Preliminary Clinical Outcomes in an IVF Program using the ProteX™ versus a Standard Specimen Cup for Semen Collection

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OBJECTIVE: The advent of ICSI has given rise to the concept that sperm need only intact DNA to complete the fertilization process. The role other semen parameters might play a role in later embryo development is more controversial. Recently, a new sperm collection device (NSCD — ProteX), specifically designed to maximize the quality of samples used in clinical procedures, was introduced for semen collection. The following is the first report of outcomes from a large-scale study in an IVF setting.

DESIGN: Retrospective cohort comparing outcomes of IVF from semen samples produced in the NSCD containing a measured amount of culture media vs. a standard specimen cup (SSC) without media.

MATERIALS AND METHODS: A total of 1077 couples undergoing IVF used either a SSC or NSCD to collect their semen. Further, approximately 40% of the patients in each group produced their semen samples away from the clinic. Data collected included both partners' ages, standard semen parameters, stimulation and fertilization results, and embryo outcomes. As 92% of the patients were involved in freeze-all protocols, the primary embryo outcome was the percentage of embryos cryopreserved as high-quality expanded blastocysts.

RESULT: The female partners in the NSCD in-clinic arm had the highest average age (38.1; P < 0.02), and the lowest average number of oocytes recovered (10.9; P < 0.03). Male partners were of similar ages between groups. However, men producing in the NSCD device had higher initial counts and motility than men producing in the SSC (P < 0.001). In addition, while fertilization and usable blastocyst rates were similar between groups, there was an 11% higher blastocyst rate in the NSCD group (43.8% vs. 39.4%) when expressed as embryos frozen/oocyte fertilized (P < 0.04).

DISCUSSION: These retrospective data suggest that producing semen in a more physiological collection container (NSCD) may provide a larger pool of healthy sperm for IVF procedures and enhance outcomes such as the usable blastocyst rate. Furthermore, when used as designed (including a measured amount of media), it appears semen samples can be produced off-site in the NSCD without compromising IVF outcomes.

DISCLOSURES: S. D. Prien is the inventor and serves as scientific consultant to Reproductive Solutions.

FUNDING: ProteX used in this study were provided by Reproductive Solutions.

INTRODUCTION

It is well documented that as sperm cells are ejaculated, they are subjected to environmental changes, temperature fluctuations, and, in the case of collection for artificial insemination or other ART procedures, exposure to potentially toxic materials (including the collection containers). Exposure to these drastic changes leads to activation of a group of proteins referred to as shock proteins, which in turn leads to a programmed death of the cell. The original experimental device, which was dubbed the Texas Tech University Device for Improved Semen Collection (TTU-DISC), was used in experiments with the canine. The device was designed to 1) limit exposed surface area, 2) concentrate the sample to maximize internal volume while minimizing total surface area, 3) provide a buffering agent to limit shifts in pH, and 4) provide nutrients. These qualities allow the sample to maintain its temperature, pH, and osmolarity.

A commercial version of the DISC, termed the ProteX, was developed by Reproductive Solutions Inc. Physiological and biochemical studies demonstrated the ProteX to produce a superior environment for semen collection compared to the traditional standard specimen cup, as determined by higher motilities and other semen parameters, delayed acrosome reactions, and demonstration of healthier mitochondrial over extended periods of time. Further, in a small, FDA-approved equivalence trial, intrauterine insemination patients had similar conceptions rates, but those using the ProteX had significantly more pregnancies to continue to term and delivery.

The objective of the present study was to conduct the first large-scale clinical trials of the ProteX in assisted reproductive procedures. The study not only allowed a comparison of the collection device, but because of the shift in collection locations due to pandemic collection location as well. Male outcomes focused on traditional male fertility measurements. Because this program freezes most embryos before transfer, female outcomes focused on the number of embryos reaching blastocyst and cryopreservation.

FIGURE 1. Design and concept of the ProteX device.

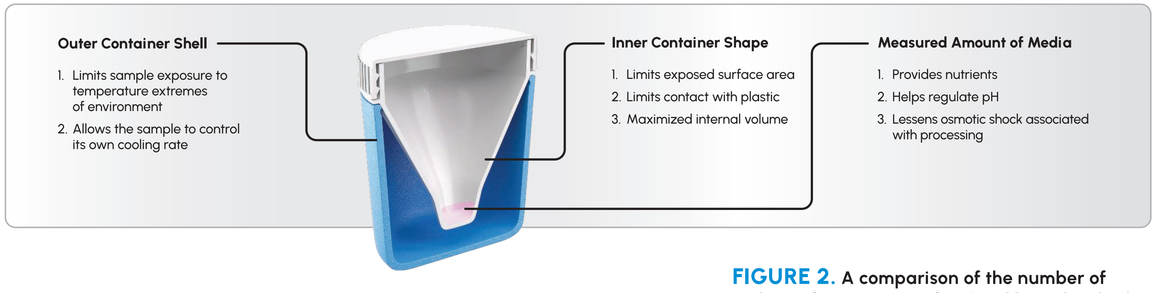


TABLE 1. Demographic data and semen parameters from the review of 1077 ART cycles using the ProteX (N=462) or Standard Specimen Cup (SSC; N=615) for semen collection. Data with a P value of < 0.05 are considered statistically different.

	ProteX in-clinic N=296	STD (+/-)	ProteX at-home N=166	STD (+/-)	SSC in-clinic N=346	STD (+/-)	SSC at-home N=269	STD (+/-)	P value
Age	39.8	5.9	38.8	5.6	39.9	6.2	39.7	5.6	**0.16**
Days of Abstinence	2.2	1.6	2.3	2.6	2.2	1.7	2.2	1.3	**0.91**
Initial Volume (mL)	2.3	1.2	2.3	1.2	2.3	1.2	2.3	1.9	**0.99**
Initial Concentration (mil/mL)	72.8[a]	67.1	74.0[a]	93.3	55.5[b]	46.8	59.5[b]	45.3	**0.001**
Initial Motility (%)	51.1[a]	16.4	45.9[b]	18.3	44.0[b,c]	17.3	40.9[c]	17.6	**0.001**
Final Concentration (mil/mL)	5.8	4.3	5.5	3.8	5.8	4.4	6.2	5.3	**0.47**
Final Motility (%)	93.0[a]	16.3	87.2[b]	26.9	90.1[a,b]	22.3	87.3[b]	26.3	**0.01**

TABLE 2. Demographic data and cycle outcomes of 1077 women whose oocytes were fertilized with either semen collected in ProteX (N=462) or a Standard Specimen Cup (SSC; N=615). Data with a P value of < 0.05 are considered statistically different.

	ProteX in-clinic N=296	STD (+/-)	ProteX at-home N=166	STD (+/-)	SSC in-clinic N=346	STD (+/-)	SSC at-home N=269	STD (+/-)	P value
Age	38.1[a]	5.6	36.7[c]	4.4	37.6[b]	4.5	37.7[b]	4.1	**0.02**
Oocytes Recovered	10.9[b]	9.5	13.3[a]	10.3	11.8[a]	9.9	13.1[a]	10.2	**0.03**
Fertilized	7.6	6.0	8	6.3	7.2	6.1	7.8	5.9	**0.44**
Cryo	3.8	4	3.5	3.8	3.2	3.7	3.4	3.6	**0.31**

ACKNOWLEDGMENTS

Reproductive Solutions supplied all ProteX for use in this retrospective review. S.D. Prien is an inventor of the technology, a consultant to Reproductive Solutions, and a stockholder in Reproductive Solutions.

FIGURE 2. A comparison of the number of embryos frozen/oocyte fertilized based on both device semen was collected in (ProteX vs. a Standard Specimen Cup (SSC)) and location (in-clinic vs. at-home) where it was collected. Columns with different superscripts are statistically different at the P < 0.02 level.

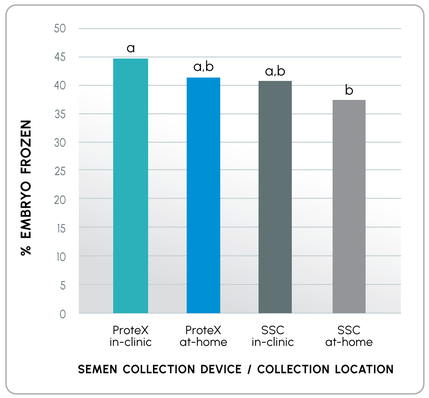
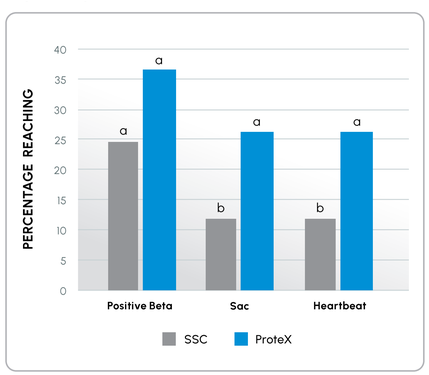


FIGURE 3. Early Pregnancy outcome of an IVF study comparing the ProteX to the Standard Specimen Cup (SSC) for semen collection. Columns within an event (pregnancy test, sac development, heartbeat) with different superscripts are different at the P < 0.02 level.



MATERIALS & METHODS

1. The ProteX was incorporated into the clinic's ART program in June 2021, using the device with the recommended inclusion of a measured amount of the lab's standard sperm wash media.
2. These data were to be compared to those patients undergoing ART during the previous six months.
3. Due to the Pandemic, patients could collect in the clinical facility or at home. Data for specimen location was available for review.
4. Limited demographic data were collected for both the male and female partner.
5. The semen sample was prepared for ART using standard laboratory procedures.
6. Data were collected on pre-and post-preparation semen parameters, including volume, concentration/mL, % motility, and total motile counts (millions).
7. Limited pregnancy data for the first 93 transfers were collected, including; initial pregnancy tests, sac development pregnancies, and pregnancy reaching heartbeat.
8. Additional data were collected for the number of embryos reaching high-quality blastocyst and frozen.

RESULTS

1. Data from 1077 ART cycles, 462 using the ProteX and 615 Standard Specimen Cup for collection, were reviewed.
2. As stated above, patients were given the option of collecting in the clinic or at home. Approximately 40% of patients in both groups selected the at-home option (35.9% ProteX vs. 43.7% SSC).
3. **TABLE 1** provides the demographic data from the male patients. These data were similar across all four groups (P = 0.16).
4. **TABLE 2** provides the demographic and the retrieval/oocyte development data for the female partner. Couples using the ProteX in the clinic appeared to have significantly older female partners (P < 0.02) who produced significantly fewer oocytes (P < 0.03) but who had similar numbers of oocytes fertilized and blastocysts selected for storage (P = 0.31).
5. Both device and location appeared to have an effect on initial motility (P < .00); **TABLE 1**), initial concentration (P < 0.001), and final motility (P < 0.01), with samples collected in the clinic with ProteX showing the best results.
6. While the number of blastocysts frozen was similar in each group (**TABLE 2**; P = 0.31). If one expressed the number of blastocysts frozen as a percentage of oocytes fertilized, a higher percentage of embryos were being frozen from the patients who used the ProteX device (**FIGURE 2**; P < 0.02)
7. Because of the low number of patients who have received transfer at this point (n=97), pregnancy outcomes were only compared between devices. Of the 97 transfers, 38 were done with embryos conceived from sperm collected in the ProteX versus the 59 in the SSC. There were 14 positive pregnancy tests in both groups resulting in initial pregnancy rates of 36.8% vs. 24.6% (ProteX vs. SSC respectfully) in patients transferred mainly on the fresh cycle (**FIGURE 3**).
8. However, more pregnancies continued to both sac development and heartbeat in the ProteX group (P < 0.02).

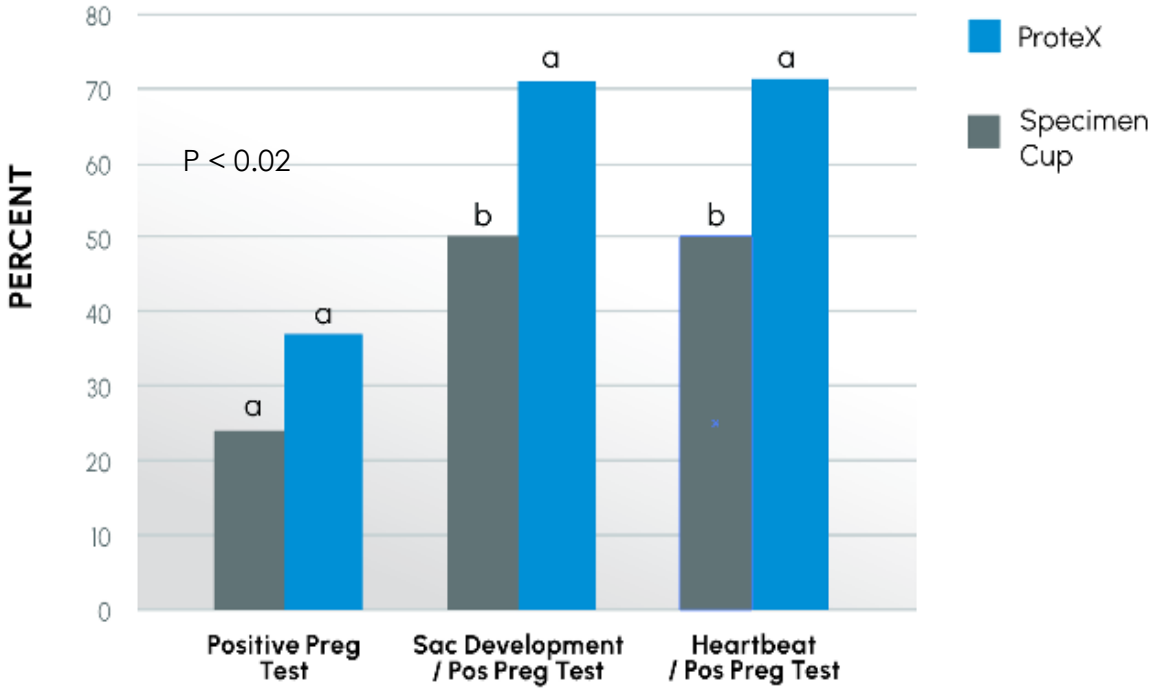
DISCUSSION

1. Data from this study involving almost 1100 patients supports earlier small-scale IUI studies.
2. Semen quality from samples collected in the ProteX demonstrated better initial parameters than those collected in the SSC.
3. As in an earlier smaller trial, initial pregnancy data suggest more pregnancies continue to heartbeat when the ProteX is used in the collection.
4. In limited pregnancy outcomes, it appears that ProteX positively affects pregnancy establishment and ongoing development. This is supported by the number of embryos frozen as blastocyst.
5. Collectively, these data suggest sperm collected in the ProteX may be in better physiological and biochemical condition than those collected in the SSC. This suggests healthier sperm may result in healthier pregnancies.
6. Additional transfers and their pregnancy outcomes are needed to support these findings.

IVF clinical trial data views

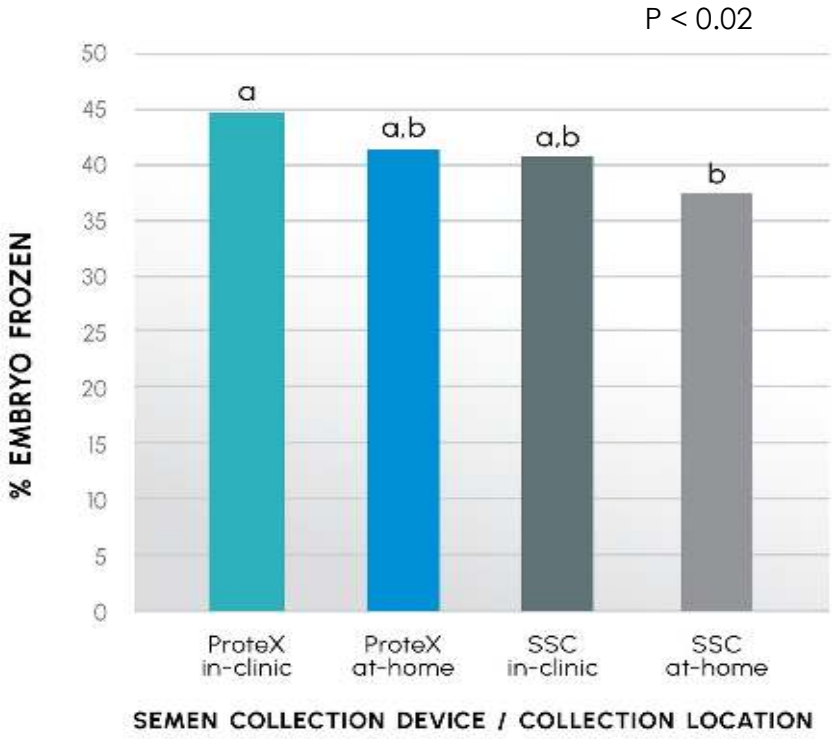
Up to **11% increase in frozen embryos/oocyte fertilized** for couples using ProteX. (P < 0.04)

Fresh transfers (n=97) comparing the ProteX (N=38) to the Standard Specimen Cup (SSC; N=59)) for semen collection.



a = Uses harmonic means sample size
b = The group sizes are unequal. The harmonic mean of the group sizes is used.

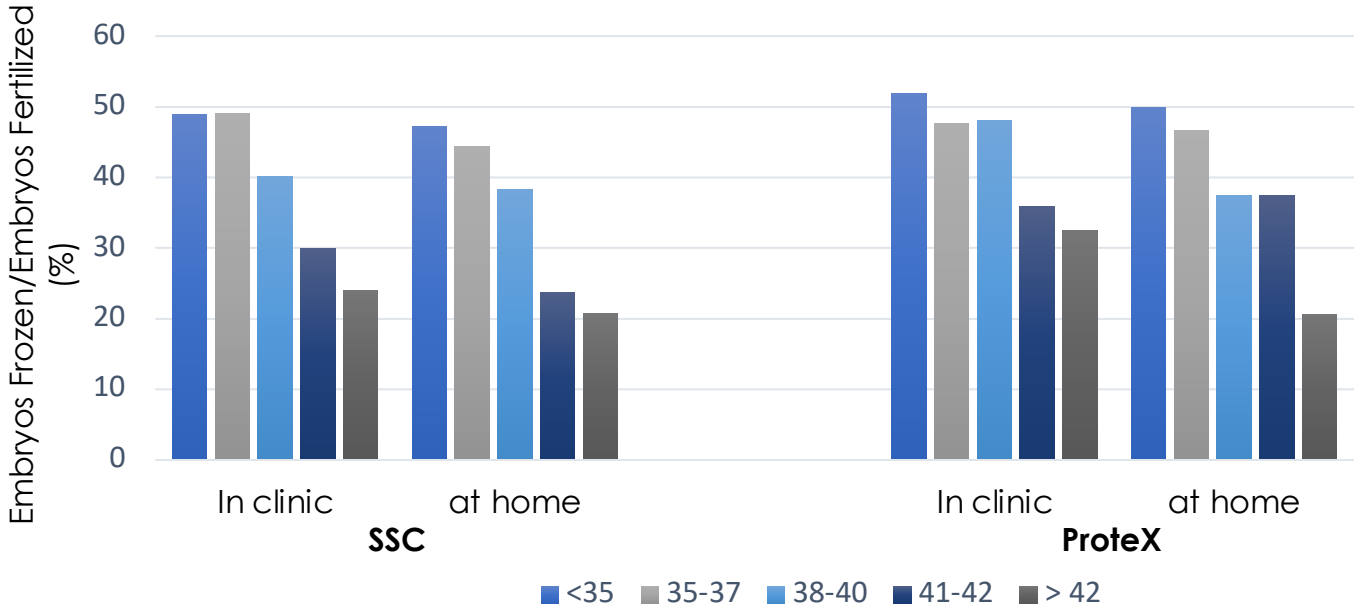
IVF study (n=1077) comparing the ProteX (N=462) to the Standard Specimen Cup (SSC; N=615)) for semen collection.



A comparison of the number of embryos frozen/oocyte fertilized based on both device semen was collected in and location where it was collected.

Source: S.D Prien[1], Z. Williams[2], E. Forman[2]. (2022). Preliminary Clinical Outcomes in an IVF Program using the ProteX™ versus a Standard Specimen Cup for Semen Collection. American Association of Bioanalysts — poster session. [1]Reproductive Solutions, Dallas, TX. [2]Columbia Center for Fertility, Columbia University, NY.

% Embryos frozen/embryos fertilized by female partner age and site of collection



- Difference in # Embryos frozen and female age p<0.001
- Difference in # Embryos frozen and sperm collection site p<0.001
- Difference in # Embryos frozen and collection device p<0.04

Number of Patient per Age Group/Site of Collection/Device

	SSC (N=596)			ProteX (N=449)		
Age	In clinic	at home	% of Total	In clinic	at home	% of Total
<35	79	62	23.66	69	50	26.50
35-37	75	54	21.64	57	32	19.82
38-40	90	76	27.85	76	43	26.50
41-42	53	41	15.77	41	26	14.92
> 42	37	29	11.07	44	11	12.25

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