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Use of semen quality scores to predict pregnancy rates in couples undergoing intrauterine insemination with donor sperm

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Objective: To establish semen quality scores in a population of sperm donors and determine whether the scores can be used to predict pregnancy rates after donor insemination.

Design: Retrospective study.

Setting: Infertility clinic at a tertiary care teaching hospital between 1993–2001.

Patient(s): One hundred eleven women who underwent IUI with sperm from 27 anonymous donors.

Intervention(s): None.

Main Outcome Measure(s): The semen analysis results before freezing and after thawing were analyzed, and overall donor insemination semen quality (DI-SQ) and donor insemination relative quality (DI-RQ) scores were calculated. After adjusting for female characteristics, the scores were compared with samples that did and did not result in pregnancy.

Result(s): Of 111 patients, 70 had at least one pregnancy, and 60 had at least one live birth, with a mean of 6.52 ± 4.67 IUI cycles per patient. Five significant risk factors for low pregnancy and live birth rates were identified: female infertility factor, positive laparoscopy, older maternal age, low number of previous births, and lack of ovulatory stimulation. After adjusting for these factors, both prefreeze and postthaw DI-SQ scores were statistically significantly associated with IUI live birth rates. Using only the samples with a DI-SQ score of >110 doubled the expected live birth rate, compared with using samples with a DI-SQ score less than 100, from 8.5% to 16.1%.

Conclusion(s): The DI-SQ score was an effective predictor of pregnancy and live birth outcomes in IUI patients who underwent artificial insemination with anonymous donor semen. The DI-SQ score could also be used by sperm banks to help select donors. (Fertil Steril® 2004;82:606–11. ©2004 by American Society for Reproductive Medicine.)

Key Words: Semen quality score, donor semen, intrauterine insemination, pregnancy rate, infertility

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The development of assisted reproductive techniques has allowed many infertile couples to conceive children. Such techniques include IUI, either with fresh sperm from the male partner or with frozen sperm from anonymous donor; IVF; and intracytoplasmic sperm injection (ICSI). Intrauterine insemination with donor semen is a common treatment for couples with severe male-factor infertility. The advent of ICSI has allowed homologous conception in many couples with severe male-factor infertility, but many of the couples who are candidates for ICSI may choose IUI with donor semen because of the increased cost, possible risks associated with ICSI, and the invasiveness of IVF and ICSI (1). Intrauterine insemination with donor semen has also become a widely accepted and successful treatment for single women or for women with azoospermic partners.

The recruitment of donors for artificial insemination programs has become increasingly difficult. Donors are accepted only after a thorough evaluation. The most important parameter that is assessed is semen quality. Traditionally, routine semen analysis has been employed, and this method is still used to assess prefreeze and postthaw samples to discriminate between donors of high and low fecundity. The most common reasons for rejection of potential donors who are otherwise healthy are poor sperm count and poor motility (2). However, individual semen parameters seem to have little accuracy in predicting pregnancy rates (3–8). Most semen characteristics seem to be positively correlated, suggesting that the different parameters are not independent. That is, a semen sample with poor values for one parameter (e.g., count) is likely to have poor values for other parameters as well, such as linearity or motility (9).

Previous studies have shown that combining multiple semen characteristics into a linear score can help predict male fertility potential (10). Recent research from our center has reported a statistical model using the principal component analysis to narrow down the interrelated, elaborate measures of semen analysis to two main components or scores, known as the overall semen quality score (SQ score) and the relative quality score (RQ score) (9).

Our center previously reported that the prewash SQ score was positively correlated ($P=.02$) with pregnancy rates in couples with male-factor infertility who were undergoing IUI with the male partner's semen (11). It is not known whether the SQ and RQ scores could be used to predict pregnancy after IUI with donor semen in cases in which a couple is unable to use the male partner's semen. This is important to study because the cost of IUI mainly depends on the number of cycles required to achieve pregnancy. If couples could predict their chances of conceiving with a given semen sample, they could reduce the total number of cycles necessary to achieve pregnancy.

The two main purposes of our current study were [1] to calculate the overall DI-SQ and DI-RQ scores for each semen sample used for IUI in a group of female patients undergoing IUI with anonymous donor semen and [2] to determine whether the DI-SQ and DI-RQ scores can predict pregnancy in this population.

MATERIALS AND METHODS

The Cleveland Clinic Foundation Institutional Review Board approved this study. We reviewed the medical charts of 134 women who participated in the Cleveland Clinic Foundation's donor insemination program between 1993–2001 because of the infertility of their male partners. Of the 134 patients, 23 were excluded because they had either never undergone any insemination cycles with donor semen or because the records for the donors that they used were not available, leaving 111 patients for our study.

The medical records of these 111 patients were examined for relevant details. The pertinent obstetric history (including the number of full-term deliveries, miscarriages, and elective abortions) and gynecological history (including history of abnormal pap tests and history of sexually transmitted diseases) were recorded. Notes on the patients' infertility history were taken, including type of infertility, duration of infertility, presence and type of any contributing female factors, and type of contributing male factors. The records were also examined for any diagnostic studies on the female patients, such as laparoscopies, hysterosalpingograms, or endometrial biopsies. Any abnormal tests were noted. We also noted the dates of all inseminations and which specific donor semen sample was used for each insemination cycle. Any pregnancies were noted, along with the outcomes of the pregnancies (miscarriage or live birth).

Donor Selection

Semen samples from 27 different anonymous donors who donated between 1987 and 1995 were used for insemination. All of the donors were healthy volunteers who had tested negative for sexually transmitted diseases as per the guidelines of the American Society for Reproductive Medicine (12). The donors' semen had been cryopreserved and quarantined for 6 months before being used for insemination. We reviewed the semen analysis reports from these 27 donors.

The SQ and RQ scores are based on nine semen parameters, which account for most of the variability expressed by these semen characteristics individually. The nine parameters used in our Center's previous study were concentration, motility, World Health Organization morphology, Kruger's morphology, linearity, curvilinear velocity, straight-line velocity, average path velocity, and amplitude of lateral head displacement. In that study, each parameter was weighted and analyzed by principal component analysis, and the two composite scores were developed (9).

In the present study, the SQ and RQ scores for each sample were determined using principal component analysis of five semen parameters: concentration, motility, curvilinear velocity, linearity, and amplitude of lateral head displacement. To differentiate these scores from those calculated from nine semen parameters, we termed them as donor insemination semen quality (DI-SQ) and donor insemination relative quality (DI-RQ) scores. We were not able to use World Health Organization morphology, Kruger's morphology, average path velocity, or straight-line velocity because information on these parameters was not available in the donors' semen analysis reports. However, results of our previous study have shown that SQ and RQ scores that are calculated by using fewer variables are still positively correlated with those scores calculated by using all nine parameters (9).

After analyzing the data for female factors that contributed to lower pregnancy and live birth rates, the DI-SQ and DI-RQ scores were compared with the outcome of the corresponding insemination cycle. Because multiple cycles from the same women were analyzed, statistical analyses were performed with logistic regression using generalized estimating equations. Statistical computations were per-

TABLE 1

Summary statistics of women undergoing IUI with donor semen.

Variables	Mean or %	SD	Median
Height (in.)	64.51	2.87	65.00
Weight (lb)	141.18	28.44	135.00
Menstrual flow (d)	5.34	1.99	5.00
No. miscarriages	0.17	0.45	0.00
Female factor (%)	29.7		
Positive laparoscopy (%)	29.7		
Age (y)	31.87	4.93	32.00
Duration of infertility (y)	2.44	1.85	2.00
Cycle length (d)	32.46	16.78	30.00
Dysmenorrhea (%)	54.1		
Previous full-term deliveries	0.56	0.84	0.00
Previous elective abortions	0.18	0.54	0.00
Stimulation drugs (%)	37.8	—	—

Allamaneni. Semen quality score—donor selection and IUI. Fertil Steril 2004.

TABLE 2

Summary statistics for anonymous donor semen samples (averaged values for 724 samples) being used for IUI.

Variable	Mean ± SD	Minimum	Maximum
	Prefreeze		
DI-SQ score	112.3 ± 5.6	96.8	131.4
DI-RQ score	110.7 ± 6.3	93.7	127.7
	Postthaw		
DI-SQ score	107.4 ± 5.6	91.9	127.8
DI-RQ score	103.6 ± 6.2	86.2	120.2

Allamaneni. Semen quality score—donor selection and IUI. Fertil Steril 2004.

formed with SAS version 8.1 (SAS institute Inc, Cary, NC), and statistical significance was assessed using two-tailed tests. A P value of $<.05$ was considered statistically significant.

RESULTS

Recipient Characteristics

One hundred eleven women underwent a total of 724 IUI cycles. Summary statistics of women undergoing donor insemination are illustrated in Table 1. The mean age of the women was 31.9 years. Seventy of the 111 patients (or 63%) had at least one pregnancy, and 60 (or 54%) had at least one live birth. Thirty-five women achieved more than one pregnancy, and 25 of these women had more than one delivery. The highest number of pregnancies achieved was four (two patients); three patients had three live births. The mean number of IUI cycles for each patient was 6.52 ± 4.67 (range, 1 to 17).

Characteristics of Donor Semen

Prefreeze and postthaw DI-SQ and DI-RQ scores for the donor semen samples are presented in Table 2. The mean prefreeze and postthaw DI-SQ scores for the donor samples were well over 100, which is considered the average for the DI-SQ score (9). Even the lowest DI-SQ score (96.8 prefreeze, 91.9 postthaw) was still within the range that is considered normal for healthy men.

Relation of DI-SQ and DI-RQ Scores With Pregnancy Outcome

Five female factors that affected the rate of pregnancy and live births were identified: female infertility factor (P=.39 for pregnancy, P=.07 for live birth), positive laparoscopy findings (P=.02 for pregnancy, P=.37 for live birth), increasing maternal age (P=.02 for pregnancy, P=.0003 for live birth), number of previous full-term deliveries (P=.01 for pregnancy, P=.02 for live birth), and lack of ovulatory stimulation (P=.26 for pregnancy, P=.049 for live birth). After adjusting for these five female factors, the prefreeze and postthaw DI-SQ and DI-RQ scores were analyzed to determine their association with pregnancy and live birth rates.

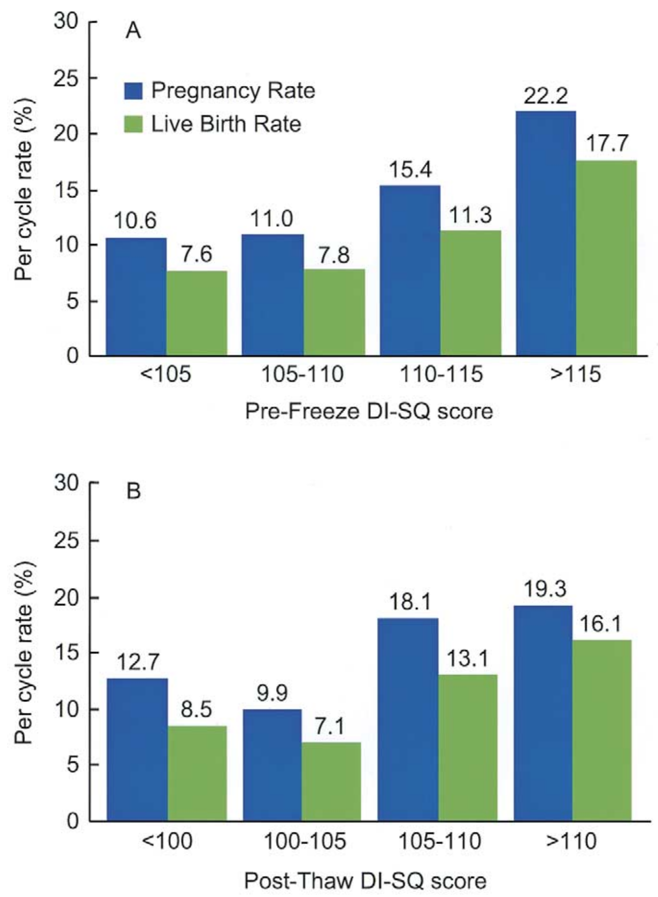
The prefreeze DI-SQ score was significantly associated with pregnancy (P=.03) and live birth rates (P=.03), whereas the postthaw DI-SQ score was significantly associated with live birth rates (P=.04). The DI-RQ score was not significantly associated with pregnancy in donor samples. The difference in the relationship of the DI-RQ scores among the donors may be due to screening, which reduces the variability of the DI-RQ score.

As the prefreeze and postthaw DI-SQ score increased, so did the pregnancy and live birth rates. The relationship between the DI-SQ score and the pregnancy and live birth rates are shown in Figure 1. The postthaw DI-SQ score is the more relevant measure because any donor semen samples used for IUI are always cryopreserved and therefore need to be thawed before insemination can occur. Both the pregnancy and the live birth rates almost doubled between the groups with DI-SQ score of <100 (12.7% pregnancy and 8.5% live birth) and with DI-SQ score of ≥110 (19.3% pregnancy and 16.1% live birth).

The predictive ability measures of DI-SQ score at different cutoff values are illustrated in Tables 3 and 4. The postthaw value with the highest sensitivity for pregnancy was at a DI-SQ score of >110, which had a sensitivity of 35.8 (Table 3). For this range of DI-SQ scores, the negative predictive value and positive predictive value was also the highest of the postthaw scores, with a value of 85.2% and 19.3%. The sensitivity for predicting live birth for DI-SQ score values in this range was 39.0 (Table 4). These values may seem low, but the normal success rate for IUI ranges from approximately 8%–13% per cycle (13–16). Therefore, using only those samples with a DI-SQ score of >110 doubled the expected pregnancy rate.

FIGURE 1

(**A**) The relationship between prefreeze donor insemination semen quality (DI-SQ) score and pregnancy or live birth rates. (**B**) The relationship between postthaw DI-SQ score and pregnancy or live birth rates.



Allamaneni. Semen quality score—donor selection and IUI. Fertil Steril 2004.

TABLE 3

Accuracy of the semen quality score as a predictor of pregnancy rates.

DI-SQ score	Sensitivity	Specificity	PPV	NPV
>120 Prefreeze	7.6	93.4	17.8	84.2
>120 Postthaw	1.0	99.1	16.7	83.8
>115 Prefreeze	42.5	71.7	22.2	86.7
>115 Postthaw	7.3	92.4	15.7	83.8
>110 Prefreeze	77.4	35.1	18.5	89.1
>110 Postthaw	35.8	71.2	19.3	85.2

Note: PPV = positive predictive value; NPV = negative predictive value.

Allamaneni. Semen quality score—donor selection and IUI. Fertil Steril 2004.

TABLE 4

Accuracy of the semen quality score as predictor of live birth rates.

DI-SQ score	Sensitivity	Specificity	PPV	NPV
>120 Prefreeze	6.3	93.1	11.1	87.8
>120 Postthaw	1.2	99.2	16.7	87.8
>115 Prefreeze	45	71.3	17.7	90.4
>115 Postthaw	8.5	92.5	13.7	87.9
>110 Prefreeze	78.8	34.9	14.3	92.3
>110 Postthaw	39	71.7	16.1	89.4

Note: PPV = positive predictive value; NPV = negative predictive value.

Allamaneni. Semen quality score—donor selection and IUI. Fertil Steril 2004.

DISCUSSION

Implications for Patients

Artificial insemination with donor spermatozoa is used worldwide to treat couples with azoospermia or severe male factor infertility. In this study, we attempted to use new semen quality scores developed in our research center to assess the quality of donor semen in a donor insemination program. We used these semen quality scores to predict the successful outcome of IUI with donor semen.

We identified five female factors that affected the rate of pregnancy and live birth: female infertility factor, positive laparoscopy findings, increasing maternal age, number of previous full-term deliveries, and lack of ovulatory stimulation. These findings are in accordance with previous studies (16–18).

After adjusting for these female factors, the DI-SQ score was positively associated with pregnancy and live birth rates, emphasizing the potential of DI-SQ score to predict outcomes in couples undergoing IUI with donor semen. A patient cannot change her female factor infertility diagnosis, positive laparoscopy findings, age, or number of previous deliveries to increase her chances of achieving pregnancy. Thus, it is especially important for these women to use semen samples with a superior DI-SQ score to maximize their chance of pregnancy and live birth.

The best IUI outcomes occurred when the patients were inseminated with a semen sample bearing a DI-SQ score of >110. Therefore, 110 could be used as a reference cutoff value for donor samples to give female patients an optimal chance of conception. If patients used only those samples with DI-SQ score of >110, this could reduce the total number of cycles necessary to achieve pregnancy, lowering the cost of IUI for the patient. Additionally, this could open up the possibility of IUI as a treatment option for many more infertile couples who may not be able to afford numerous insemination cycles.

The DI-SQ and DI-RQ scores reported in this study and SQ and RQ scores in earlier studies (9, 11) could be used for reference when counseling patients who are seeking assisted reproductive techniques. For example, if a female patient's male partner consistently submits semen samples that are below the threshold recommended for optimal success rates, the couple could be advised that they have better chances of achieving pregnancy by IVF or ICSI instead of by IUI. Therefore, they would be able to save time and money by moving directly to a more advanced assisted reproduction technique that would have a better chance of success instead of going through multiple IUI cycles that are unlikely to result in pregnancy. Likewise, if the male partner's semen samples have a DI-SQ or SQ score that are low enough that even IVF or ICSI are unlikely to work, the couple could be advised that IUI with anonymous donor semen may be their best option for achieving pregnancy.

Implications for Clinicians

Currently, there are no reliable tests that can predict a donor's fecundity before use in a recipient population. Multiple studies have attempted to use individual sperm parameters to predict an individual donor's fecundity without success (5–8, 19). Some studies have used the sperm penetration assay as a prognostic indicator of donor fecundity, with variable results (20–22). In one retrospective analysis that studied 800 insemination cycles by using the semen of 20 different donors, the investigators concluded that basic semen parameters could not identify the differences in fertility among the donors (7).

Poor semen quality is the major reason in rejecting a potential donor. Investigators have reported donor rejection rates of 10%–66% because of this specific reason (2). One prospective randomized study showed the lack of uniformity between sperm banks in the criteria used to screen potential semen donors and emphasized the need for documentation of semen quality by uniform criteria (23).

Because we found the prefreeze DI-SQ score to be significantly related to both pregnancy ($P=.03$) and live birth rates ($P=.03$), we believe that sperm banks could use this score as an initial screening test before taking the time and expense to perform a complete evaluation of any donor. In our study, using a semen sample with a prefreeze DI-SQ score of >110 resulted in the highest sensitivity (77.4% for pregnancy rates and 78.8% for live birth rates) of all of the prefreeze scores. Using 110 as a prefreeze cutoff value for semen samples could decrease the costs involved for donor insemination centers in evaluating all potential volunteers for fitness to donate sperm.

Another issue that affects pregnancy and live birth rates for sperm banks is the fact that cryopreservation decreases the quality of semen. The freezing and thawing process is usually associated with diminished viability, motility, and functional ability of the sperm (24). Sperm susceptibility to cryodamage varies both between individuals and between different samples from the same donor (25). Therefore, despite the preliminary screening of donors for semen quality, the quality of their samples after thawing can vary. Compared with fresh semen, donor insemination with thawed frozen semen is less likely to achieve pregnancy (26, 27).

Studies show conflicting results in the use of sperm motion characteristics to predict the fertility outcome of a frozen-thawed specimen (3, 21). However, in our study, the postthaw DI-SQ score was significantly related to live birth rates. Therefore, postthaw DI-SQ score could possibly be used to select the specific donor sample for use in insemination. For example, if a couple was planning to use a specific donor sample but the sperm bank found that the sample's DI-SQ score was below standard values, the couple could be advised to select another sample with a DI-SQ score of >110 to give them the best chance of conception. The DI-SQ score also could be used to periodically check the fecundity of a specific donor's samples. Sperm banks could consider dropping a donor whose prefreeze or postthaw DI-SQ score was consistently substandard.

In conclusion, the DI-SQ score is an effective predictor of pregnancy and live birth outcomes in IUI patients who are undergoing artificial insemination with anonymous donor semen. If only those semen samples with a DI-SQ score of >110 were used for IUI, success rates could significantly improve, and the time to pregnancy could also decrease. Semen quality scores can be used to counsel couples seeking assisted reproduction techniques. Sperm banks can screen donors and monitor the fertility potential of their samples by using the DI-SQ score. The use of DI-SQ score needs to be validated in prospective studies.

References

1. Goverde AJ, McDonnell J, Vermeiden JP, Schats R, Rutten FF, Schoemaker J. Intrauterine insemination or in-vitro fertilisation in idiopathic subfertility and male subfertility: a randomised trial and cost-effectiveness analysis. Lancet 2000;355:13–8.
2. Sidhu RS, Sharma RK, Kachoria S, Curtis C, Agarwal A. Reasons for rejecting potential donors from a sperm bank program. J Assist Reprod Genet 1997;14:354–60.
3. Sidhu RS, Sharma RK, Agarwal A. Effects of cryopreserved semen quality and timed intrauterine insemination on pregnancy rate and gender of offspring in a donor insemination program. J Assist Reprod Genet 1997;14:531–7.
4. Bielsa MA, Andolz P, Gris JM, Martinez P, Egozcue J. Which semen parameters have a predictive value for pregnancy in infertile couples? Hum Reprod 1994;9:1887–90.
5. Byrd W, Bradshaw K, Carr B, Edman C, Odom J, Ackerman G. A prospective randomized study of pregnancy rates following intrauterine and intracervical insemination using frozen donor sperm. Fertil Steril 1990;53:521–7.
6. Ombelet W, Vandeput H, Van de Putte G, Cox A, Janssen M, Jacobs P, et al. Intrauterine insemination after ovarian stimulation with clomiphene citrate: predictive potential of inseminating motile count and sperm morphology. Hum Reprod 1997;12:1458–63.
7. Thyer AC, Patton PE, Burry KA. Fecundibility trends among sperm donors as a measure of donor performance. Fertil Steril 1999;71:891–5.
8. Al-Inany HG, Dunselman GA, Dumoulin JC, Maas JW, Evers JL. Fertility potential of individual sperm donors. Gynecol Obstet Invest 1999;47:147–50.
9. Agarwal A, Sharma RK, Nelson DR. New semen quality scores developed by principal component analysis of semen characteristics. J Androl 2003;24:343–52.
10. Bartoov B, Eltes F, Pansky M, Lederman H, Caspi E, Soffer Y. Estimating fertility potential via semen analysis data. Hum Reprod 1993;8:65–70.
11. Bedaiwy MA, Sharma RK, Alhussaini TK, Mohamed MS, Aleem AM, Nelson DR, et al. The use of novel semen quality scores to predict

pregnancy in couples with male-factor infertility undergoing intrauterine insemination. J Androl 2003;24:353–60.
12. The American Fertility Society. New guidelines for the use of semen donor insemination: 1990. Fertil Steril 1990;53:1s–7s.
13. Byrd W, Ackerman GE, Carr BR, Guzick DS, McConnell JD. Treatment of refractory infertility by transcervical intrauterine insemination of washed spermatozoa. Fertil Steril 1987;65:127–32.
14. Dickey RP, Pyrzak R, Lu PY, Taylor SN, Rye PH. Comparison of the sperm quality necessary for successful intrauterine insemination with World Health Organization threshold values for normal sperm. Fertil Steril 1999;71:684–9.
15. Stone BA, Vargyas JM, Ringler GE, Stein AL, Marrs RP. Determinants of the outcome of intrauterine insemination: analysis of outcomes of 9963 consecutive cycles. Am J Obstet Gynecol 1999;180:1522–34.
16. Depypere HT, Gordts S, Campo R, Comhaire F. Methods to increase the success rate of artificial insemination with donor semen. Hum Reprod 1994;9:661–3.
17. Kang BM, Wu TC. Effect of age on intrauterine insemination with frozen donor sperm. Obstet Gynecol 1996;88:93–8.
18. Shenfield F, Doyle P, Valentine A, Steele SJ, Tan SL. Effects of age, gravidity and male infertility status on cumulative conception rates following artificial insemination with cryopreserved donor semen: analysis of 2998 cycles of treatment in one centre over 10 years. Hum Reprod 1993;8:60–4.
19. Paraskevaides EC, Pennington GW, Naik S, Gibbs AA. Pre-freeze/post-freeze semen motility ratio [letter]. Lancet 1991;337:336–7.
20. Navarrete T, Johnson A, Mixon B, Wolf D. The relationship between fertility potential measurements on cryobanked semen and fecundity of sperm donors. Hum Reprod 2000;15:344–50.
21. Marshburn PB, McIntire D, Carr BR, Byrd W. Spermatozoal characteristics from fresh and frozen donor semen and their correlation with fertility outcome after intrauterine insemination. Fertil Steril 1992;58:179–86.
22. Barratt CL, Clements S, Kessopoulou E. Semen characteristics and fertility tests required for storage of spermatozoa. Hum Reprod 1998;13 Suppl 2:1–11.
23. Carrell DT, Cartmill D, Jones KP, Hatasaka HH, Peterson CM. Prospective, randomized, blinded evaluation of donor semen quality provided by seven commercial sperm banks. Fertil Steril 2002;78:16–21.
24. Kliesch S, Behre HM, Jurgens H, Nieschlag E. Cryopreservation of semen from adolescent patients with malignancies. Med Pediatr Oncol 1996;26:20–7.
25. Kolon TF, Phillips KA, Buch JP. Custom cryopreservation of human semen. Fertil Steril 1992;58:1020–3.
26. Hammond MG, Jordan S, Sloan CS. Factors affecting pregnancy rates in a donor insemination program using frozen semen. Am J Obstet Gynecol 1986;155:480–5.
27. Brown CA, Boone WR, Shapiro SS. Improved cryopreserved semen fecundability in an alternating fresh-frozen artificial insemination program. Fertil Steril 1988;50:825–7.