How to improve the embryo transfer technique

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Factors affecting embryo transfer success

- ease of the procedure
- embryo transfer catheter
- use of ultrasound guidance
- position of embryo in the uterus
- experience of the physician
- use of cervical introducer
- precence or absence of blood on the catheter
- removal of the mucus
- bacterial contaminationof the catheter
- retention of embryos in the catheter

Optimizing the technique of embryo transfer

Lindsay Mains, M.D., and Bradley J. Van Voorhis, M.D.

Objective: To review currently available literature on various technical aspects of the ET procedure.

Result(s): Numerous technical aspects of the ET procedure have been studied to determine their effect on pregnancy outcome. Although much of the published data that evaluates these factors is conflicting or confounded, good and consistent evidence does appear to support the following:

optimizing the ‘‘ease’’ of the transfer, ultrasound guidance, and soft catheters.

Limited evidence also supports trial transfers, removal of cervical mucus, deposition of embryos in the mid portion of the uterus, avoiding negative pressure from the catheter, and completion of the procedure in a timely manner.

Conclusion(s): Although there is no consensus on the optimal technique of ET, there is evidence that certain methods in the ET are associated with improved outcomes after IVF.

(Fertil Steril 94:785–90. 2010

Ultrasound measurement of the uterocervical angle before embryo transfer: a prospective controlled study

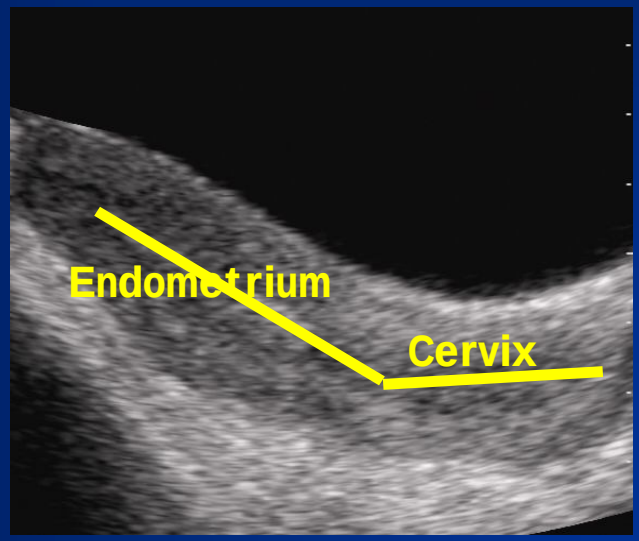
H.N.Sallam et al, Human Reproduction 2002,17;1767-1772

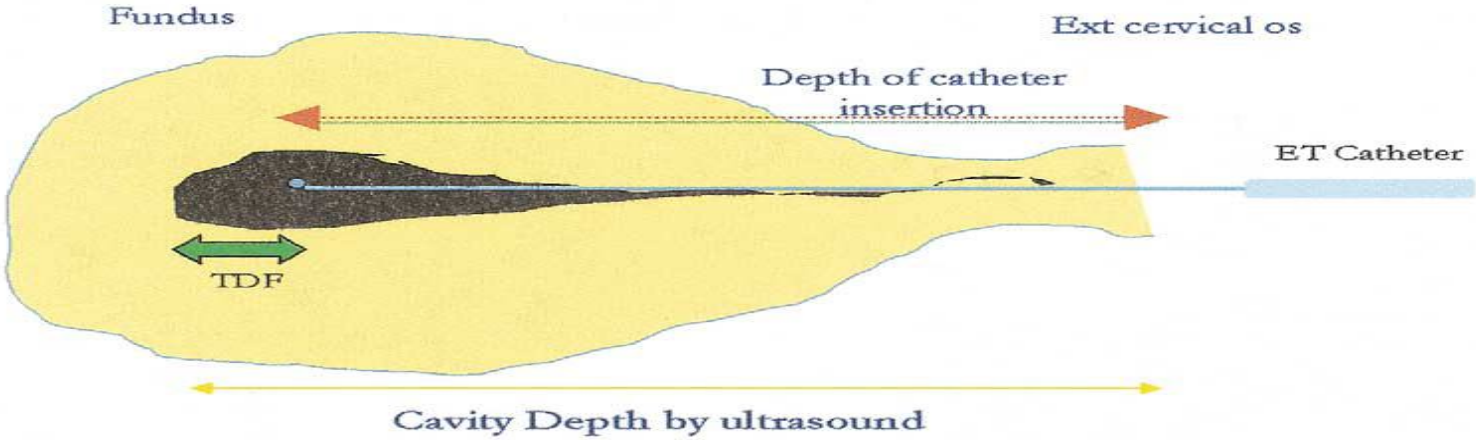
- to investigate whether moulding the catheter according to the uterocervical angle could improve the pregnancy rate
- 640 embryo transfer

Clinical pregnancy rate	ultrasound-guided	26.25%
	no ultrasound	18.43%

Conclusions

moulding the catheter according to the uterocervical angle could improve the implantation and pregnancy rate and diminishes the incidence of difficult and bloody transfer.





Transfer Distance from Fundus (TDF) =

cavity depth by ultrasound - depth of catheter insertion

os

Ultrasound-guided soft catheter embryo transfer will improve pregnancy rates in in.vitro fertilization

E.Wood et al, Human Reproduction 2000,15;107-112

- To compare different catheters and ultrasound-guided embryo transfer
- 518 embryo transfers with hard (Tefcat, Tomcat, Norfolk) or soft (Frydman, Wallace)

Implantation rate	without US 14.1% and with US 19.9%
Clinical pregnancy rate	without US 25.4% and with US 38.4%
Implantation rate	hard catheter 8.1% and soft catheter 19.1%
Clinical pregnancy rate	hard catheter 17% and soft catheter 36%

Conclusions

Performance of embryo transfer with a soft catheter system under ultrasound guidance with a good visualization resulted in a significant increase in clinical pregnancy rates

Difficult embryo transfer is associated
with decreased pregnancy rate (Sallam et al 2005)

Soft embryo transfer catheter should find its own way into the uterine cavity, rather then being forced in, to avoid trauma to all tissues and, possibly, to the embryo (Abou-setta et al 2005)

Soft catheters are sometimes associated with higher degree of failure to negotiate the cervix and higher incidence of retained embryos
(Abou-Setta et al 2005)

ET with soft catheter

- Over 876 ET (Wood et al 1985)
  - 1.3 % impossible
  - 3.2 very difficul
  - 5.2 difficult

- 37.6% of difficult transfer with soft catheter (Mansour et al 1990)

Cervical mucus may become a source of contamination and reduce the rate of embryo implantation from 9 to 16% (Fanchin et al 1998)

Presence of germs in the mucus has a significant impact on the preagnancy rate (Egbase et al 1996)

INTRODUCER

evidence

- Methylene blue was visualized at the external os in 42% of the cases (Mansour 1994)
- Presence of endometrial movements (Ijland 1996, Kunz 1996)
- The embryos can move toward the cervical canal or toward the Fallopian Tube (Woolcott 1997)
- Poor embryo transfer technique may account for as much as 30% of all failures in assisted reproduction (Cohen 1998)

•Only 45% of transferred embryos were present within the uterine cavity 1 hr after the embryo transfer (Menezo 1985)

•15% of transferred embryos have been collected from the external cervical os, the catheter or speculum after embryo transfer (Poindexter 1986)

•Radio-opaque dye remained in the uterine cavity in only 58% of cases (Knutzen 1992)

Impact of some factors on embryo transfer - I

•Removal of hydrosalpinges	340
•Absence of bleeding/blood	330
•Type of catheter	255
•Not touching the fundus	292
•Avoid tenaculum	283
•Removal of cervical mucus	258

Kovacs, Human Reproduction 14;590, 1999

Type of catheter

Soft
Echogenic
Able to negotiate the internal os
Rounded tip
Little diameter
Centimeter marked
Easy-to-use
Transparent
With introducer

Evaluation of the embryo transfer protocol by a laboratory model of the uterus

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Objective: To investigate the dispersion of transferred matter within a uterine laboratory model during and after embryo transfer (ET) as a function of uterine position, catheter placement, and injection speed.
Design: Experimental setup.
Setting: Reproductive bioengineering laboratory.
Patient(s): N/A
Intervention(s): N/A
Main Outcome Measure(s): Laboratory simulations of ET into a rigid transparent uterine model. The catheter was loaded with sequences of liquid and air as in the clinical setting. Experiments were conducted for different inclinations of the uterine model, various transfer speeds of the catheter load, and placement of the catheter tip near and remote from the fundus.
Result(s): Dispersion of the transferred matter depended on the position of sagittal cross-section of the uterine cavity with respect to the horizon. The air bubbles were pulled up by buoyant forces toward the highest point of the cavity (e.g., the fundus) and thereby dragged behind them the transferred media with the embryos. Placement of the catheter tip near the fundus appeared to transfer the embryos into the tube when transfer was performed at fast speeds, possibly leading to ectopic pregnancies.
Conclusion(s): Fundal level of the uterine cavity, location of the catheter tip, and transfer speed determine the potential for embryo implantation. Adjustment of ET protocol to individual patient anatomy is recommended. (Fertil Steril® 2007;88:485–93. ©2007 by American Society for Reproductive Medicine.)

Key Words: Mock ET, uterine laboratory model, injection speed of embryo transfer, uterine position

CONCLUSIONS

Fundal level of the uterine cavity, location of the catheter tip and transfer speed determine the potential for embryo implantation

nical parameters, such as catheter position, catheter loading, injection speed, and posture of the patient. Thus, the only

placed very close to the fundus (<5 mm) (8–11).

Many clinics have adopted an ET routine of transferring a volume of media containing the embryos, preceded and followed by air volumes, into the uterine cavity (12–14). The effect of loading air in the catheter-syringe system, as well as the actual size of these volumes, on the implantation and pregnancy rates has not been fully determined (15, 16). The speed of transferring the catheter load has never been inves-

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•*BIOFLUID ASPECTS OF EMBRYO TRANSFER*

…the speed at which the embryos are ejected from the catheter dominates the procedure and controls the velocity of their transport whitin the uterine cavity ET at excessively high injection speeds may lead to ectopic pregnancies, while uterine peristalsis affects transverse dispersion only during injection at low ejection speed

Yaniv S et al Ann Biomed Eng 2003

•*BIOENGINEERING STUDIES OF THE EMBRYO TRANSFER PROCEDURE*

…the load be delivered slowly, that is, not less than 10 s

Eytan O et al Ann N Y Acad Sci 2007

Simulation of how ectopic pregnancy may occur.

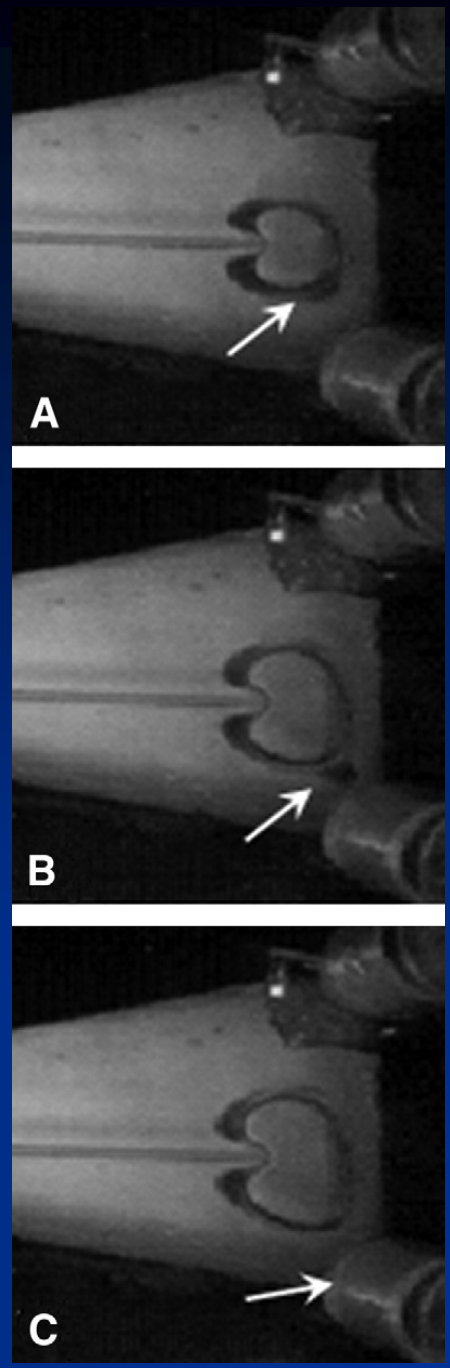
Dispersion of the transferred volume injected at a high speed (T 1 s) in a horizontal uterine model (0 °) while the catheter is close to the fundus:

(A) t 0.5 s,

(**B**) t 0.75 s, and

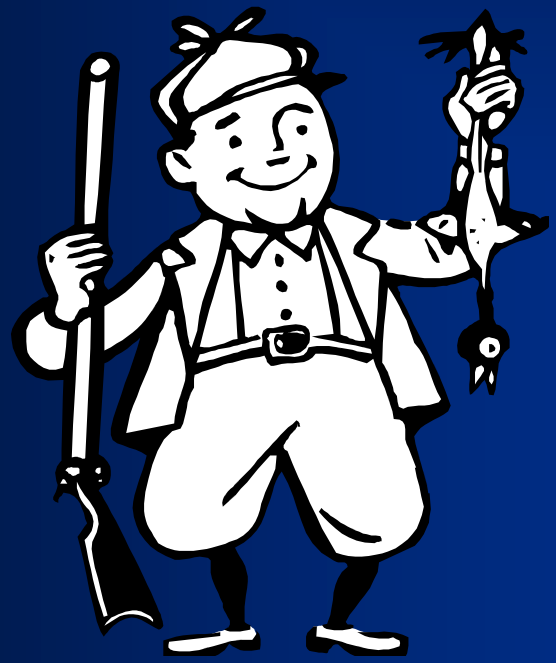
(**C**) t 0.875 s.

The *arrows* mark the part of the liquid that enters into the glass tube.



Eytan. Physical features of ET protocol. Fertil Steril 2007.

Embryo release



World in Vitro Fertilization Units
www.IVF-Worldwide.com

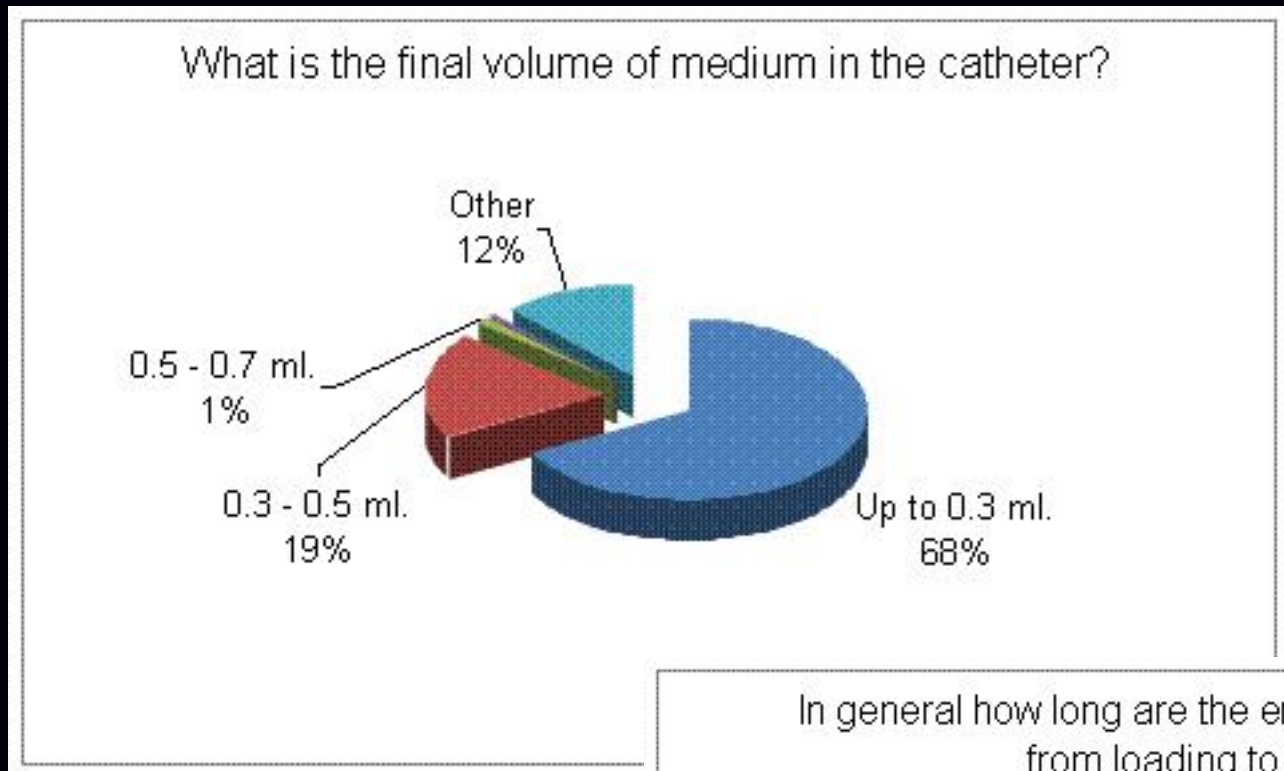
The statistics are based on the number of cycles each unit performed and not on the number of units.

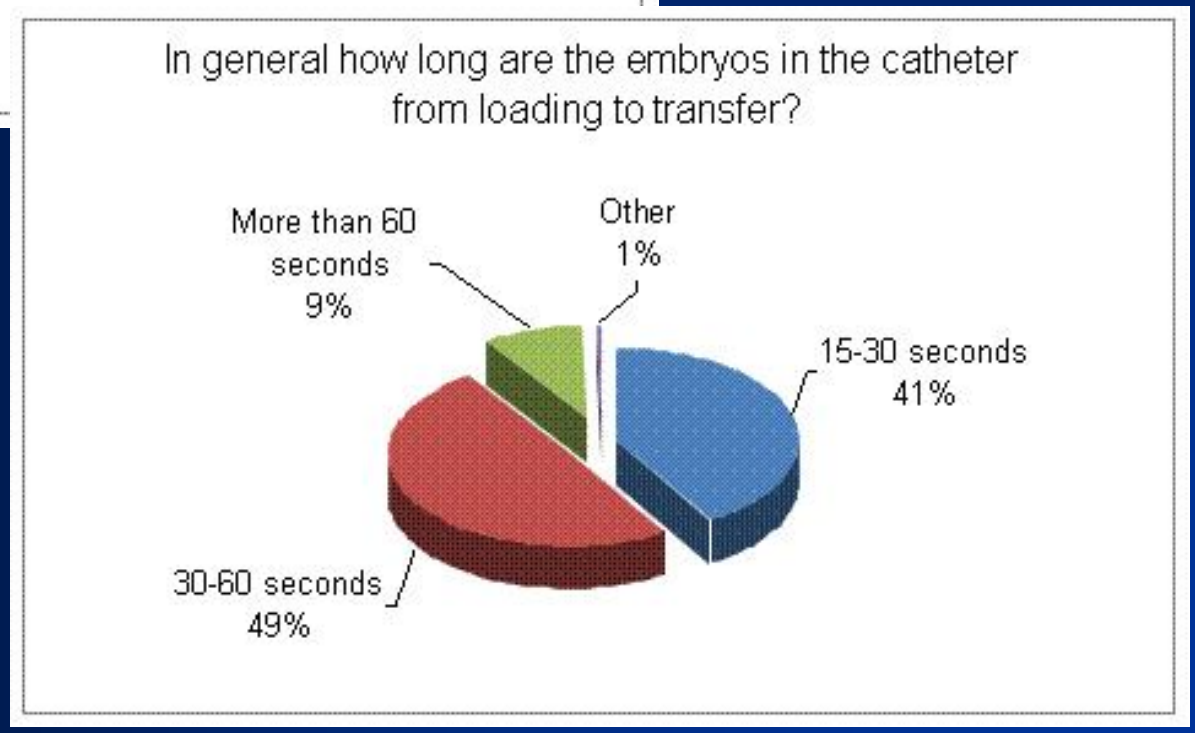
Newsletter – June 2, 2011

The number of IVF units registered on the website is now 3,221

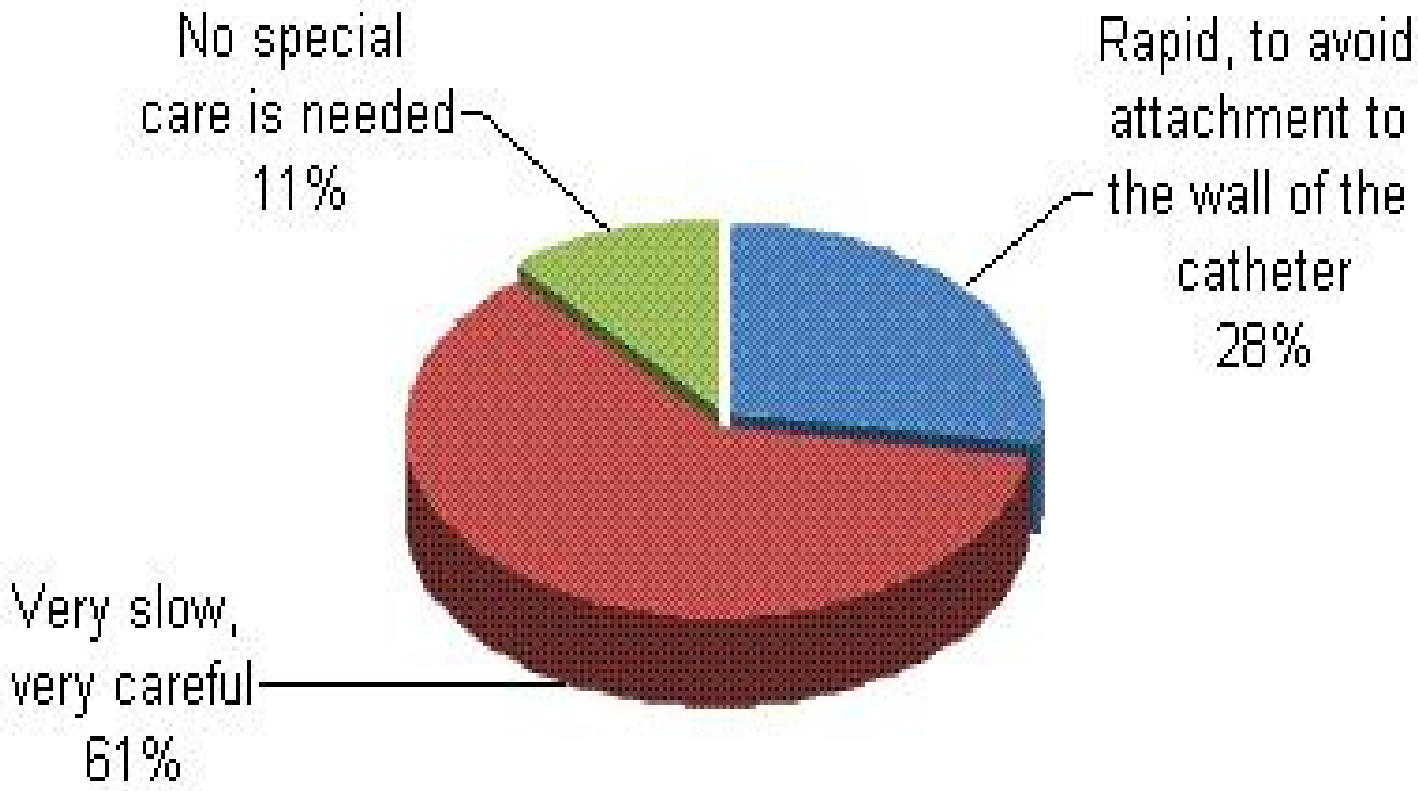
Results of the Survey
"Embryo Culture and Catheter Loading"

Results of 161,300 IVF Treatment Cycles (265 centres from 71 countries)

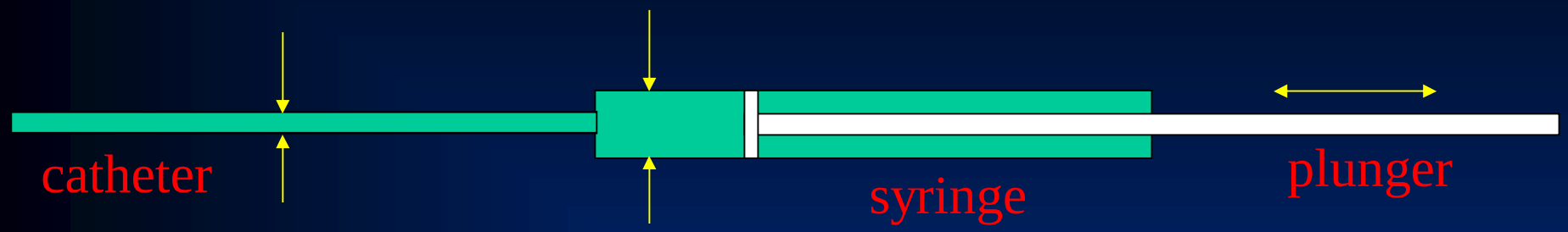

What is the final volume of medium in the catheter?
Other
12%
0.5 - 0.7 ml.
1%
0.3 - 0.5 ml.
19%
Up to 0.3 ml.
68%


In general how long are the embryos in the catheter from loading to transfer?
More than 60 seconds
9%
Other
1%
15-30 seconds
41%
30-60 seconds
49%

What is the rate at which embryos are injected into the uterus:



The plunger of the insulin syringe has a diameter of 4.75 mm with a corresponding surface of 17.34 mm^2 (A)



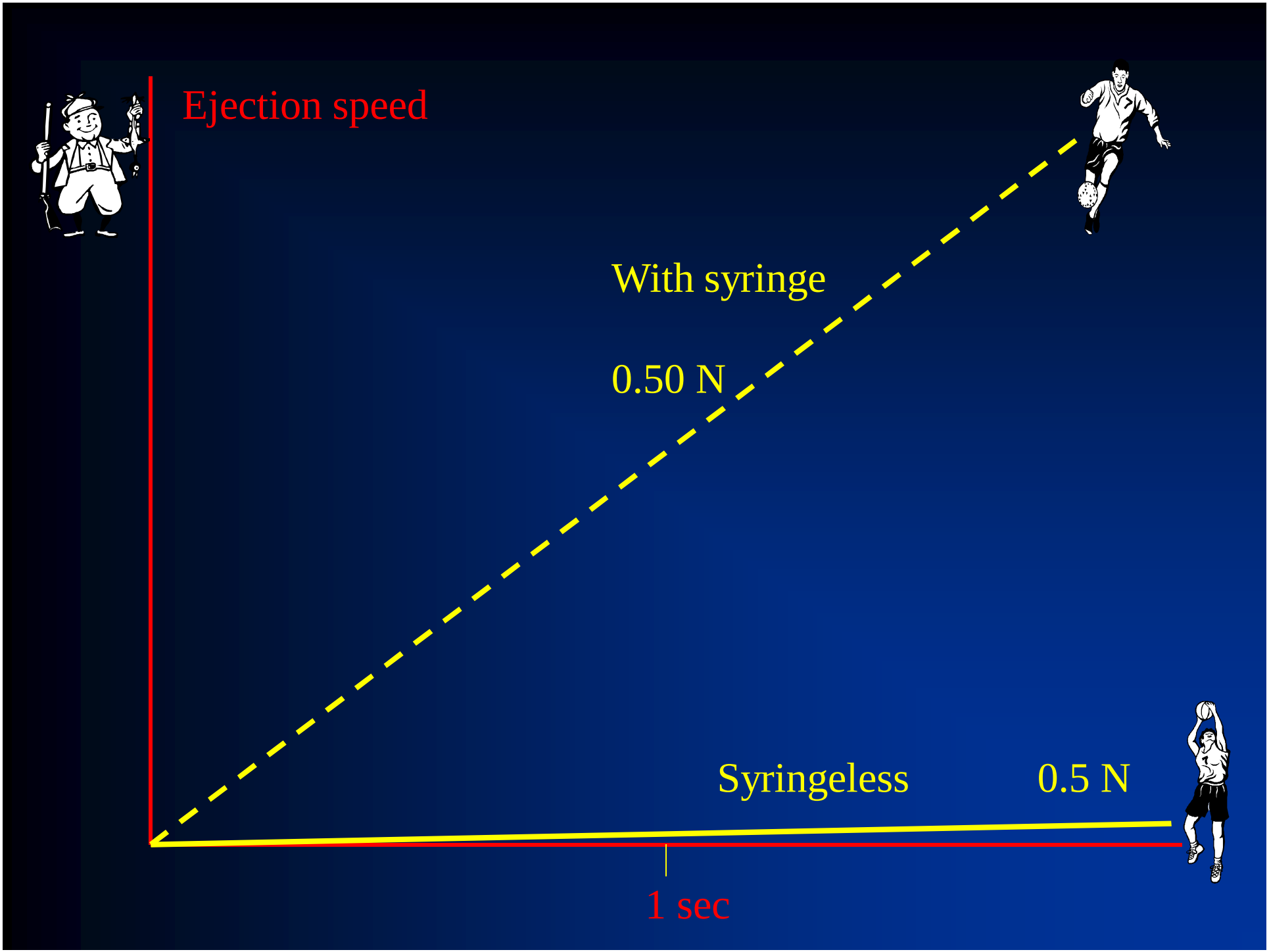
the plunger inside the catheter has a diameter of 0.4 mm with a corresponding surface of 0.125 mm^2 (B).

The immediate consequence of those data is that when both plungers move by 1 mm , A transport 140 times more water than B.

If a force of 0.50 Newton (approx 50 gr), representing the minimal force able to move the plunger, is applied to the situation A, the consequence is that 1 gr of water is ejected in 55 sec. which corresponds to a velocity of 18×10^{-3} gr/sec.

On the other hand if a force of 0.50 N (approx 50 gr) is applied to the plunger B, we obtain that 1 gr of water is ejected in 3300 sec with an ejection speed of 3.03×10^{-4} gr/sec

i.e. **60 times less**.


Ejection speed
With syringe
0.50 N
Syringeless
0.5 N
1 sec

Ejection speed

5 N

With syringe

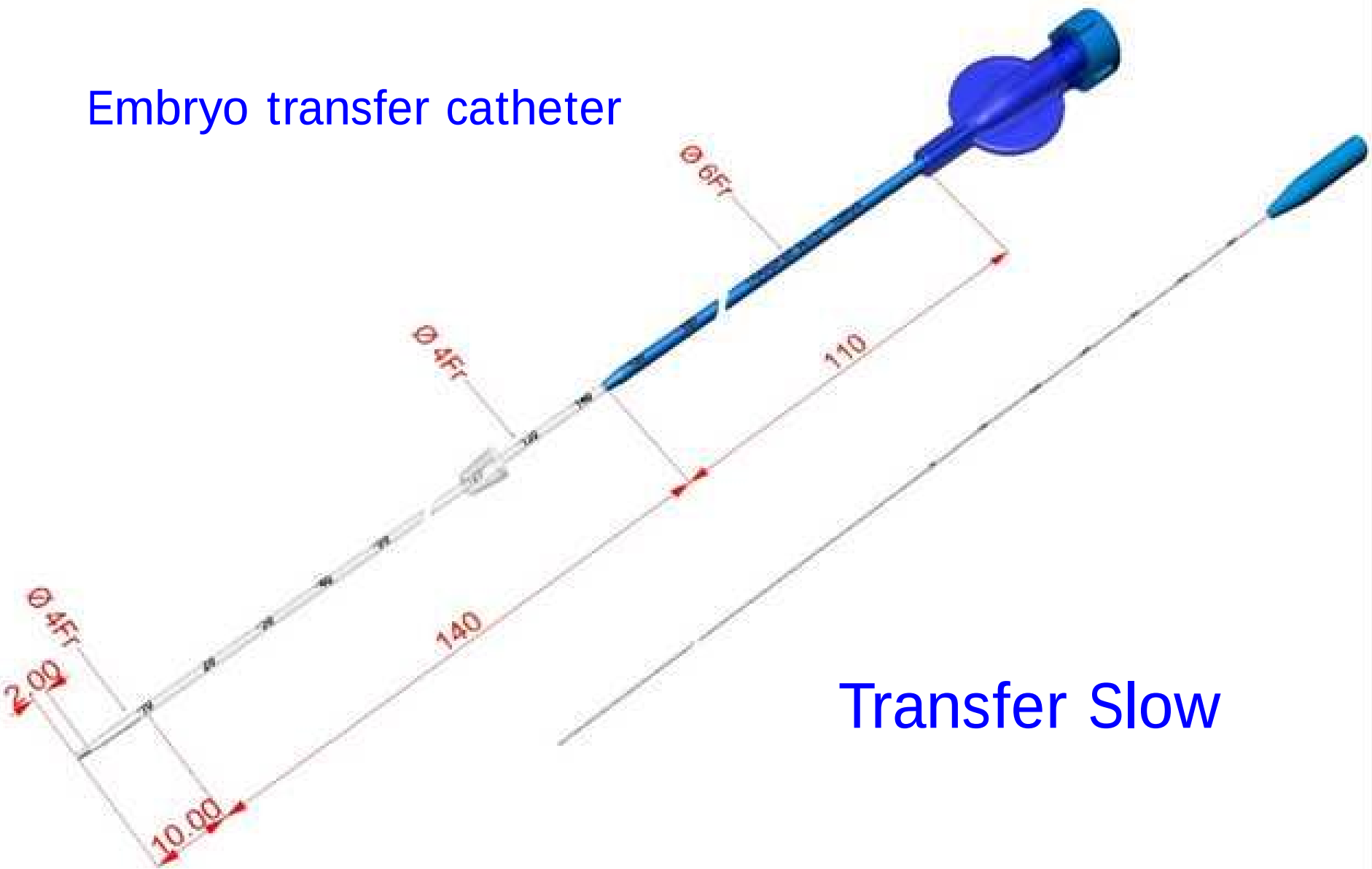
If the maximun force (500 gr = 5 N) is applied in the two conditions, A and B, the velocity increases dramatically with the syringe.

Syringeless

5 N

1 sec

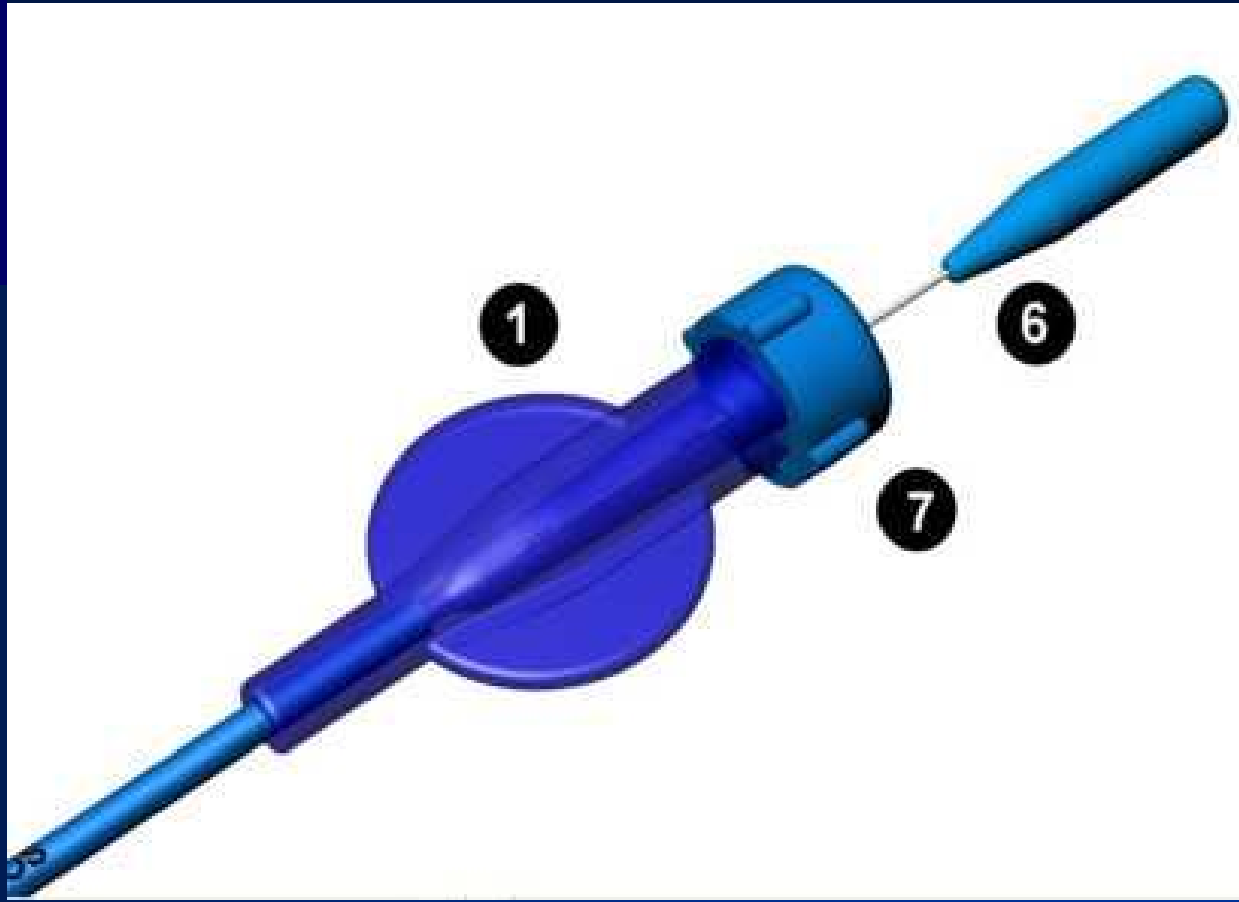
Embryo transfer catheter



Transfer Slow

1) Female connector finger-grip.

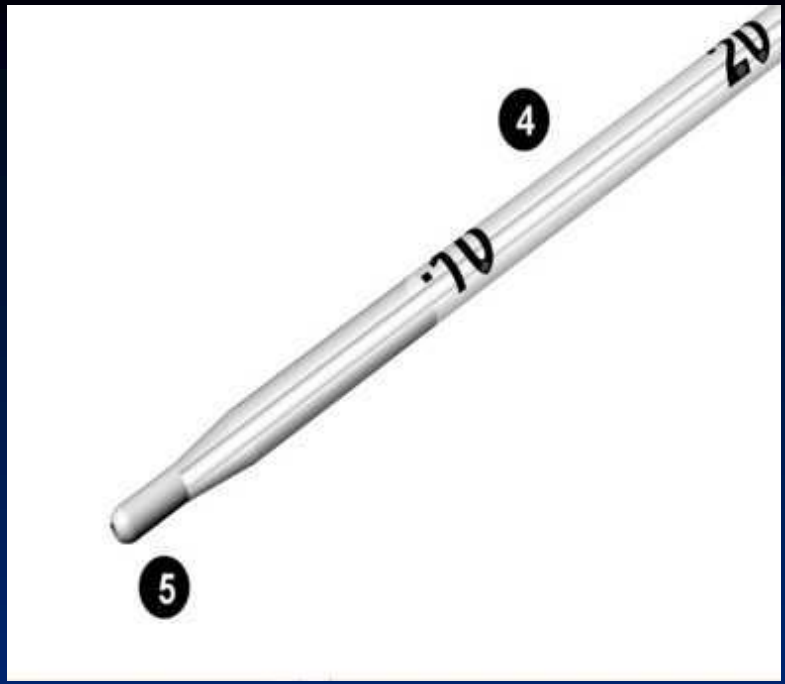
6) Centimeter-marked stylet with OD 0,40 mm acting as a microplunger grants a very slow & gentle embryo aspiration through the medial portion with ID 0,50 mm.



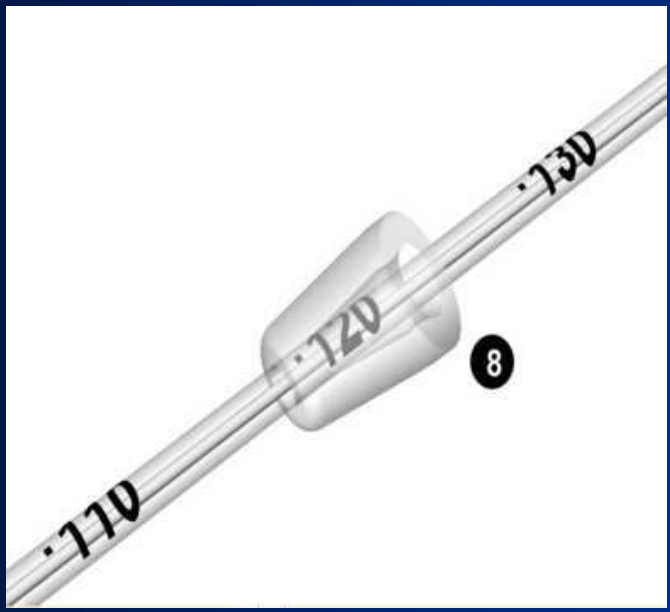
7) Guidance system on finger-grip connector for enhanced control of the stylet/microplunger.

4) Soft & transparent distal portion OD 1,33 mm for atraumatic penetration into the uterus.

5) Special rounded echogenic tip allows precise positioning under ultrasound visualization.

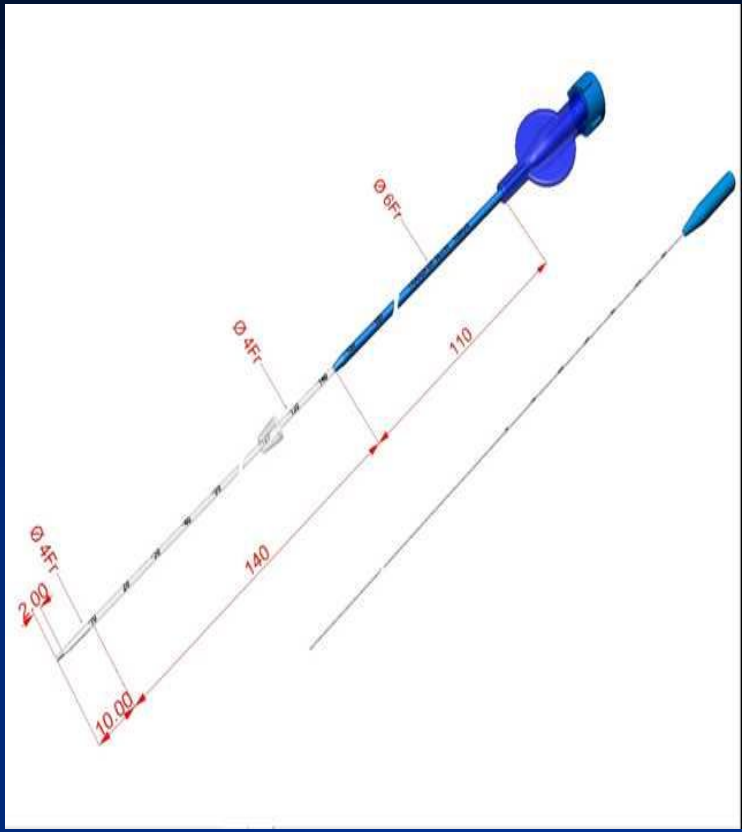


8) Stopper system on the semirigid portion of the catheter for a controlled penetration into the uterus.

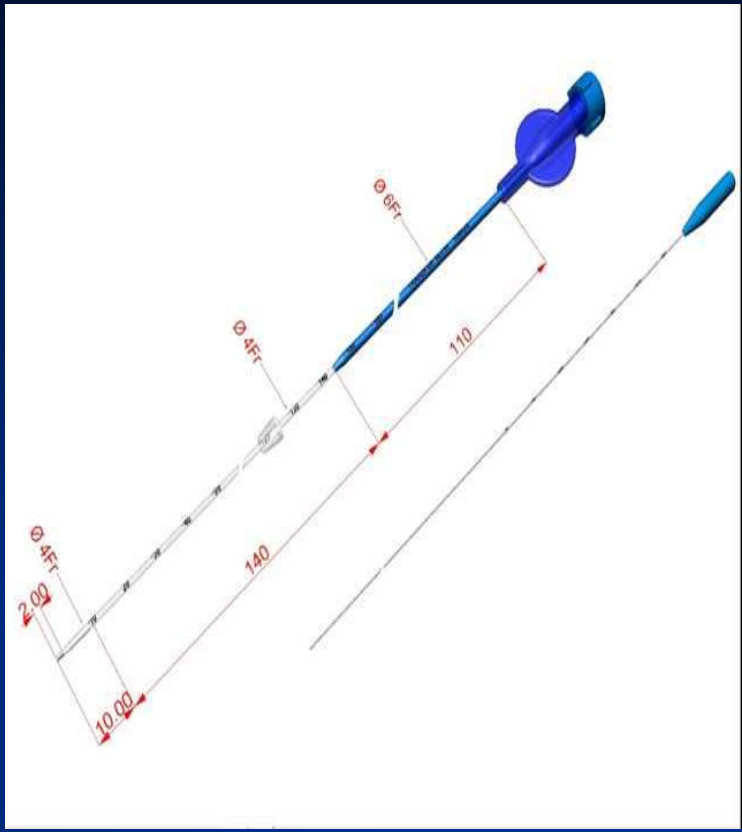


This system avoids the use of the syringe during embryo aspiration/expulsion phases. This largely excludes the risk of excessive pressure or turbulence to the embryos and makes the procedure definitely less traumatic.

	Slow Transfer		
Age (years)	34.75±2.8		
Duration of infertility (years)	3.9±0.8		
r-FSH (IU)	1630±462		
Stimulation length (days)	12.2 ± 0.28		
NS			
ultrasound (N °)	3.16 ± 0.64		
NS			
endometrium (mm) the day of hCG	12.0 ± 0.33		
NS			
follicles (N) ≥16 mm the day of hCG	3.80 ± 0.43		
collected oocytes (N)	8.00 ± 0.60		
matures oocytes (N)	6.21 ± 0.22		
NS			
fertilization rate (%)	81.0 ± 2.90	78.5 ± 2.7	NS
Embryos Transferred (N)	2.0±0.67	2.1±0.5	NS



	Slow Transfer Catheter
Pregnancies (N)	68/150
Pregnancy rate (%)	45.3
Multiple pregnancy rate %	36.4
Implantation rate (%)	32.0
Blood on the catheter (%)	2
Easy transfer (%)	126/150 (84)
Moderately difficult transfer (%)	18/150 (12)
Difficult transfer (%)	6/150 (4)



Type of catheter

Soft
Echogenic
Able to negotiate the internal os
Rounded tip
Little diameter
Centimeter marked
Easy-to-use
Transparent
With introducer

Syringeless for low embryo ejection speed

With this new catheter, the embryos cannot be fired into the uterine cavity.