) | G1 (n=50) | 27.86†,** (4.17) | 41.30†,*** (5.21) |

| Measurement | Group | Baseline | After |
|---|---|---|---|
| | G2 (n=25) | 24.80 (3.12) | 32.69 (1.88) |
| | G3 (n=20) | 41.96 (2.51) | 62.25 (3.68) |

*P < .05, **P < .01, ***P < .001.

### Pelvic Floor Impact Questionnaire Short Form 7

The patient's subjective evaluation is summarized in Table 3 and Figure 1. The minimal variation in the baseline score of both symptomatic groups was insignificant. Nonetheless, after the last treatment, there was a significant difference in the PFIQ score between the G1 and G2 groups (P < .01). Although both treatment modalities resulted in highly substantial subjective improvement, the patients treated with HIFEM experienced more remarkable outcomes. In addition, 16 patients (35.56%) from the G1 group reached a score of zero after the HIFEM treatments (meaning 100% improvement against the baseline). Contrary to this, only three patients (12.00%) from the G2 group who underwent electrical stimulation reported zero scores at their last visit. The shift in PFIQ scores is visualized in Figure 1. As can be seen, the relative frequency of scores was remarkably changed in the G1 group, while almost 90% of patients fell into the low score categories (0-10 or 10-20) after the treatments. In addition, scores of more than 50 were eliminated from patient's responses. The G2 group showed minimal changes in patients' PFIQ scores distribution, corresponding to a moderate average improvement of 5.15 points (see Table 3).

***Table 3.*** ***Results of the Pelvic Floor Impact Questionnaire Short Form 7 (PFIQ-7) for both treated groups (G1 and G2) at baseline and after the last therapy session presented as mean followed by a 95% confidence interval in brackets***

| Group | Baseline | After |
|---|---|---|
| G1 (n=45) | 37.16 (4.68) | 15.95 (2.55) |
| G2 (n=22) | 32.28 (5.92) | 21.96 (3.37) |

## DISCUSSION

Our examination of PFM electrogenesis in patients who showed signs of PFD revealed a significant reduction of the generated EMG signal compared with the asymptomatic patients at baseline (MVC, mean MVC, and endurance). The results of intervention groups G1 and G2 denote that noninvasive PFM strengthening can positively influence PFM activity. As seen in Table 2, the sEMG measurements obtained after therapies with the BTL EMSELLA device or electrical stimulation showed increased values of maximum possible voluntary contraction and endurance. It suggested that at the end of the study, patients could have more robust and more complex PFM contractions, resulting in a reduction of PFD symptoms (whether incontinence or sexually based), also demonstrated by a significant decrease in the PFIQ-7 score.

In contrast to sEMG measurements, which demonstrated considerable PFM weakening in the G1 and G2 groups at baseline, the PFIQ resulted in relatively low scores in both groups. We attribute this to perhaps a less specific grading system of the PFIQ when evaluating patients who showed various PFD-related symptoms of different severity. In future studies, it might be beneficial to focus on evaluating a particular patient's symptoms by using condition-specific questions assessed by a visual analog scale or a 5 to 7-point Likert scale, for instance, to enhance grading possibilities.

A magnetic and electrical stimulation comparison showed a significant improvement in EMG values, observed in the G1 group, which was treated by HIFEM technology. Compared with electrical stimulation, the BTL EMSELLA device was shown to be substantially more effective in restoring muscle strength as the MVC, mean MVC and endurance parameters uniformly increased from 48 to 59% after HIFEM treatments. On the contrary, electrical stimulation induced only mild changes in MVC (7.34%) or mean MVC (6.81%) while reaching mild to moderate improvement (36.26%) in endurance. The sEMG measurements coincide with the results of the PFIQ. The patient's subjective evaluation showed more pronounced improvement in the G1 group (57.16%) than in the G2 group (32.18%), corresponding to the improvement rate in EMG values. The HIFEM procedure also substantially reduced high PFIQ scores after the last therapy session (see Figure 1).

### PFM Electrical Activity and sEMG Measurements

Given the specific patient group and scarce evidence in the literature, control group G3 was established to obtain normative EMG values that were valid for the studied sample. In general, the results presented here coincide with the previously published findings. It has been documented by numerous authors[13-15,17,18,20] that women who are suffering from PFD show lower MVC and endurance values because of the impairment of the PFM. Properly stimulating the PFM allows patients to produce more significant voluntary contractions for longer durations. In addition, the PFD influences muscle activity at rest as the PFMs are less electrically active.

However, the PFM resting level evaluation revealed significant differences between both modalities in our study. Although the G1 group, after treatments, reached similar EMG values as the healthy population, patients from group G2 showed altered muscle activation with relatively high electromyogenesis at rest (3.94 mV on average, see Table 2). This indicates that G2 patients cannot correctly relax their PFM after treatments because they cannot isolate and control the appropriate muscle activation patterns, which was then reflected by the lower MVC amplitudes. The correct activation pattern during PFM contraction is associated with increased activation of the PFM and lower transverse abdominal wall with markedly less activation of the upper abdominal and chest wall. The inappropriate activation refers to increased abdominal and chest wall activation while PFM activation decreases,[16] resulting in lessened strength (MVC amplitude) of contraction.

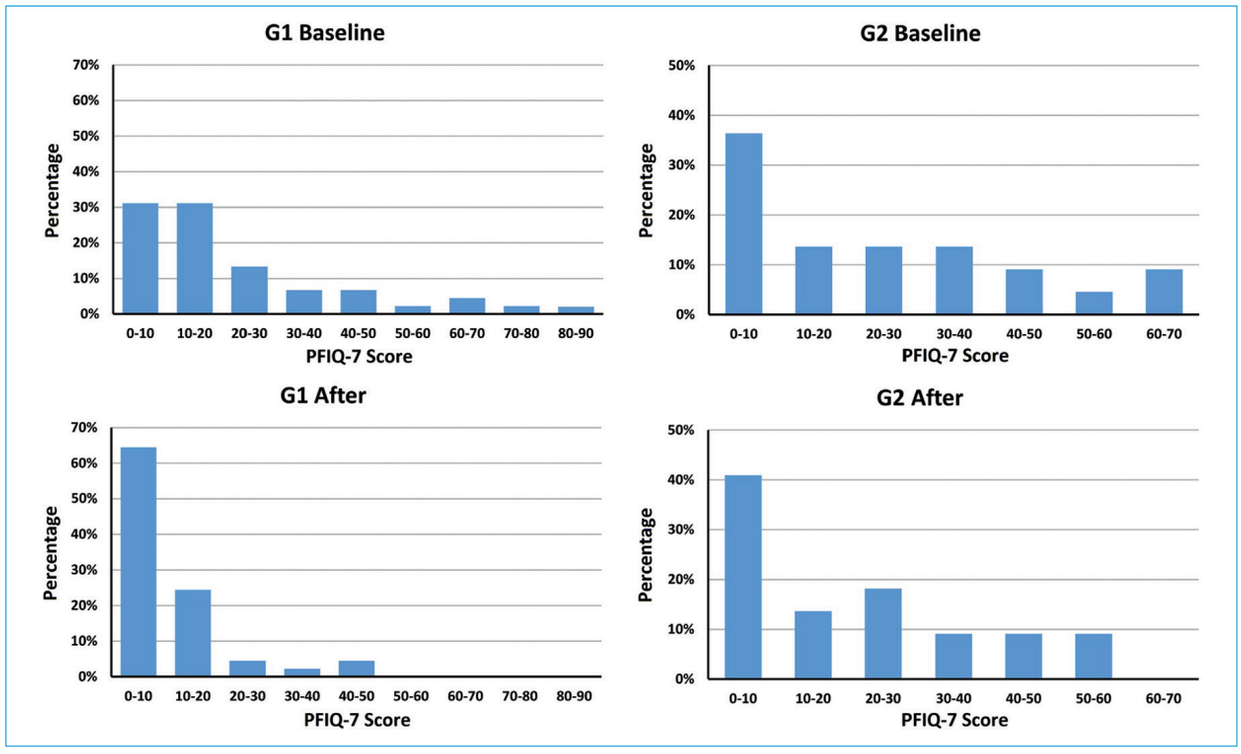
Showing high test-retest reliability,[13,14] the sEMG measurement is a valuable tool for detecting PFM activity. To record PFM electrical activity, we used an intravaginal electrode with a large surface to obtain EMG signals of sufficient amplitude with high sensitivity.[2,3] Fortunately, the PFM encompasses only a partial amount of subcutaneous tissue, possibly further attenuating the amplitude of EMG.[35] To prevent any systematic error during measurements, the skilled physiotherapist supervised the insertion and the position of the measuring electrode. Data normalization was

unnecessary as we assessed the same muscle group during one measurement session without removing the active electrode.[3] The selectivity of measured values was accomplished by the reference electrode placed on the abdomen. The signal obtained by the abdominal electrode was subtracted from the recording site to eliminate standard components and received EMG values, thus representing the summation activity of the whole PFM. To achieve an even greater degree of selectivity, the specific design of the vaginal electrode is required. For instance, Voorham-van et al.[14] have been able to successfully measure and compare the activity of selected pelvic muscles (pubococcygeus, puborectalis, bulbospongiosus, and ischiocavernosus) by using an experimental intravaginal probe with a matrix of 24 electrodes.

## Study Limitations

Still, an sEMG measurement faces various challenges. The nature of the recorded electrical signal (amplitude, frequency, or noise) is influenced by several factors, such as the composition of measured muscle and the structure and position or placement of electrodes.[35] The core and skin temperature[36] or different humidity of measured environments may also influence the signal parameters. Because of the moisture and temperature within the vaginal lumen, it is challenging to ensure identical conditions at each visit during the intravaginal measurements. The moisture between the electrode and tissue may lead to decreased EMG amplitude. Furthermore, the electrode positioning is crucial for the reliability of sEMG measurement. Therefore, the operator must consistently insert the intravaginal probe into the measured muscles, as the electrode orientation affects the signal's power.[37] In addition, the intravaginal probes should be designed in such a way

***Figure 1.*** ***The comparison of PFIQ-7 scores per group and appointment. The relative frequencies of scores reported by the patients of group 1 (G1) and group 2 (G2) are plotted in the graphs. There is a substantial shift toward the lower PFIQ-7 scores in the G1 group after the treatments.***



as to minimize any impact on the PFM by its insertion to avoid cross-talk and motion artifacts.[14] Indisputably, the appropriate planning of treatments is essential to achieve desired results. Unlike electrical stimulation, HIFEM is a relatively new technology that is still being investigated to some extent. In our study, the HIFEM treatments were administered at least 48 hours apart (2-3 per week) to maximize treatment outcomes and avoid muscle fatigue caused by overtreatment of the PFM, as the therapy with maximum settings produces intense muscle contractions. Presumably, the results would differ because of changes in the treatment frequency; however, this should be verified by future studies.

## CONCLUSION

Electromyographic measurement of PFM activity proved to be a valid method for examination of patients with PFD (suffering from urinary incontinence and/or accompanied by sexual dysfunction) treated with HIFEM and electrical stimulation. Surface EMG of the PFMs showed more profound muscle activation after HIFEM treatments, along with improved relaxation and enhanced endurance. The PFIQ also indicates a greater effect of the HIFEM procedure based on the significant change in patient scores. Documented outcomes imply that the HIFEM procedure is substantially more effective in restoring PFM strength and treating PFD when compared with the electrical stimulation applied correspondingly in postpartum women.

**Corresponding Author**: Silantyeva Elena, MD, Hospital Lapino MD Medical Group, 111, Lapino village, Odintsovo District 143081, Moscow Region, Russia. Tel: +7-916-060-20-00; Fax: +7-495-433-73-79; E-mail: essdoktor@yandex.ru

**Conflict of interest**

None.

**Funding**

None.

**Statement of Authorship**

**Category 1**

(a) Conception and Design: Silantyeva Elena(b) Acquisition of Data: Silantyeva Elena; Zarkovic Dragana; Soldatskaia Ramina; Astafeva Evgeniia(c) Analysis and Interpretation of Data: Silantyeva Elena; Astafeva Evgeniia; Mekan Orazov; Soldatskaia Ramina

**Category 2**

(a) Drafting the Article: Soldatskaia Ramina; Astafeva Evgeniia(b) Revising It for Intellectual Content: Silantyeva Elena; Zarkovic Dragana; Mekan et al.

**Category 3**

(a) Final Approval of the Completed Article: Silantyeva Elena

Elena S., Dragana Z., Ramina S., et al. Electromyographic Evaluation of the Pelvic Muscles Activity After High-Intensity Focused Electromagnetic Procedure and Electrical Stimulation in Women With Pelvic Floor Dysfunction. Sex Med 2020;XX:XXXeXXX. 

## REFERENCES


1. Selvan VA. Single-fiber EMG: a review. *Ann Indian Acad Neurol.* 2011; 14: 64-67.
2. Bø K, Sherburn M. Evaluation of female pelvic-floor muscle function and strength. *Phys Ther.* 2005; 85: 269-282.
3. Ribeiro AM, Mateus-Vasconcelos ECL, Silva TD da, et al. Functional assessment of the pelvic floor muscles by electromyography: Is there a normalization in data analysis? A systematic review. F*isioter e Pesqui.* 2018; 25: 88-99.
4. Raez MBI, Hussain MS, Mohd-Yasin F. Techniques of EMG signal analysis: detection, processing, classification, and applications. *Biol Proced Online*. 2006; 8: 11-35.
5. Salsi G, Cataneo I, Dodaro MG, et al. Three-dimensional/four-dimensional transperineal ultrasound: clinical utility and future prospects. *Int J Womens Health.* 2017; 9: 643-656.
6. Braekken IH, Majida M, Engh ME, et al. Test-retest reliability of pelvic floor muscle contraction measured by 4D ultrasound. *Neurourol Urodyn.* 2009; 28: 68-73.
7. García del Salto L, de Miguel Criado J, Aguilera del Hoyo LF, et al. MR imaging-based assessment of the female pelvic floor. *RadioGraphics*. 2014; 34: 1417-1439.
8. Angelo PH, Varella LRD, de Oliveira MCE, et al. A manometry classification to assess pelvic floor muscle function in women. *PLoS One.* 2017; 12.
9. Chamochumbi CCM, Nunes FR, Guirro RRJ, et al. Comparison of active and passive forces of the pelvic floor muscles in women with and without stress urinary incontinence. *Braz J Phys Ther.* 2012; 16: 314-319.
10. Faubion SS, Shuster LT, Bharucha AE. Recognition and management of nonrelaxing pelvic floor dysfunction. *Mayo Clin Proc.*2012; 87: 187-193.
11. Strohbehn K. Normal pelvic floor anatomy. Obstet Gynecol Clin North Am 1998; 25: 683-705.
12. Pemberton J, Swash M, Henry MM, eds. The pelvic floor: its function and disorders. London: Saunders; 2002.
13. Koenig I, Luginbuehl H, Radlinger L. Reliability of pelvic floor muscle electromyography tested on healthy women and women with pelvic floor muscle dysfunction. *Ann Phys Rehabil Med.* 2017; 60: 382-386.
14. Voorham-van der Zalm PJ, Voorham JC, van den Bos TWL, et al. Reliability and differentiation of pelvic floor muscle electromyography measurements in healthy volunteers using a new device: the multiple array probe Leiden (MAPLe). *Neurourol Urodyn*. 2013; 32: 341-348.
15. Zhang Q, Wang L, Zheng W. Surface electromyography of pelvic floor muscles in stress urinary incontinence. *Int J Gynecol Obstet*. 2006; 95: 177-178.
16. Thompson JA, O'Sullivan PB, Briffa NK, et al. Altered muscle activation patterns in symptomatic women during pelvic floor muscle contraction and Valsalva maneuver: altered Muscle Activation Patterns. *Neurourol Urodyn.* 2006; 25: 268-276.
17. Smith MD, Coppieters MW, Hodges PW. Postural response of the pelvic floor and abdominal muscles in women with and without incontinence. *Neurourol Urodyn*. 2007; 26: 377-385.
18. Sapsford RR, Richardson CA, Maher CF, et al. Pelvic floor muscle activity in different sitting postures in the continent and incontinent women. *Arch Phys Med Rehabil.* 2008; 89: 1741-1747.
19. Pereira LC, Botelho S, Marques J, et al. Are transversus abdominis/oblique internal and pelvic floor muscles coactivated during pregnancy and postpartum? *Neurourol Urodyn.* 2013; 32: 416-419.

20. Lauper M, Kuhn A, Gerber R, et al. Pelvic floor stimulation: What are the good vibrations? *Neurourol Urodyn*. 2009; 28: 405-410.
21. Junginger B, Baessler K, Sapsford R, et al. Effect of abdominal and pelvic floor tasks on muscle activity, abdominal pressure, and bladder neck. *Int Urogynecol J.* 2010; 21: 69-77.
22. Gagnon L-H, Boucher J, Robert M. Impact of pelvic floor muscle training in the postpartum period. *Int Urogynecol J.* 2015; 27: 255-260.
23. Zuchelo LTS, Bezerra IMP, Da Silva ATM, et al. Questionnaires to evaluate pelvic floor dysfunction in the postpartum period: a systematic review. *Int J Womens Health.* 2018; 10: 409-424.
24. Radziminska A, Straczynska A, Weber-Rajek M, et al. The impact of pelvic floor muscle training on the quality of life of women with urinary incontinence: a systematic literature review. *Clin Interv Aging.* 2018; 13: 957-965.
25. Correia GN, Pereira VS, Hirakawa HS, et al. Effects of surface and intravaginal electrical stimulation in treating women with stress urinary incontinence: randomized controlled trial. *Eur J Obstet Gynecol Reprod Biol.* 2014; 173: 113-118.
26. Schreiner L, Santos TG dos, Souza ABA de, et al. Electrical stimulation for urinary incontinence in women: a systematic review. *Int Braz J Urol.* 2013; 39: 454-464.
27. Samuels JB, Pezzella A, Berenholz J, et al. Safety and efficacy of a noninvasive high-intensity focused electromagnetic field (HIFEM) device for treating urinary incontinence and enhancing quality of life. *Lasers Surg Med.* 2019; 51: 760-766.
28. Hlavinka T, Turcan P, Bader A. The use of HIFEM technology in the treatment of pelvic floor muscles as a cause of female sexual dysfunction: a multi-center pilot study. *J Womens Health Care.* 2019; 08.
29. Alinsod R, Vasilev V, Yanev K, et al. Hifem technology is a new perspective in the treatment of stress urinary incontinence. *Lasers Surg Med.* 2018; 50
30. Omar A, Marwaha K, Bollu PC. Physiology, neuromuscular junction. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2019; Available at: http://www.ncbi.nlm.nih.gov/books/NBK470413/. Accessed December 5, 2019.
31. Faraday MV. Experimental research in electricity. *Philos Trans R Soc Lond.* 1832; 122: 125-162.
32. Kanjanapanang N, Chang K-V. Peripheral magnetic stimulation (transcutaneous magnetic stimulation). In: *StatPearls*. Treasure Island, FL: StatPearls Publishing; 2019; Available at: http://www.ncbi.nlm.nih.gov/books/NBK526087/. Accessed May 29, 2019.
33. Mehler B, Larsson KM. Electromyographic (EMG) biofeedback in the treatment of pelvic floor disorders. In: Mostofsky DI, ed. The handbook of behavioral medicine. Oxford, UK: John Wiley & Sons, Ltd; 2014; 313-338.
34. Barber MD, Kuchibhatla MN, Pieper CF, et al. Psychometric evaluation of 2 comprehensive condition-specific quality of life instruments for women with pelvic floor disorders. *Am J Obstet Gynecol.* 2001; 185: 1388-1395.
35. De Luca CJ. The use of surface electromyography in biomechanics. *J Appl Biomech.* 1997; 13: 135-163.
36. Coletta NA, Mallette MM, Gabriel DA, et al. Core and skin temperature influences on the surface electromyographic responses to an isometric force and position task. *PLoS One.* 2018; 13
37. Basmajian JV, Luca CJD. Muscles alive: their functions revealed by electromyography. Subsequent edition. Baltimore: Williams & Wilkins; 1985.

# DURING THE CORONAVIRUS DISEASE 19 (COVID-19) PANDEMIC, WE ENCOUNTERED SEVERAL CLINICAL DILEMMAS THAT NEEDED TO SOLVE

***AIZER ADVA**, PhD*
*Department of Obstetrics and Gynecology, Chaim Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel*
***ORVIETO RAOUL**, MD*
*The Tarnesby-Tarnowski Chair for Family Planning and Fertility Regulation, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel*

## SUMMARY

This study investigates the effects of COVID-19 infection and mRNA SARS-CoV-2 vaccination on fertility outcomes in women and men's subsequent in vitro fertilization (IVF) cycles.

**Keywords:** COVID-19, mRNA SARS-CoV-2 vaccination, fertility outcomes, IVF cycles, infection effects, reproductive health, COVID-19 and fertility

## INTRODUCTION

1. Assess the effect of COVID-19 infection on subsequent IVF cycle outcomes.
2. Evaluate the impact of mRNA SARS-CoV-2 vaccination on subsequent IVF cycle outcomes.
3. Investigate whether mRNA SARS-CoV-2 vaccination influences semen analysis parameters in fertile males.
4. Analyze the effect of mRNA SARS-CoV-2 vaccination on Anti-Müllerian Hormone (AMH) levels.
5. Examine the relationship between patients' immunization following COVID-19 infection or mRNA vaccination and endometrial receptivity, as measured by outcomes in frozen-thawed embryo transfer (FET).

## METHODS

A series of studies assessed the impact of COVID-19 infection and mRNA vaccines on fertility parameters.

## RESULTS

The findings revealed that mRNA vaccination had no significant effects on IVF treatment outcomes, ovarian reserve, gamete or embryo quality, or endometrial receptivity. Conversely, COVID-19 in-

fection was found to detrimentally affect gamete and embryo quality, mainly when IVF treatment was initiated within 3-6 months following recovery from the infection. No significant effects were observed on IVF treatment or ovarian reserve.

## CONCLUSION

The results indicate that while COVID-19 vaccination does not adversely impact IVF outcomes, COVID-19 infection poses a significant risk to gamete and embryo quality. Therefore, it is advisable to consider the timing of IVF treatment in relation to COVID-19 infection recovery.

# ENDOMETRIOSIS AND INFERTILITY

***BOCHORISHVILI REVAZ**, MD, PhD, Prof.*
*Obstetrician-Gynecologist, Laparoscopic Surgeon, Tbilisi, Georgia*

## SUMMARY

The surgical treatment of endometriosis remains a contentious topic, particularly regarding the preservation of ovarian function. This paper reviews the arguments for and against surgical intervention, including the effects on pain reduction, ovarian cancer risk, and fertility outcomes.

**Keywords:** Endometriosis, surgical treatment, ovarian function, pain reduction, ovarian cancer risk, fertility outcomes, surgical intervention

## INTRODUCTION

Endometriosis, a condition characterized by the presence of endometrial-like tissue outside the uterus, can significantly impact fertility. The management of endometriosis often involves surgical intervention; however, the implications for ovarian reserve and overall fertility remain a critical consideration. This paper explores the current understanding of the surgical treatment of endometriosis, particularly in the context of preserving ovarian function.

## METHOD

A literature review was conducted, focusing on studies related to surgical techniques for endometriomas, including cystectomy and laparoscopic aspiration. Data on ovarian reserve markers, particularly Anti-Müllerian Hormone (AMH) levels, were analyzed to assess the impact of surgical interventions on fertility outcomes.

## RESULTS

Surgical cystectomy can lead to the removal of the normal ovarian cortex, with reports indicating rates of 6% to 50% in various studies (Muzii et al., 2002; Hachisuga et al., 2005) and >90% in spe-

cific populations (Roman et al., 2010; Dogan et al., 2011). Although surgery may provide benefits such as pain relief and reduced cancer risk, the impact on fertility is concerning. Postoperative AMH levels often decline, particularly in patients with pre-existing low levels. Furthermore, studies indicate that laparoscopic aspiration or cystectomy prior to assisted reproductive technology (ART) shows no significant advantage over expectant management concerning clinical pregnancy rates.

## DISCUSSION

Surgical intervention for endometriosis is fraught with challenges, particularly regarding its potential to harm ovarian reserve. Risk factors for negative surgical outcomes include age over 38, low AMH/AFC, and the presence of multiple or bilateral endometriomas. The ESHRE guidelines advocate for the excision of the endometrioma capsule rather than ablative techniques to enhance postoperative pregnancy rates. Patients must be fully informed of the potential risks, including diminished ovarian reserve and loss of ovarian tissue.

Research indicates that endometriomas have toxic effects on ovarian tissue, including oxidative stress and fibrosis, which may further complicate the reproductive potential of affected individuals. While some studies suggest that AMH levels may improve post-surgery, this is contingent on the quality of the surgical intervention.

## CONCLUSION

Surgical treatment of endometriosis continues to be a standard approach, but careful consideration must be given to preserving ovarian function and reserve. The surgeon's expertise plays a vital role in minimizing damage to ovarian tissue. Ultimately, the goal should be to address endometriomas with a single surgical intervention to optimize fertility outcomes.

**International Conference "Infertility 35+ "**

**1 February, 2020**

**9:00 - 10:00 |** Registration

I SECTION

Chairman: **ARCHIL KHOMASURIZE**
Moderator: **NINO MUSERIDZE**

**10:00 - 10:15 |** Opening ceremony. Welcome addresses

**ARCHIL KHOMASURIDZE** (GEORGIA)
MD, Ph.D., Professor, President of Georgian Reproductive Association.

**10:15 - 11:15 |** Poor Responders

**DOV FELDBERG** (ISRAEL)
MD, Ph.D., Gynecologist, Reproductologist, Co-Chairman Reproductive Endocrinology & Infertility (REI), Committee of International Federation of Gynecology and Obstetrics (FIGO).

**11:15 - 11:45 |** ART 35+

**VLADISLAV KORSAK** (RUSSIA)
MD, Ph.D., Professor
General Director of ICRM (International Center of Reproductive Medicine.
President of Russian Association of Human Reproduction (RAHR),
ESHREEIM Community Council member.

**11:45 - 12:30 |** *Coffee break*

II SECTION

Chairman: **ARCHIL KHOMASURIDZE**
Moderator: **NINO MUSERIDZE**

**12:30 - 13:00 |** Endometrium and ART Outcomes

**VLADISLAV KORSAK** (RUSSIA)
MD, Ph.D., Professor

**13:00 - 13:30 |** Micro TESE

**IVAN HOFFMANN** (GERMANY)
MD, Ph.D, Urologist, Secretary of the German Society of Andrology (DGA), Berlin Andrology Center

**13:00 - 13:45 |** Sperm DNA fragmentation: where and how it occurs?

**ALEKSANDER KHELAIA** (GEORGIA)
Md, Ph.D., Urologist, National Center of Urology,Tbilisi, Georgia.
Associated Professor of European University.
Co-chair of Androlgy section of Georgian Urological Association,
EAU Section of Andrological Urology member (ESAU)

**13:45 - 14:00 |** Study cases in IVF

**TAMAR MAGULARIA** (GEORGIA)
MD, Ph.D., Reproductologist, Georgian-German Reproductive Center.

**NINO MUSERIDZE** (GEORGIA)
MD, Ph.D., Embryologist,
Clinical Director of Georgian-German Reproductive Center.

**14:00 - 14:30 |** Infertility and Thrombophilia

**DOV FELDBERG** (ISRAEL)
MD, Ph.D.

**14:30 - 16:30 |** *Lunch*

**DOV FELDBERG** (ISRAEL)
MD, Ph.D.

III SECTION

Chairman: **TENGIZ ASATIANI**
MD, Ph.D., Professor,
Chairman of Georgian Obstetrician's and Gynecologists Association.
Moderator: **NINO MUSERIDZE**

**16:30 - 17:00 |** Genetic Test in Reproductology

**GÜLAY ÖZGÖN** (TURKEY)
MD, Ph.D., Geneticist, Nesiller Genetik Tanı Merkezi.

**17:00 - 17:30 |** Discuss the book

Authors: **VLADISLAV KORSAK, NINO MUSERIDZE**

**17:30 - 18:45 |** Workshop - "Embryotransfer"

**SEMRA SERTYEL** (TURKEY)
MD, Embryologist, Head of IVF Department of Medical Park.

**YASHAR TAYFUN ALPER** (TURKEY)
MD Ph.D., Reproductologist, IVF Department of Medical Park.













ERENCE AND WORKSHOP
GEORGIAN-GERMAN REPRODUCTIVE
TBILISI, GEORGIA
TY 35+


INTERNATIONAL CONFERENCE AND WORKSHOP 2020
1 FEBRUARY, 2020
GEORGIAN-GERMAN REPRODUCTIVE CENTER


ank you for your attention...
tayfunalper@yahoo.com
MEDICALPARK


















1 FEBRUARY, 2020
TBILISI, GEORGIA







**2nd International Conference "Infertility 35+"**

**12-13 June, 2021, Tbilisi, Georgia**

**12/06/2021 Day 1**

**8:30 - 9:00 |** Registration

**I SECTION**
**9:00 - 12:00**

Chairman: **ARCHIL KHOMASURIDZE**
Moderator: **NINO MUSERIDZE**

**9:00 - 9:20 |** Opening ceremony. Welcome addresses

**ARCHIL KHOMASURIDZE (GEORGIA)**
MD, Ph.D. Professor, President of Georgian Reproductive Association

**9:20 - 9:40 |** Micro TESE State of the Art

**IVAN HOFFMANN (GERMANY)**
MD, Urologist, Andrologist, Europian Academy of Andrology EAA,
Secretary of the German Society of Andrology (DGA),
Berlin Andrology Center

**09:40 - 10:00 |** The Role of LH for Ovarian Stimulation 35+

**ROBERT FISCHER (GERMANY)**
MD, MVZ Fertility Center Hamburg GmbH,
Medical Director, Reproductive Endocrinologist

**10:00 - 10:20 |** Overcoming Infertility of Women in Older of Reproductive Age. Is the Result of ART Predictable?

**VYACHESLAV LOKSHIN (KAZAKHSTAN)**
Professor, Academician of the National Academy of Sciences of the RK,
President of the Kazakhstan Association of Reproductive Medicine (KARM), CEO of the ICCR "PERSONA"

**10:20 - 10:40 |** Is There a Place for Gestagens in the Stimulation of Superovulation in IVF Programs

**SHOLPAN KARIBAYEVA (KAZAKHSTAN)**
Candidate of Medical Sciences, Reproductologis,
Director for Strategic Development of the ICCR "PERSONA"

**10:40 - 11:00 |** Covid 19 and ART

**VLADISLAV KORSAK (RUSSIA)**
MD, Ph.D., Professor, General Director of ICRM.
President of Russian Association of Human Reproduction (RAHR),
ESHREEIM Community Council member

**11:00 - 11:20 |** "Pure" IVM has Opened the Way to a "Peaceful" Consensus in the Collaboration of an Oncologist and a Reproductologist! Experience of St. Petersburg

**MAKA OSEPAISHVILI (RUSSIA)**
MD, Ph.D., Obstetrician-Gynecologist, Reproductologist, NGC St. Petersburg

**11:20 - 11:40 |** ART in Women of Late Reproductive Age

**NATO SHAMUGIA** (RUSSIA)
MD, Ph.D., Associate Professor of the Department of Obstetrics and Gynecology, RMANPO, Medical Director of the GMS IVF Clinic, obstetrician-gynecologist, reproductologist, Member of the Education Committee of the Russian Association of Human Reproduction (RAHR)

**11:40 - 12:00 |** IVF. How Not to Turn Your Last Hope into a Missed Opportunity

**TAMARA NADIRASHVILI** (GEORGIA)
MD, Ph.D., Obstetrician-Gynecologist, Reproductologist, Georgian-German Reproductive Centre (GGRC)

**12:00 - 12:20 |** *Coffee break*

**II SECTION**
**12:00 - 14:00**

**12:20 - 12:40 |** How is IVF Done at GGRC Clinic

**VENIAMIN KAZARINOV** (RUSSIA)
Embryologist, Head of Embryo Laboratory, Georgian-German Reproductive Centre (GGRC)

**12:40 - 13:00 |** PGT in Clinical Practice

**EKATERINA POMERANTSEVA** (RUSSIA)
MD, Ph.D., Genetic Laboratory, GMS Clinic

**13:00 - 13:20 |** Long-Dreamt Pregnancy and Then...

**MAKA GEGECHKORI** (GEORGIA)
MD, Ph.D., TSMU Professor, Zurab Sabakhtarashvili Reproductive center Head of Medical science department, Head of Association Georgian Gynecology and Endocrinology

**13:20 - 13:40 |** Fertility Preservation In Cancer Patients

**FOAD AZEM** (ISRAEL)
MD, Director - IVF Unit, Lis Maternity Hospital

**13:40 - 14:00 |** Advanced Maternal Age (up to 35) Require Advance Lab Technologies

**BIROL AYDIN** (TURKEY)
Head of Embryology laboratory, Leading clinic embryologist and management consultant

**14:00 -15:00 |** *Lunch*

**III SECTION**
**15:00 - 16:30**

**15:00 - 15:20 |** Estrogen Deficiency and Modern Principles of management

**JENARO KRISTESASHVILI** (GEORGIA)
MD, Ph.D., Vice president of Georgian Association of Reproductive Health, Professor of TSU Medicine School, Deputy chief of

Reproductive Medicine Center Universe, Associated member of
Human reproduction International Academy

**15:20 - 15:40 |** Expert Approach for Oocyte Donation

**ULIANA DOROFEYEVA (UKRAINE)**
MD, MRCOG, Medical Director OVOGENE Egg Bank,
Founder of Ukrainian Association of Medical Transportation "Biotransfer",
Expert Advisor of IVF Media

**15:40 - 16:00 |** Sperm Aneuploidy and Infertility

**ALEKSANDRE KHELAIA (GEORGIA)**
MD, PhD Urologist, National Center of Urology.
Professor of European University, Co-chair andrology section of
Georgian Urological Association

**16:00 - 16:20 |** Ovarian Stimulation in PCO Patients in ART

**BOTROS RIZK (USA)**
MD, MA, FACOG, FACS, HCLD, FRCOG, FRCS, Professor of Obstetrics
and Gynecology and the head of Reproductive Endocrinology
and Infertility and Medical and Scientific Director of In Vitro Fertilization
and Assisted Reproduction at the University of South Alabama,
Lab Director to Odessa fertility lab at Odessa Regional Medical center.
Faculty member at Texas Tech University in Odessa, TX

**16:20 - 16:40 |** ERPeak and Personalized Embryo Transfer

**TAMAR BADRIDZE (USA)**
MD, NYC IVF, New York, USA

**16:40 - 17:00 |** *Coffee break*

**IV SECTION**
**17:00 - 18:30**

**17:00 - 17:20 |** Corona Pandemic will End But Old, Familiar Viruses will Remain

**MADONA JUGELI (GEORGIA)**
MD, Ph.D., Gynecologist-reproductologist, President of
the Federation of Colposcopy of Georgia

**17:20 - 17:40 |** Ovarian Endometriosis and Reproduction: Is Surgery Necessary?

**REVAZ BOCHORISHVILI (FRANCE)**
Ph.D., Professor, MD, Obstetrician-Gynecologist, laparoscopic Surgeon.
Director of the International Centre of Endoscopic Surgery (CICE)
and Head of the Diagnostic and Treatment Centre of Endoscopic Surgery
of Policlinique de Hotel-Dieu (France), Head of gynecological department
of the Centre Hospitaller Universitaire Clermont-Ferrad

**17:40 - 18:40 |** *Discussion*

**18:40 - 19:00 |** Presentation of the new Magazine of GGRC

**NINO MUSERIDZE (GEORGIA)**
MD, Ph.D., Clinical Director of Georgian-German Reproductive Centre (GGRC)

**13/06/2021 Day 2**

**9:30 - 10:00 |** Registration

Workshop - Preliminary Registered Participants only

**10:00 - 10:15 |** Conference Conclusion

**ARCHIL KHOMASURIDZE (GEORGIA)**
MD, Ph.D. Professor, President, Georgian Association of Reproductive Health

**10:15 - 10:30 |** Legal Aspects of surrogacy and donation

**GIORGI ARCHVADZE (GEORGIA)**
General Director of Georgian-German Reproductive Centre

**10:30 - 12:00 |** Round Table - Actual Topics in the Reproductive medicine, Regional experiences

**VALERIA AGLONIETE (LATVIA)**
Gynecologist, Medical Director of "Your doctors" privet clinic,
Head of Latvian Human Reproduction Society,
Chairman of the board of Baltic society of reproductologists

**VIYACHESLAV LOKSHIN (KAZAKHSTAN)**
Professor, Academician of the National Academy of Sciences of the RK,
President of the Kazakhstan Association of Reproductive Medicine (KARM), CEO of the ICCR "PERSONA"

**12:00 - 12:15 |** *Coffee break*

**12:15 - 12:40 |** Round Table - Actual Topics in the Reproductive medicine

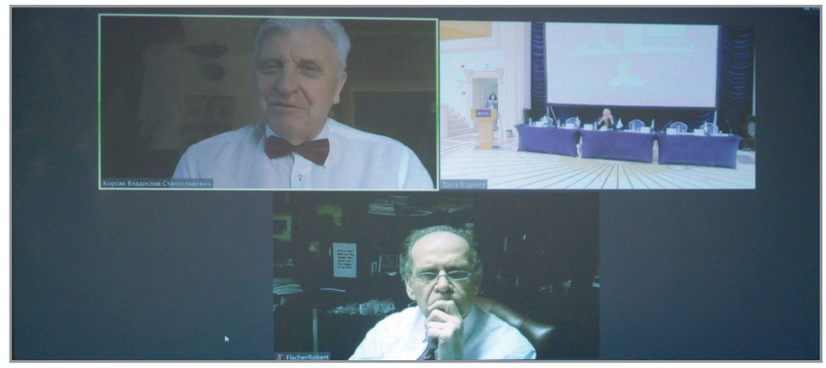
**NATO SHAMUGIA (RUSSIA)**
Member of the Education Committee of the Russian Association of Human Reproduction (RAHR), member of the Scientific Committee of the Association of Gynecologists, Endocrinologists and Therapists

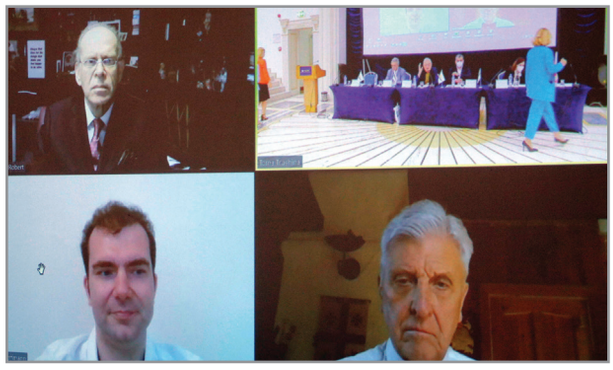
**12:40 - 14:00 |** *Discussion*

**14:00 - 15:00 |** *Lunch*

**15:30 - 18:30 |** *Tbilisi Sightseeing Tour*

**19:00 - 20:45 |** *Dinner in the Hotel*






Fero


ESI
onna life
VALERIA AGLONETE


Security
Participants
Chat
Share Screen
Record
Interpretation


GGRC


GGRC
GEORGIAN-GERMAN REPRODUCTIVE CENTER


INTERNATIONAL CONFERENCE


INTERNATIONAL CONFERENCE


GGRC


GGRC


GGRC


Ferolain


Donna life

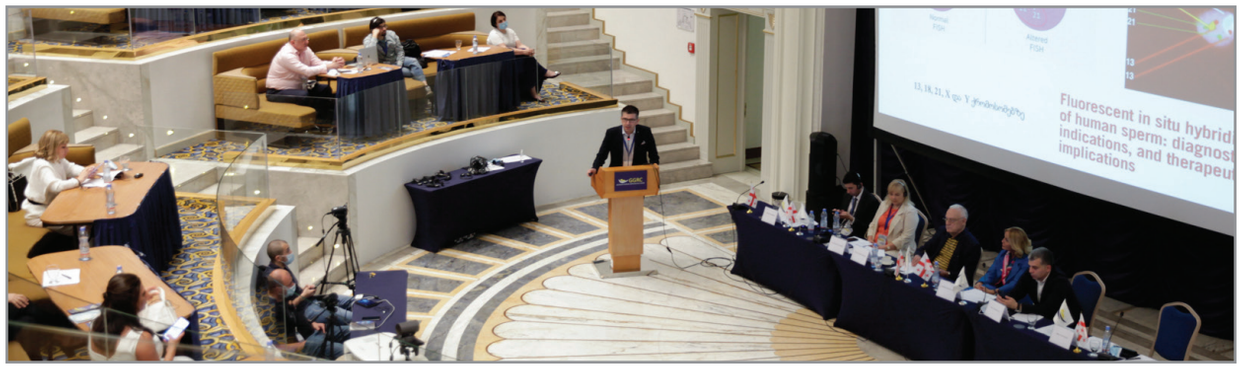

GGRC


GGRC


GGRC
GEORGIAN-GERMAN REPRODUCTIVE CENTER


GGRC
GEORGIAN-GERMAN REPRODUCTIVE CENTER


Unmute
Start Video


Fluorescent in situ hybrid
of human sperm: diagnost
indications, and therapeu
implications

Printed by ColorPress

Ekaterine Baghdavadze 3, Tbilisi

# INTERNATIONAL CONFERENCE AND WORKSHOP 2022

**GEORGIAN-GERMAN REPRODUCTIVE CENTER** — **TBILISI, GEORGIA**

## WORKSHOP
**Stem cell and PRP Therapy**

## INFERTILITY 35+

Medicine for Life
International Association

GEORGIAN-GERMAN REPRODUCTIVE CENTER
GGRC

ADAPHARM · RICH GROUP · Abbott A Promise for Life · AVERSI · GEOGROUP MEDICAL

YURIA-PHARM · ABM · ThermoFisher SCIENTIFIC · saf farma PHARMACY MARKETING · IBSA · STEMBIO

LL Group · PROFERTIL · InnoTeam FOLLOW THE INNOVATION · TBILISI MEDIC · GEA PHARMACEUTICAL COMPANY

GEDEON RICHTER · kromos genetics laboratory · MC Group · regenlab PRP & CELL THERAPY SPECIALISTS · CP COHA ФАРМ

## 18-19 SEPTEMBER 2022

*The Biltmore Hotel Tbilisi*