TESE for non-obstructive azoospermia 30 years after

Prof. Dr. Herman Tournaye

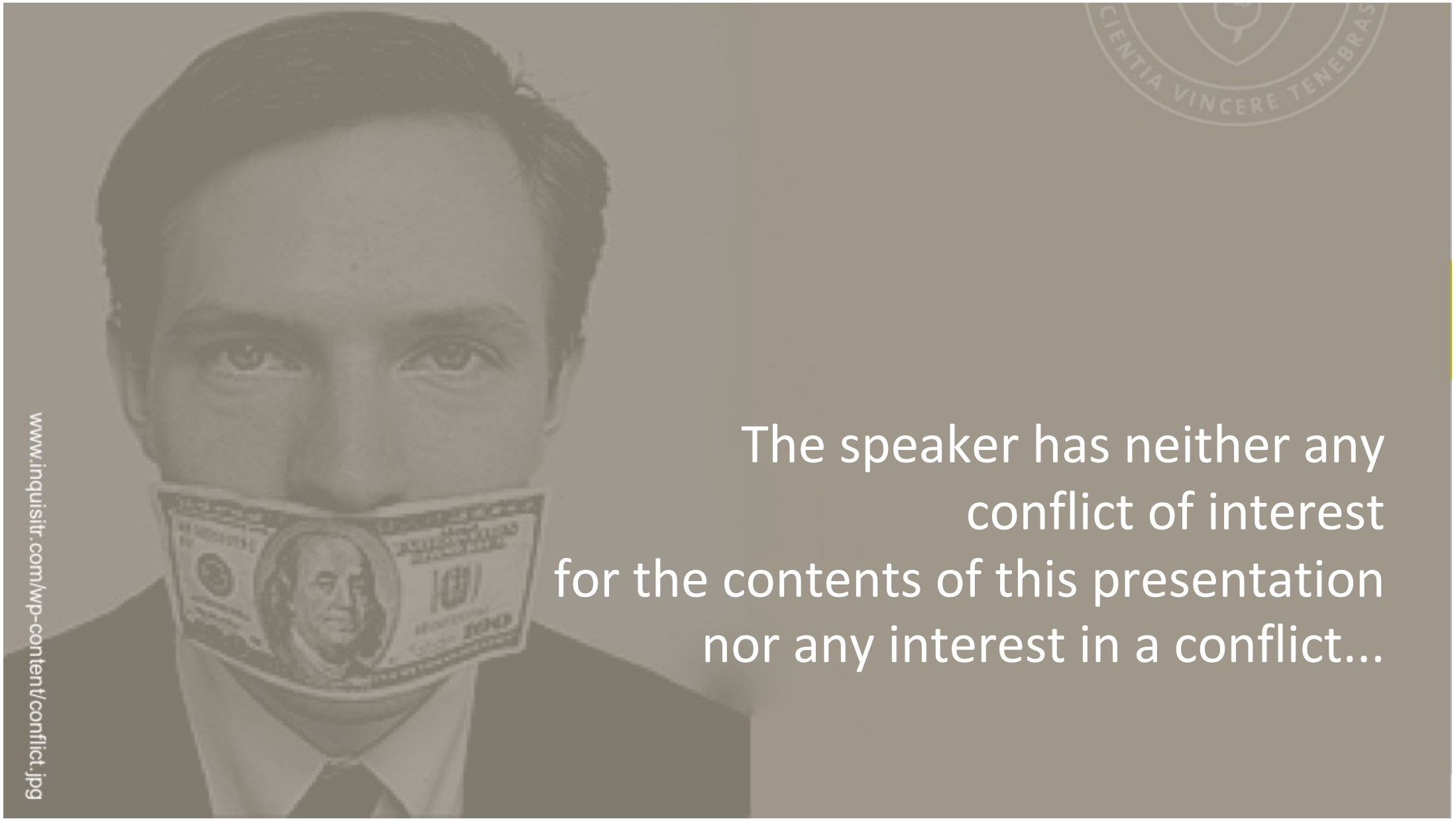
Brussels IVF

Universitair Ziekenhuis Brussel

Brussels IVF

VUB VRIJE UNIVERSITEIT BRUSSEL

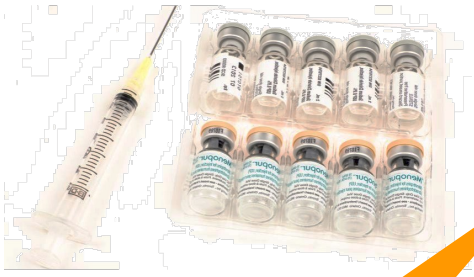
Universitair Ziekenhuis Brussel



The speaker has neither any
conflict of interest
for the contents of this presentation
nor any interest in a conflict...

Treatment of male infertility

The FSH algorithm in azoospermia

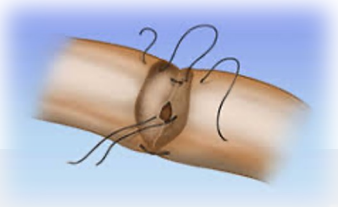


Secondary hypogonadism
(LH,FSH ↓, T↓)
- Hypothalamic disorders

(e.g. Kallmann syndrome,

FSH ↓	FSH nl	FSH ↑
hypogonadotropic	normogonadotropic	hypergonadotropic
Pre-testicular hormonal dysfunction	>> Post-testicular dysfunction	Primary testicular dysfunction
Hormonal treatment	Surgical correction	Donor sperm

Primary hypogonadism
(LH,FSH↑, T↓)
- cryptorchidism
- testicular damage
- torsion
- orchitis
- unexplained …



Intracytoplasmic sperm injection (ICSI)

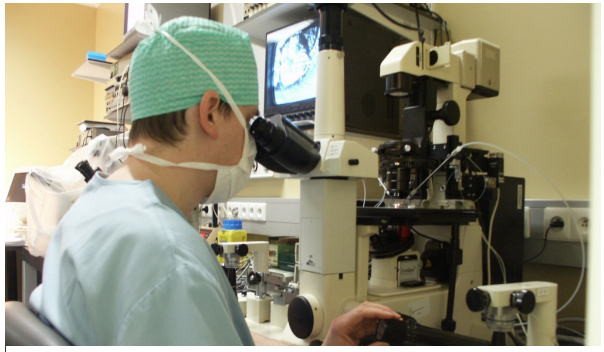
A gamechanger in male infertility

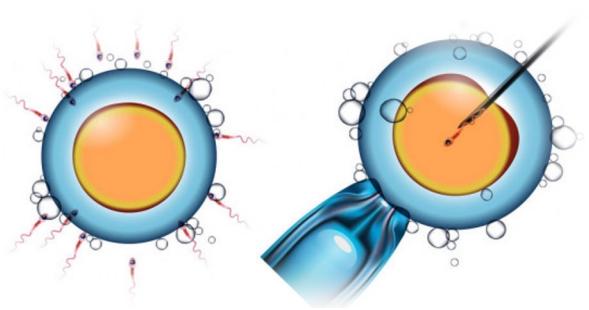
Pregnancies after intracytoplasmic injection of single spermatozoon into an oocyte

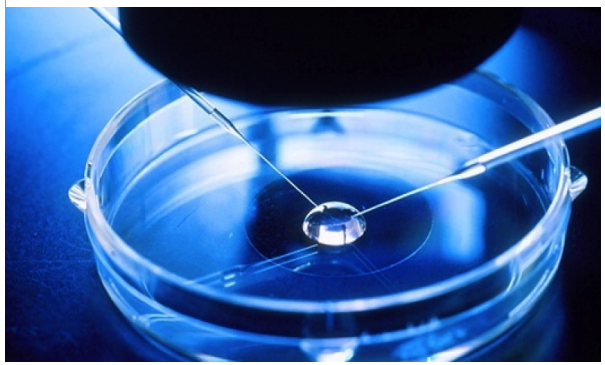
GIANPIERO PALERMO HUBERT JORIS
PAUL DEVROEY ANDRE C. VAN STEIRTEGHEM

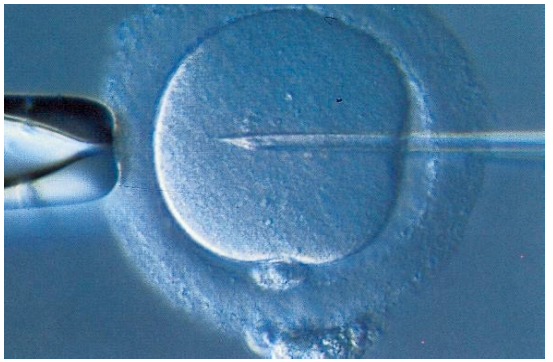
Intracytoplasmic sperm injection (ICSI) is a promising assisted-fertilisation technique that may benefit women who have not become pregnant by in-vitro fertilisation (IVF) or subzonal insemination (SUZI) of oocytes. We have used ICSI to treat couples with infertility because of severely impaired sperm characteristics, and in whom IVF and SUZI had failed. Direct injection of a single spermatozoon into the ooplasm was done in 47 metaphase-II oocytes: 38 oocytes remained intact after injection, 31 became fertilised, and 15 embryos were replaced in utero. Four pregnancies occurred after eight treatment cycles—two singleton and one twin pregnancy, and a preclinical abortion. Two healthy boys have been delivered from the singleton pregnancies and a healthy boy and girl from the twin pregnancy.

Lancet 1992; **340**: 17–18.









Intracytoplasmic sperm injection (ICSI)

A gamechanger for obstructive azoospermia

Pregnancy after fertilisation with human testicular spermatozoa

SIR—We routinely accept patients with agenesis or obstruction of the vas deferens for microsurgical epididymal spermatozoa aspiration (MESA). Although pregnancies have been reported after MESA,[1,2] it is generally accepted that the fertilising capacity of spermatozoa is reduced; in 7% of our patients no spermatozoa could be retrieved. The fertilising ability of testicular spermatozoa has been shown in animals. We therefore tried in patients with failed collection of epididymal spermatozoa biopsy of the testis and isolation of spermatozoa.

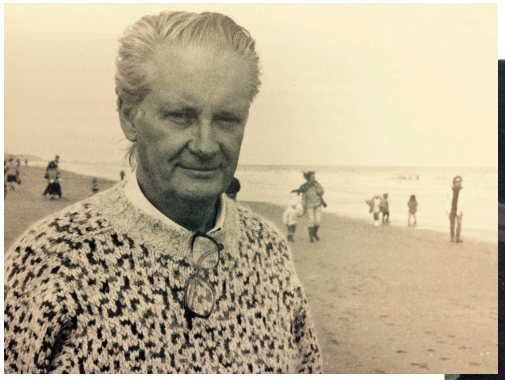
We investigated 6 excretory azoospermic men, referred because of congenital absence of the vas (patients 1–5) or failed vasoepididymostomy (patient 6). The fertilising capacity of testicular spermatozoa was evaluated in 3 (patients 1–3) entering the MESA programme. They underwent positive epididymal spermatozoa aspiration and testis biopsy. In patients 4–6, no spermatozoa were obtained from the epididymis at several levels. Peripheral testicular biopsy was then done.

R Schoysman, P Vanderzwalmen, M Nijs, L Segal, G Segal-Bertin, L Geerts, E van Roosendaal, D Schoysman

Schoysman Infertility Management Foundation, van Helmont-Ziekenhuis, IVF Laboratory, 1800 Vilvoorde, Belgium

Vol 342 • November 13, 1993

THE LANCET



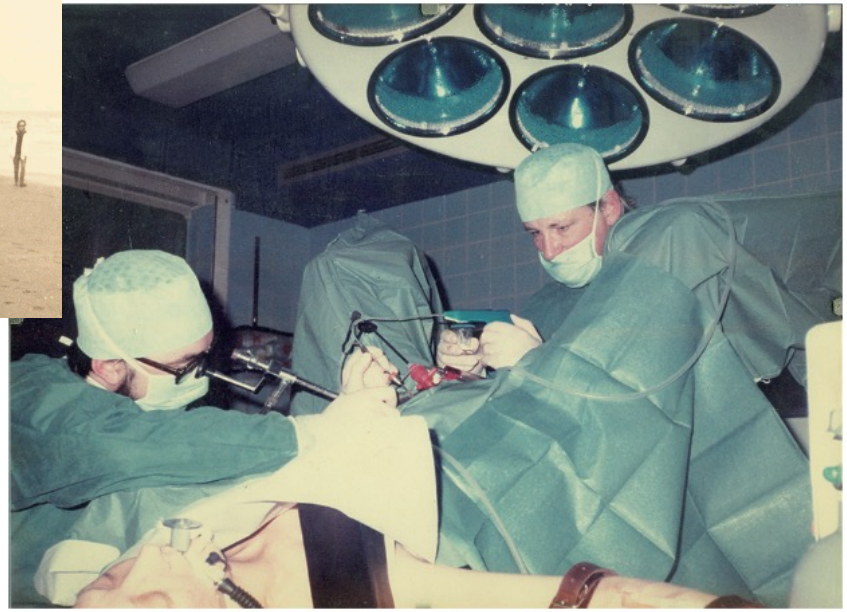


Fig. 2. — October 1981, at 3 am during a Saturday night, Jan Gerris (President VVOG) and Bob Schoysman performing a laparoscopic oocyte aspiration in the IVF centre of Vilvoorde.

Human Reproduction vol.10 no.6 pp.1457–1460, 1995

Pregnancies after testicular sperm extraction and intracytoplasmic sperm injection in non-obstructive azoospermia

P.Devroey[1,4], J.Liu[1], Z.Nagy[1], A.Goossens[2], H.Tournaye[1], M.Camus[1], A.Van Steirteghem[1] and S.Silber[3]

[1]Centre for Reproductive Medicine, [2]Department of Pathology, University Hospital, Dutch-speaking Brussels Free University,

Table I. Histological analysis of testicular biopsy in non-obstructive azoospermic patients

Patient no.	Hormonal evaluation		Histological report
	FSH (IU/l)	LH (IU/l)	
1	19.0	12.0	Sertoli cell only
2	21.9	13.1	Sertoli cell only
3	-	-	maturation arrest
4	10.6	5.5	tubular fibrosis
5	4.8	3.1	maturation arrest
6	17.0	3.7	maturation arrest
7	14.2	5.4	hypospermatogenesis
8	22.8	5.9	Sertoli cell only
9	7.9	4.5	hypospermatogenesis
10	40.0	20.0	not available
11	17.5	6.7	Sertoli cell only
12	24.0	10.0	tubular fibrosis
13	3.0	1.5	hypospermatogenesis
14	9.0	5.9	Sertoli cell only
15	7.5	4.5	Sertoli cell only

FSH = follicle stimulating hormone; LH = luteinizing hormone.

Human Reproduction Volume 10 Supplement 1 1995

Recent concepts in the management of infertility because of non-obstructive azoospermia

Herman Tournaye[1,4], Michel Camus[1], Anita Goossens[2], Jiaen Liu[1], P.Nagy[1], S.Silber[3], A.C.Van Steirteghem[1] and Paul Devroey[1]

[1]Centre for Reproductive Medicine, University Hospital, Dutch-speaking Brussels Free University (Vrije

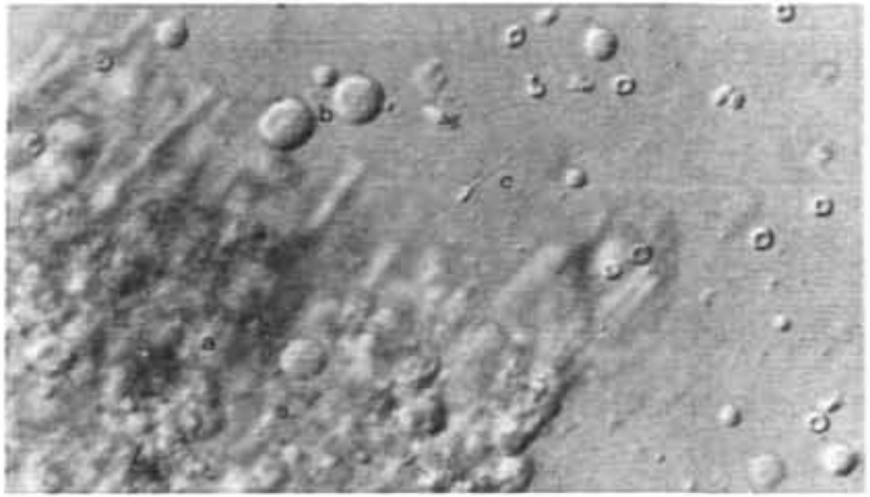
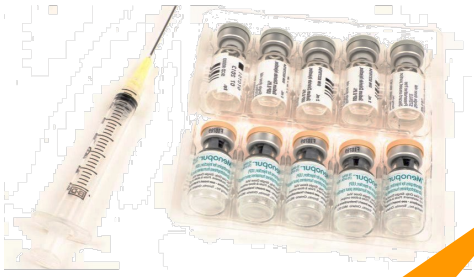


Figure 1. 'Wet preparation' of a testicular biopsy specimen demonstrating a bulky Sertoli cell (**a**), a germinal cell (**b**) and a mature spermatozoon (**c**).

Treatment of male infertility

The FSH algorithm in azoospermia



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	Surgical sperm recovery	Surgical sperm recovery

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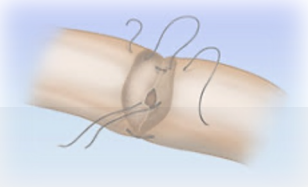
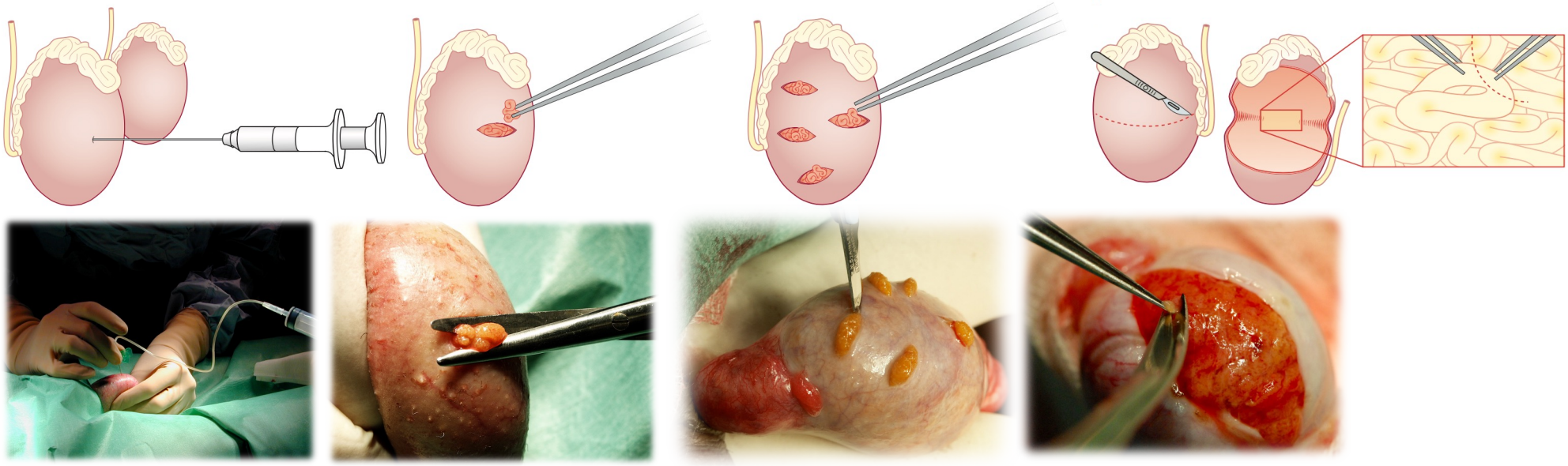


ICSI for azoospermia

Conventional and microsurgical testicular sperm extraction techniques

FNA: fine-needle aspiration TESE: testicular sperm extraction Conventional and microsurgical testicular sperm extraction



Concepts in diagnosis and therapy for male reproductive impairment

Herman Tournaye, Csilla Krausz, Robert D Oates
***Lancet Diabetes Endocrinol* 2016**

Surgical sperm recovery in non-obstructive azoospermia

multiple biopsies is the key to success

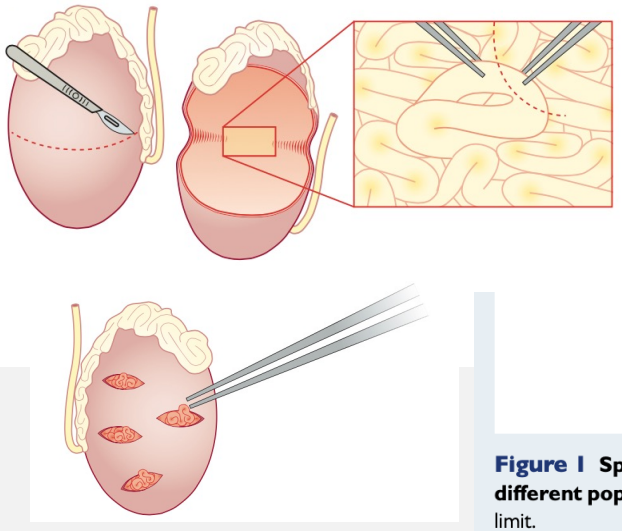
Human Reproduction Update, Vol.26, No.4, pp. 606–609, 2020

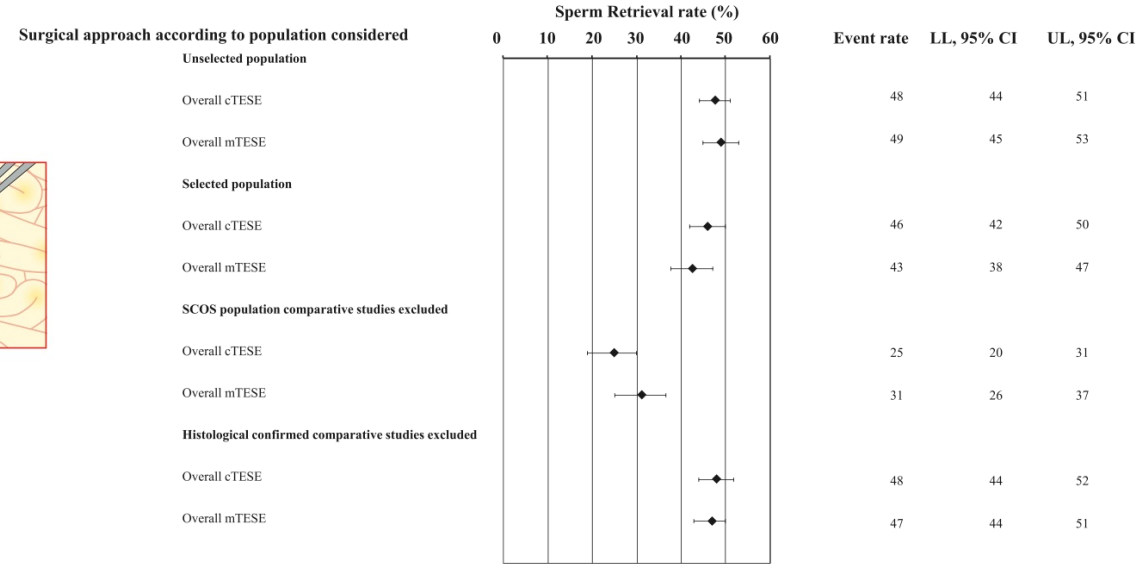
human reproduction update

LETTER TO THE EDITOR

Reply: Sperm retrieval rates by micro-TESE versus conventional TESE in men with non-obstructive azoospermia—the assumption of independence in effects sizes might lead to misleading conclusions

Giovanni Corona [1,*], Suks Minhas[2], Carlo Bettocchi[3], Csilla Krausz[4], Alessandro Pizzocaro[5], Walter Vena[5], Mario Maggi[7], and Nikolaos Sofikitis[6]





Surgical approach according to population considered	Event rate	LL, 95% CI	UL, 95% CI
Unselected population			
Overall cTESE	48	44	51
Overall mTESE	49	45	53
Selected population			
Overall cTESE	46	42	50
Overall mTESE	43	38	47
SCOS population comparative studies excluded			
Overall cTESE	25	20	31
Overall mTESE	31	26	37
Histological confirmed comparative studies excluded			
Overall cTESE	48	44	52
Overall mTESE	47	44	51

Figure 1 Sperm retrieval rate (SRR) per testicular sperm extraction (TESE) cycle according to the type of surgical approach in different populations. cTESE = conventional TESE; mTESE = microsurgical-TESE. SCOS = Sertoli cell only syndrome; UP = lower limit; UL = upper limit.

Sperm retrieval as an outcome

Add-ons to improve retrieval

Human Reproduction Update, Vol.28, No.5, pp. 609–628, 2022
Advance Access Publication on May 8, 2022 https://doi.org/10.1093/humupd/dmac016

human reproduction update

Does hormonal therapy improve sperm retrieval rates in men with non-obstructive azoospermia: a systematic review and meta-analysis

Tharu Tharakan[1,2,*], Giovanni Corona[3], Daniel Foran[2], Andrea Salonia[4,5], Nikolaos Sofikitis[6], Aleksander Giwercman[7], Csilla Krausz[8], Tet Yap[9], Channa N. Jayasena[2,†], and Suks Minhas[1,†]

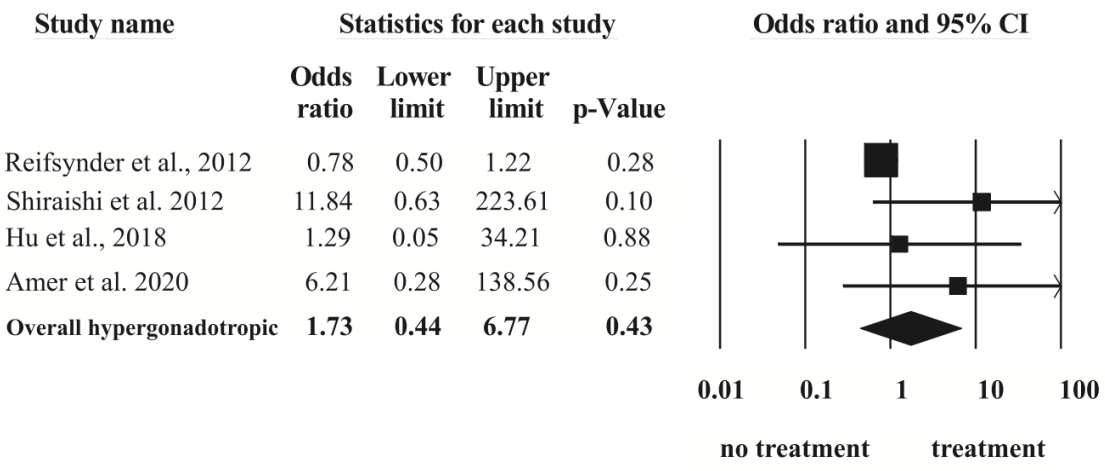


Figure 6. Effect of hormone therapy on surgical sperm retrieval rate in hypergonadotropic men with non-obstructive azoospermia. A Forest plot demonstrating the individual and cumulative odds ratios for surgical sperm retrieval.

Sperm retrieval as an outcome

Add-ons to improve retrieval

Clinical factors impacting microdissection testicular sperm extraction success in hypogonadal men with nonobstructive azoospermia

Fertil Steril® VOL. 122 NO. 4 / OCTOBER 2024

Sandro C. Esteves, M.D., Ph.D.,[a,b] Arnold P. P. Achermann, M.D.,[a,c] Ricardo Miyaoka, M.D., Ph.D.,[a,b] Sidney Verza Jr., M.Sc.,[a] Adriano Fregonesi, M.D., Ph.D.,[b] and Cassio L. Z. Riccetto, M.D., Ph.D.[b,c]

Crude and adjusted odds ratios for sperm retrieval success in patients receiving (treated) or not (untreated) pre-sperm retrieval hormonal stimulation according to follicle-stimulating hormone threshold levels.

Patient groups	Crude OR (95% CI)	*P* value[a]	Adjusted OR[b] (95% CI)	*P* value[c]
Normogonadotropic (n = 295):				
Untreated (n = 164)[d]	1	—	1	—
Treated (n = 131)	2.25 (1.34–3.80)	.01	3.20 (1.59–6.44)	.001
Hypergonadotropic (n=321):				
Untreated (n = 161)[d]	1	—	1	—
Treated (n = 160)	1.71 (1.10–2.68)	.01	1.46 (0.74–2.88)	.27

Note: Hypergonadotropic: FSH levels >12 IU/L; normogonadotropic: FSH levels ≤12 IU/L. *P* value < .05 was considered statistically significant. CI = confidence interval; FSH = follicle-stimulating hormone; IU = international units; OR = odds ratio.

Sperm retrieval as an add-on

still to be proven…

Review – Andrology

Does Testicular Sperm Improve Intracytoplasmic Sperm Injection Outcomes for Nonazoospermic Infertile Men with Elevated Sperm DNA Fragmentation? A Systematic Review and Meta-analysis

Christopher C. Khoo [a,], Axel Alberto Cayetano-Alcaraz [a], Razi Rashid [a], Tharu Tharakan [a], Tet Yap [b], Nikolaos Sofikitis [c], Andrea Salonia [d,e], Giovanni Corona [f], Aleksander Giwercman [g], Channa N. Jayasena [h], Suks Minhas [a]*

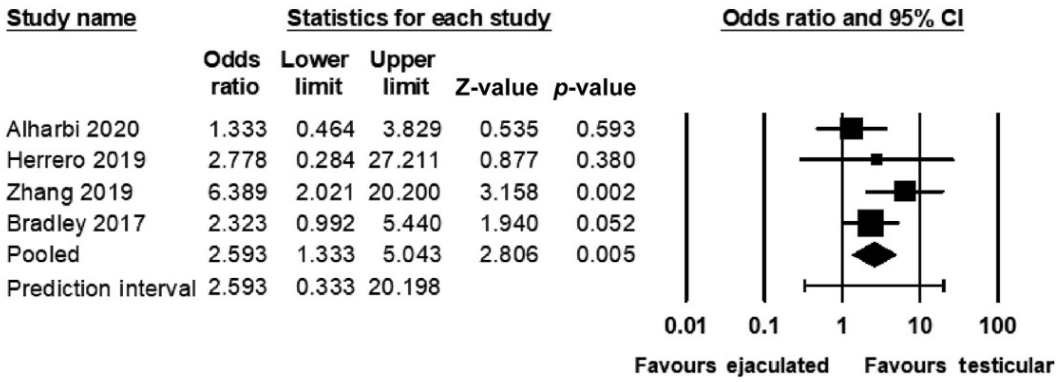


Fig. 5 – Live birth rate (Begg's test: p = 0.496, I^2 = 24%). CI = confidence interval.

Patient summary: Our review showed that for infertile men with a high level of DNA damage in their sperm, use of sperm extracted from the testicles may give better results than ejaculated sperm for a particular IVF (in vitro fertilisation) technique. However, there is a lack of high-quality data.

Sperm retrieval as an outcome

The lab may be more important

Enzymatic tissue processing after testicular biopsy in non-obstructive azoospermia enhances sperm retrieval

Human Reproduction Open, 2023, **2023(4)**, hoad039

V. Vloeberghs [1,*], N. De Munck[1], A. Racca [2], I. Mateizel[1], K. Wouters[1], and H. Tournaye[1]

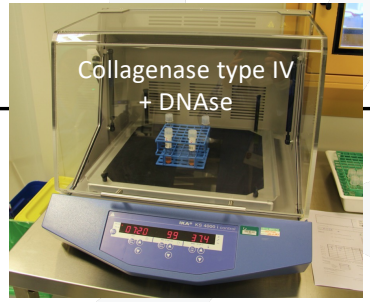
118 NOA patients

- Strict NOA diagnosis
- First TESE ever

Spermatozoa found for ICSI

N = 28 (23.7%)

Cryopreservation of supernumerary sperm for later ICSI



No (or insufficient) spermatozoa found for ICSI

N = 90 (76.3%)

Enzymatic digestion

Spermatozoa found for ICSI

N = 44 (48.9%)

No spermatozoa found

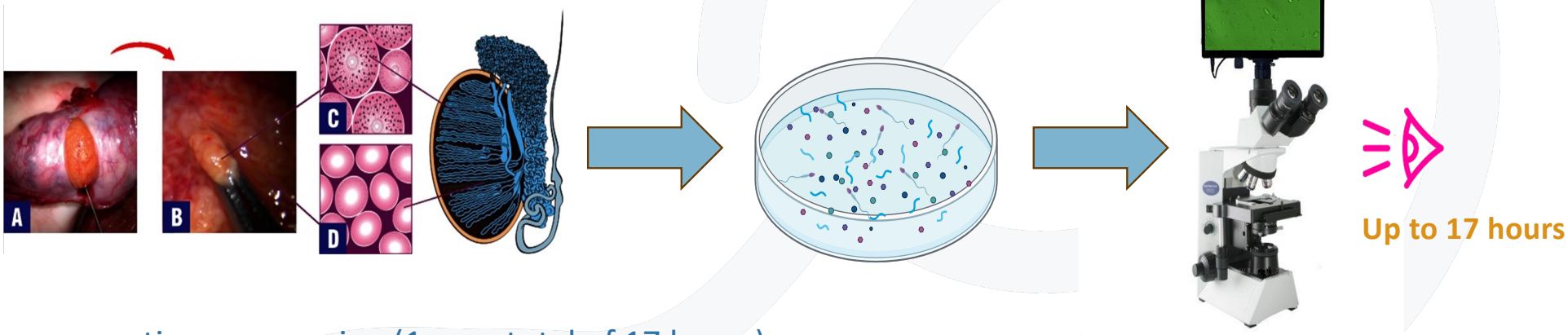
N = 46 (51.1%)

Sperm retrieval after mechanical and enzymatic digestion = 28 + 44 / 118 = 61.0%

ADDITIONAL VALUE OF ENZYMATIC DIGESTION 44/90 = 48.9%

Sperm retrieval as an outcome

The lab may be more important



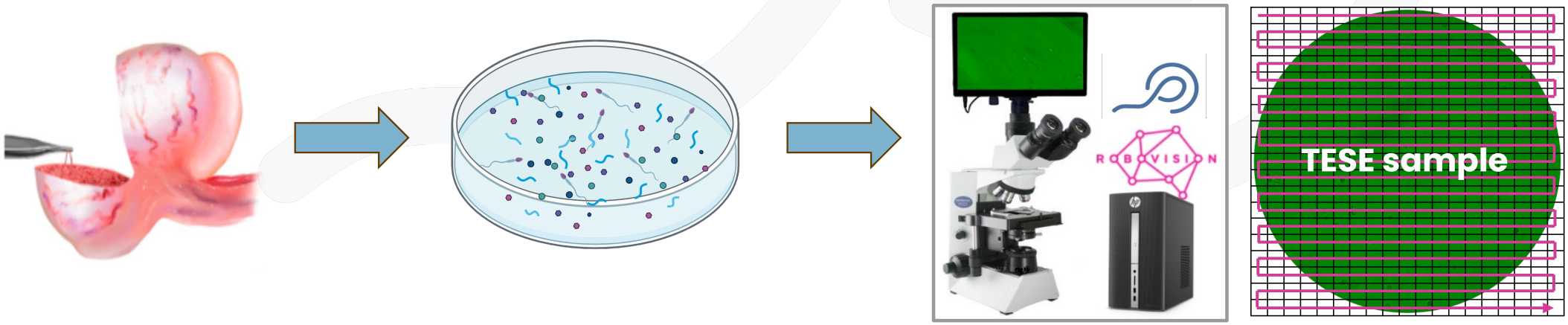
- very time consuming (1 case total of 17 hours)
- average 61 minutes (average 8 oocytes / n=479 cycles)
- total search time (2023-2024): 258 hours = 32 working days

Sperm retrieval as an outcome

T'Easy, making TESE easy…

Koen Wouters · 1st
Deputy head of the ART lab
Brussels, Brussels Region, Belgium

- new fully automated sperm detection tool
- visual control of progress
- motile vs immotile
- X,Y and Z coordinates: go back to findings to pick up the sperm
- objective support for deciding when to stop searching



Sperm retrieval as an outcome

T'Easy, making TESE easy…

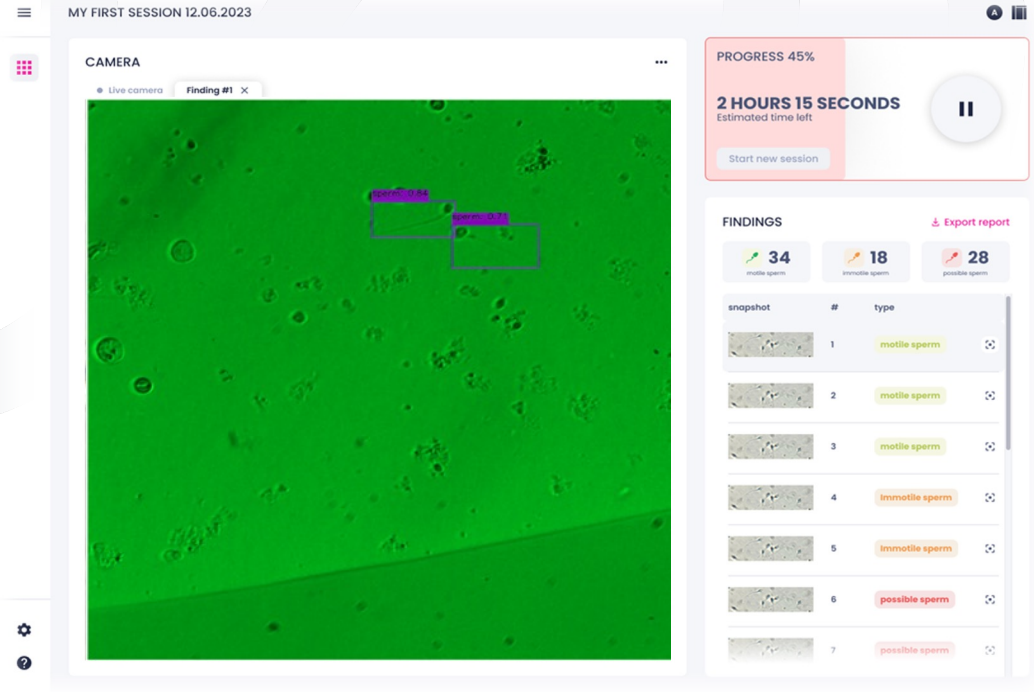
Abstract citation ID: deaf097.228

O-228 T'easy: redefining sperm detection after testicular sperm extraction (TESE) – A faster, smarter and more efficient approach to sperm retrieval in IVF Labs

K. Wouters[1], M. De Meyer[2], M. Larmuseau[2], N. Franceus[1], M. Krunic[1], A. Witdouck[1], S. Lingier[2], H. Tournaye[1], S. Willaert[2], N. De Munck[1]

[1]UZ Brussel, Brussels IVF, Brussel, Belgium
[2]Robovision AI, Robovision AI, Gent, Belgium

- accurate detection rate ≥98%
- higher detection rate than lab technician
- faster: 10 min vs 24 min (lab tech)
- low false positives and negatives



Pregnancy as an outcome

Does NOA equal OA ?

Comparison of the outcome of intracytoplasmic sperm injection in obstructive and non-obstructive azoospermia in the first cycle: a report of case series and meta-analysis

MOHAMED GHANEM,* NAGWA I. BAKR,† MAHA A. ELGAYAAR,‡ SHYMAA EL MONGY,‡ HANAN FATHY‡ and ABDEL-HAMID A. IBRAHIM‡

Table 5. Odds ratio and 95% CI for pregnancy in obstructive azoospermia (OA) and non-obstructive azoospermia (NOA): meta-analysis

Number	Reference	Pregnancy in OA and NOA OR (95% CI)	*p*-value
1	Ghanem *et al.* (present study results)	1.3 (0.68–2.6)	0.49
2	Friedler *et al.* (2002)	1.14 (0.64–2.05)	0.76
3	Mansour *et al.* (1997)	3.7 (1.62–7.4)	<0.01
4	Palermo *et al.* (1999)	1.38 (0.79–2.41)	0.25
5	De Croo *et al.* (2000)	1 (0.56–1.77)	1.1
6	Overall	1.53 (0.83–2.74)	0.17

Pregnancy as an outcome

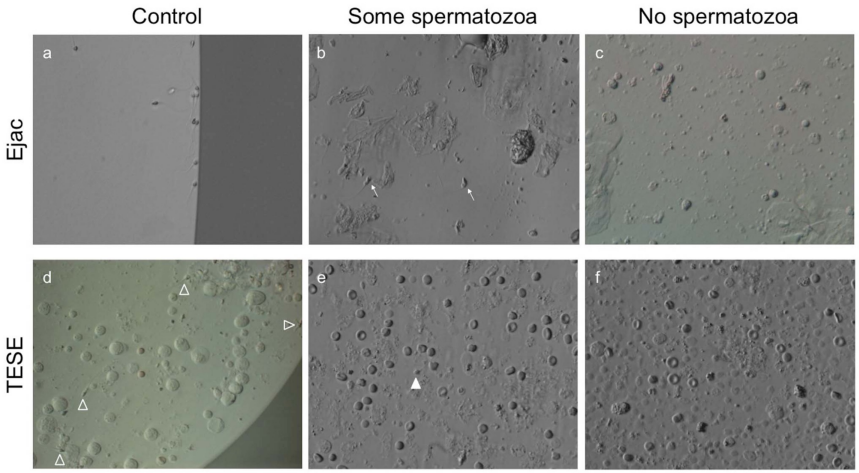
NOA does not equal OA

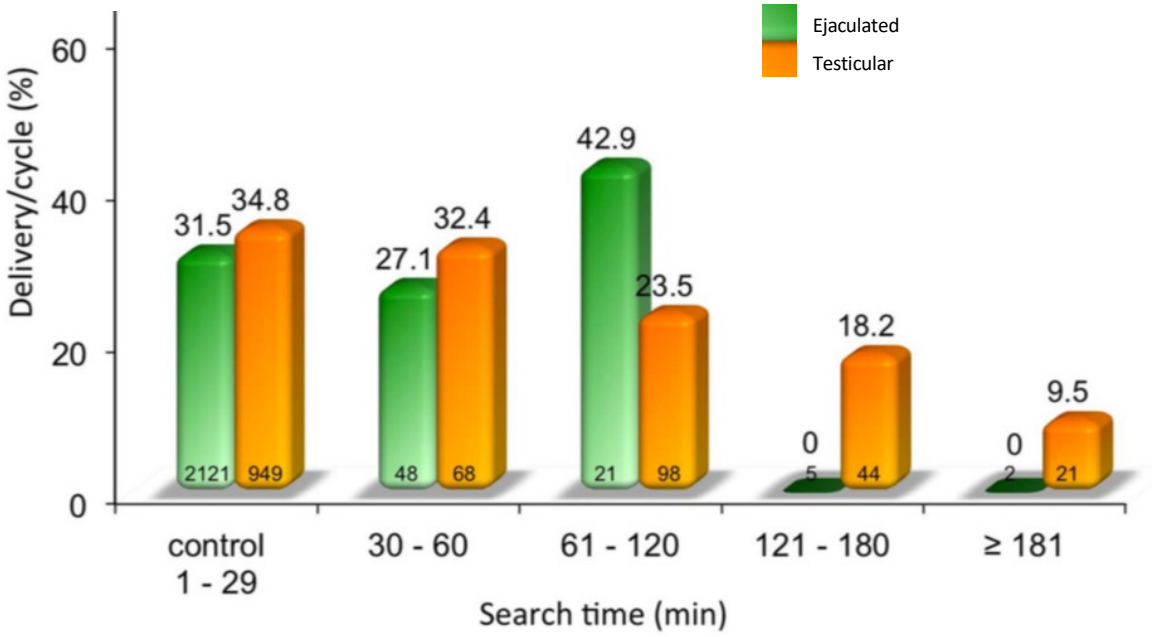
Intracytoplasmic Sperm Injection (ICSI) in Extreme Cases of Male Infertility

Gianpiero D. Palermo*, Queenie V. Neri[1], Peter N. Schlegel[2], Zev Rosenwaks[1]

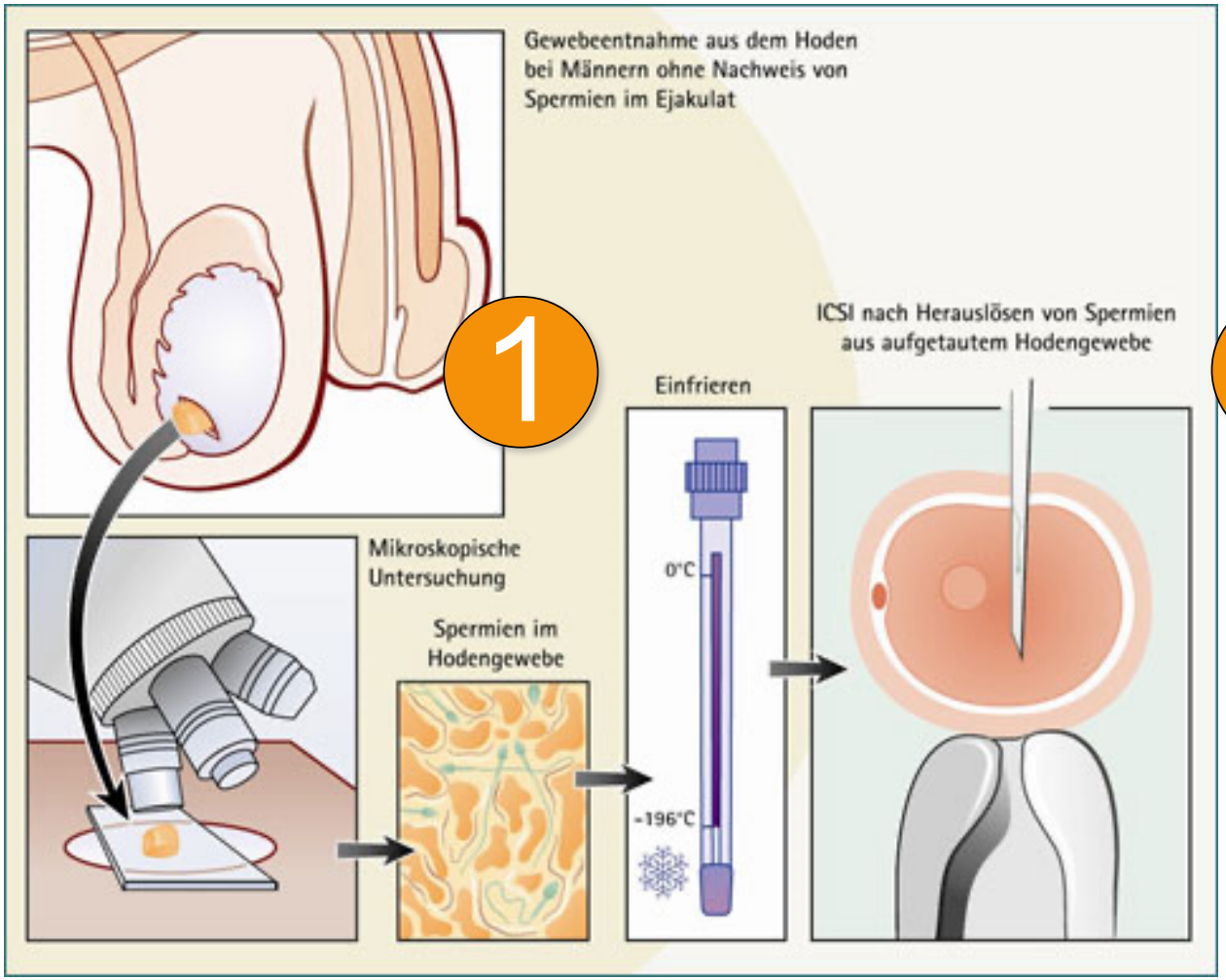
1. The Ronald O. Perelman & Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medical College, New York, New York, United States of America, **2.** Department of Urology, Weill Cornell Medical College, New York, New York, United States of America

PLOS ONE | DOI:10.1371/journal.pone.0113671 December 1, 2014





How to counsel candidate patients ?



http://www.aim-schulungen.de/

How to counsel candidate patients ?

Intention-to-treat approach

Human Reproduction, Vol.30, No.8 pp. 1790–1796, 2015
Advanced Access publication on June 16, 2015 doi:10.1093/humrep/dev139

human reproduction ORIGINAL ARTICLE *Andrology*

1 + 2

How successful is TESE-ICSI in couples with non-obstructive azoospermia?

V. Vloeberghs[1,*], G. Verheyen[1], P. Haentjens[2], A. Goossens[3], N.P. Polyzos[1], and H. Tournaye[1]

- 714 couples: 826 TESE with SSR rate: 40,5% (48%)
- 261 couples had ICSI and 129 got pregnant: 49%

- **but on 714 starting TESE couples 96 delivered: 13%**

Delivery as an outcome

How to counsel patients?

1 + 2 + 3

118 NOA patients

- Strict NOA diagnosis
- First TESE ever

Spermatozoa found for ICSI

N = 28 (23.7%)

Cryopreservation of supernumerary sperm for later ICSI

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ADDITIONAL VALUE OF ENZYMATIC DIGESTION 44/90 = 48.9%

giving rise to a total CLB per TESE of 32/118 (27.1%)

Vloeberghs V et al. Enzymatic tissue processing after testicular biopsy in non-obstructive azoospermia enhances sperm retrieval and cumulative live birth rates. 2023 HR Update

Is genetic fatherhood within reach for all azoospermic Klinefelter men?

Veerle Vloeberghs[1]*, Greta Verheyen[1], Samuel Santos-Ribeiro[1], Catherine Staessen[2], Willem Verpoest[1], Inge Gies[3], Herman Tournaye[1]

1 Centre for Reproductive Medicine, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Brussels,

PLOS ONE | https://doi.org/10.1371/journal.pone.0200300 July 25, 2018

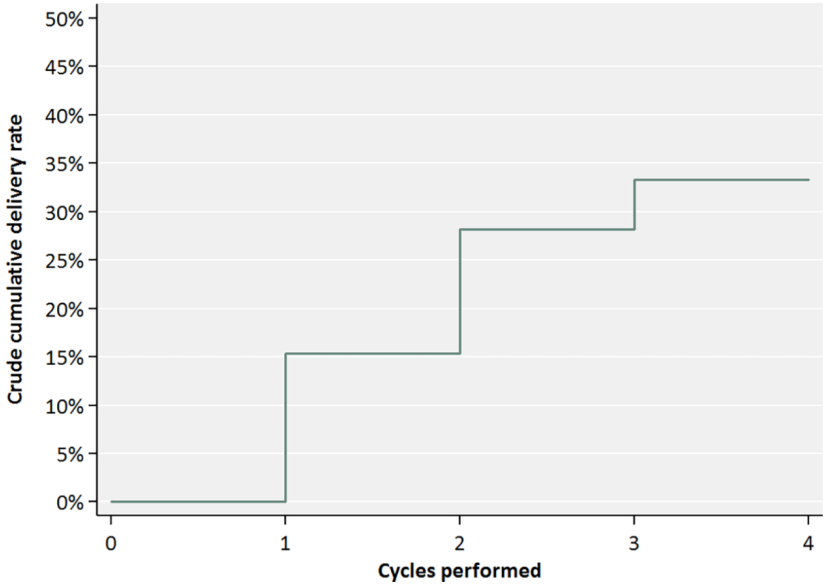


Fig 2. Crude cumulative delivery rates in non-mosaic azoospermic KS patients.

Sperm recovery and ICSI outcomes in Klinefelter syndrome: a systematic review and meta-analysis

Giovanni Corona[1,†], Alessandro Pizzocaro[2,†], Fabio Lanfranco[3,†], Andrea Garolla[4,†], Fiore Pelliccione[2], Linda Vignozzi[5], Alberto Ferlin[4], Carlo Foresta[4], Emmanuele A. Jannini[6], Mario Maggi[5], Andrea Lenzi[7], Daniela Pasquali[8], Sandro Francavilla[9,*], and On behalf of the Klinefelter ItaliaN Group (KING)

Human Reproduction Update, pp. 1–11, 2017

chemical parameters, including age, testis volume and hormonal status at baseline. In addition, the use of retrieved sperm allows live children to be born in ~40% of ICSI cycles meaning a final LBR of 16% for the couples who initiated the assisted reproductive techniques.

In 1996, Tournaye *et al.* reported a successful recovery of sperm-atozoa by cTESE in men with azoospermia and KS for the first time.

What about the children born?

paucity of data on NOA pregnancies

Karyotyping, congenital anomalies and follow-up of children after intracytoplasmic sperm injection with non-ejaculated sperm: a systematic review

G.H. Woldringh[1,4], D.E. Besselink[1], A.H.J. Tillema[2], and I.A.M. Kremer[1]

Human Reproduction Update, Vol.16, No.1 pp. 12–19, 2010

Table IV RRs with 95% CI for major malformations of ICSI children with epididymal or testicular sperm compared with major malformations of ICSI children with ejaculated sperm

Authors	RR (95% CI)	
	Epid/ejac	Test/ejac
Bonduelle *et al.*	1.12 (0.42–2.98)	0.86 (0.38–1.94)
Källén *et al.*	1.13 (0.47–2.72)	0.62 (0.20–1.93)
Ludwig and Katalinic	0.46 (0.07–3.13)	1.09 (0.71–1.66)
Palermo *et al.*	1.09 (0.39–3.03)	0.62 (0.09–4.47)
Wennerholm *et al.*	1.04 (0.33–3.28)	0

Epid, epididymal; Ejac, ejaculated; Test, testicular.

Table III Major malformations per study group (%)

Authors	Major malformations					Outcome[#]
	ICSI with ejac. sperm	ICSI with epid. sperm	ICSI with testic. sperm	IVF	Natural conceived children	
Bonduelle *et al.*	84/2477 (3.4)	4/105 (3.8)	6/206 (2.9)	112/2955 (3.8)	NA	No statistical difference (ejaculated sperm versus non-ejaculated sperm; testicular sperm versus epididymal sperm; ICSI versus IVF)
Källén *et al.*	139/4248 (3.3)	5/135 (3.7)	3/147 (2.0)	284/ 10 116 (2.8)	NA	No significant difference (between different methods of ICSI; between standard IVF and ICSI)*
Ludwig and Katalinic	248/2944 (8.4)	1/26 (3.8)	21/229 (9.2)	NA	2140/30 940 (6.9)	No influence of sperm origin; increased risk after ICSI compared with natural conceived children[¶]
Palermo *et al.*	33/1774 (1.9)	4/198 (2.0)	1/87 (1.1)	30/1796 (1.7)	NA	No difference in frequency (between IVF and ICSI; between ejaculated, epididymal and testicular sperm)
Wennerholm *et al.*	39/934 (4.2)	3/69 (4.3)	0/31 (0.0)	NA	NA	Similar rate in different subgroups

[#]Outcome of the study as mentioned in article.
*Adjusted for potential confounders: year of birth, maternal age and parity, years of involuntary childlessness and maternal smoking in early pregnancy.
[¶]Included stillbirths.
Ejac., ejaculated; Epid., epididymal; Testic., testicular; NA, not available.

What about the children born?

paucity of data on NOA pregnancies

Neonatal outcome of 724 children born after ICSI using non-ejaculated sperm

F. Belva[1,*], F. De Schrijver[1], H. Tournaye[2], I. Liebaers[1,2], P. Devroey[2], P. Haentjens[3], and M. Bonduelle[1]

[1]Center for Medical Genetics, UZ Brussel, Brussels 1090, Belgium [2]Center for Reproductive Medicine, UZ Brussel, Brussels, Belgium
[3]Center for Outcomes Research and Laboratory for Experimental Surgery, UZ Brussel, Brussels, Belgium

Human Reproduction, Vol.0, No.0 pp. 1–7, 2011

Table V **Outcome parameters of live and stillborns conceived with testicular sperm according to obstructive (OA) or non-obstructive (NOA) cause of azoospermia.**

	OA (n = 360)	NOA (n = 168)	OR (95% CI) or P-values
Live born singletons	206	117	
Birthweight (g)	2830	2950	0.9
Gestational age (weeks)	38.4	38.5	0.9
Gestational age <37 weeks	16 (7.7)	15 (12.8)	0.2 (0.3–1.2)
Live born twins	134	38	
Birthweight (g)	2395	2373	0.9
Gestational age (weeks)	35.8	35.2	0.9
Gestational age <37 weeks	74 (55.2)	24 (63.1)	0.7 (0.3–1.5)
Male gender	183 (51)	78 (46)	1.2 (0.8–1.7)
Children with major malformations	19 (5.2)	7 (4.2)	1.2 (0.5–3.1)
Children with major genital malformations	2	3	0.3 (0.0–1.8)
De novo karyotype anomaly (pre- and post-natally detected)	3	0	3.2 (0.2–64.3)

Data are presented as numbers (%). OR, odds ratio; 95% CI, 95% confidence interval.

What about the children born?

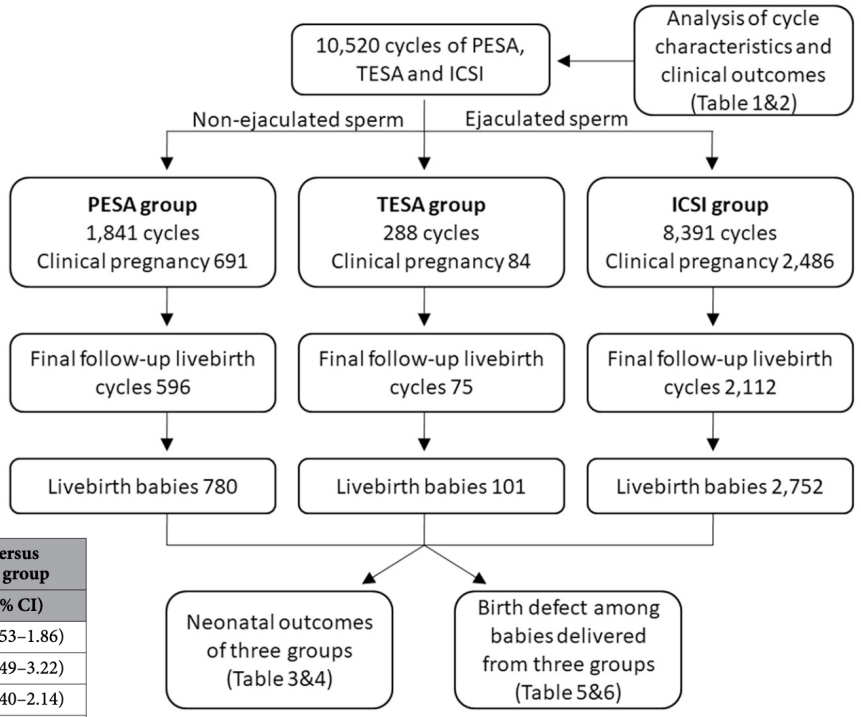
paucity of data on NOA pregnancies

Neonatal outcome of children born after ICSI with epididymal or testicular sperm: A 10-year study in China

Lei Jin[1,2], Zhou Li[1,2], Longjie Gu[1] & Bo Huang[1*]

SCIENTIFIC REPORTS
nature research

(2020) 10:5145 | https://doi.org/10.1038/s41598-020-62102-y



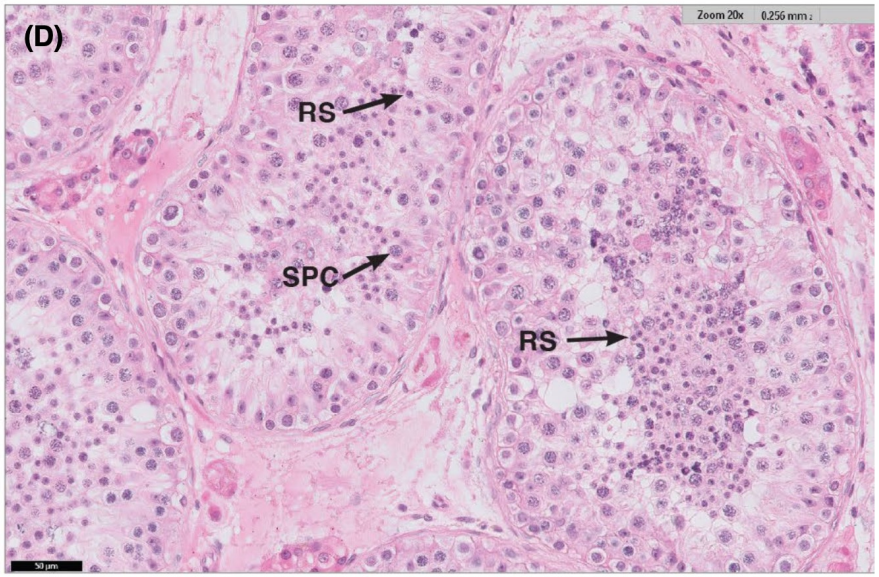
Parameter	Non-ejaculated sperm			Ejaculated sperm	Non-ejaculated versus ejaculated sperm group	
	Total	Epididymal sperm	Testicular sperm		P value	OR (95% CI)
Numbers of birth defect (% per total live birth)[a]	13 (1.48)	12 (1.54)	1 (1.00)	41 (1.49)	NS	0.99 (0.53–1.86)
Male with birth defect (% per total male live birth)[a]	6 (1.48)	5 (1.31)	1 (2.04)	16 (1.19)	NS	1.25 (0.49–3.22)
Female with birth defect (% per total female live birth)[a]	7 (1.64)	7 (1.76)	0 (0)	25 (1.78)	NS	0.92 (0.40–2.14)
Singletons with birth defect (% per total singletons live birth)[a]	9 (1.95)	8 (1.94)	1 (2.04)	14 (0.95)	NS	2.07 (0.89–4.82)
Twins with birth defect (% per total multiples live birth)[a]	4 (0.95)	4 (1.09)	0 (0)	27 (2.11)	NS	0.45 (0.16–1.28)

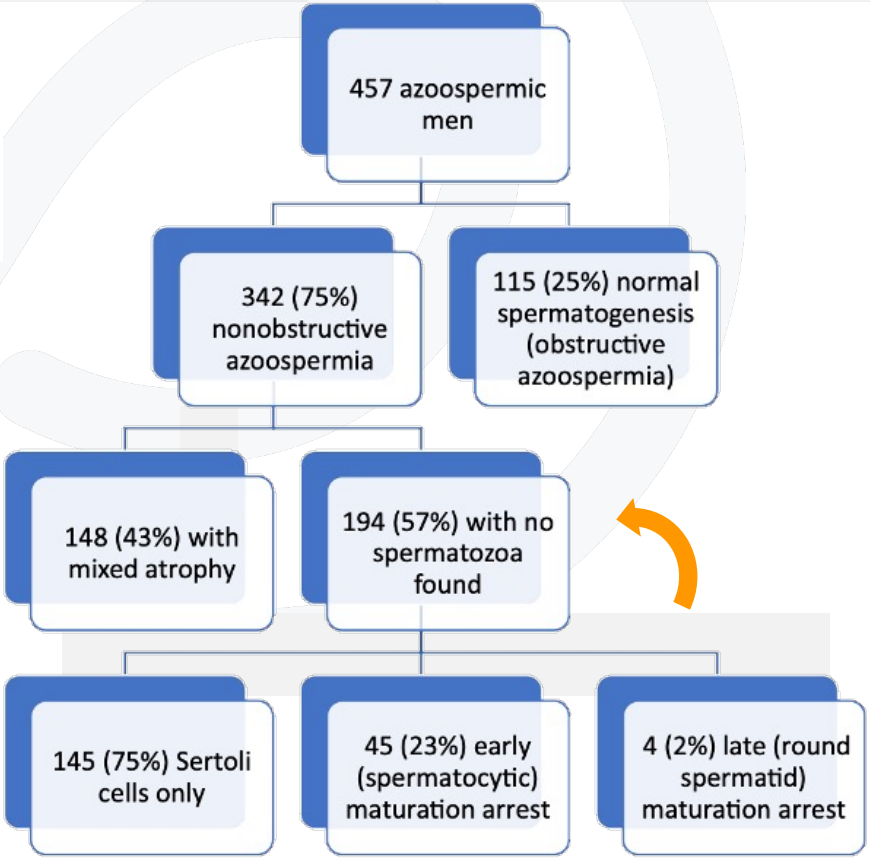
What if no spermatozoa ?

Round spermatid injection?

Questioning the utility of round spermatid injections in men with non-obstructive azoospermia

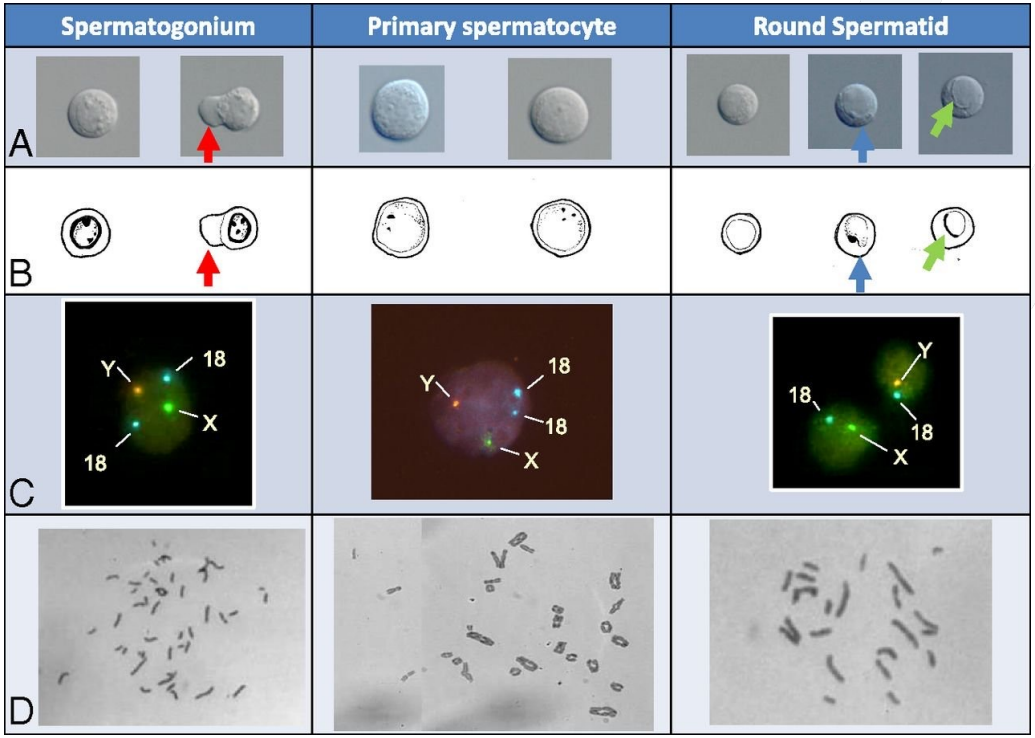
Shimi Barda[1,2] | Roy Mano[3] | Ofer Lehavi[1] | Sandra E. Kleiman[1] | Ofer Yossepowitch[3] | Foad Azem[4] | Ron Hauser[1] | Snir Dekalo[1,3]





What if no spermatozoa ?

Round spermatid injection



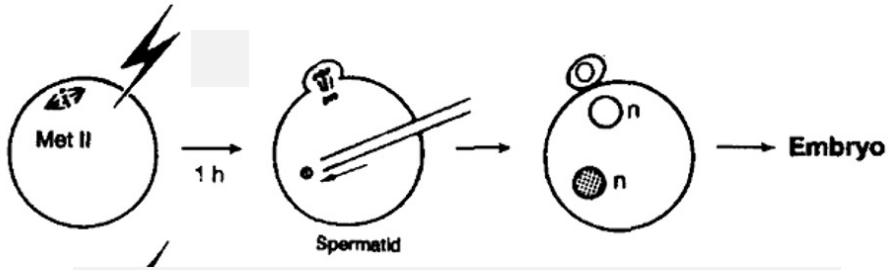
Tanaka A et al.2015

Development 121, 2397-2405 (1995)

Mouse oocytes injected with testicular spermatozoa or round spermatids can develop into normal offspring

Yasuyuki Kimura and R. Yanagimachi

Department of Anatomy and Reproductive Biology, University of Hawaii School of Medicine, Honolulu, Hawaii 96822, USA



Round spermatid injection

An efficient strategy?

Predictive value of testicular histology in secretory azoospermic subgroups and clinical outcome after microinjection of fresh and frozen–thawed sperm and spermatids

M.Sousa[1,3], N.Cremades[1], J.Silva[1], C.Oliveira[1], L.Ferraz[1], J.Teixeira da Silva[1], P.Viana[1] and A.Barros[2]

Human Reproduction Vol.17, No.7 pp. 1800–1810, 2002

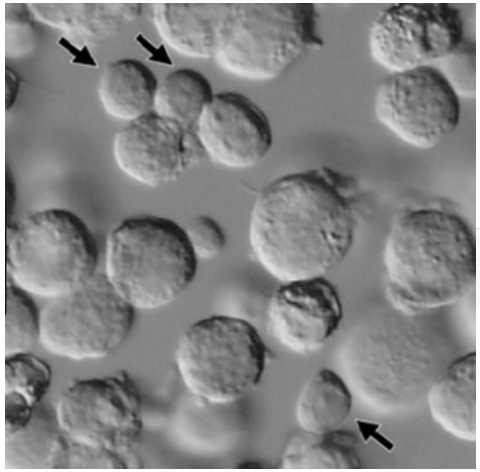


Table V. Review of outcome in round spermatid injection (ROSI) cycles

Author	Cycles	MII injected	2PN zygotes	Cleaved (from 2PN)	Viable clinical pregnancies
Tesarik *et al.*, 1995, 1996	7	39	14	14	2[a]
Amer *et al.*, 1997	56	610	110	79	0
Antinori *et al.*, 1997a,b	21	150	82	62	3[b]
Vanderzwalmen *et al.*, 1997	32	260	57	49	1[b]
Yamanaka *et al.*, 1997	9	53	34	30	0
Barak *et al.*, 1998	8	37	10	–	1[a]
Bernabeu *et al.*, 1998	8	69	7	7	0
Kahraman *et al.*, 1998	20	199	51	31	0
Al Hasani *et al.*, 1999	4	49	9	–	0
Sousa *et al.*, 1999	50	394	43	43	0
Tesarik *et al.*, 1999	1	6	2	2	0
Present results	33	200	31	24	0
Total (%)	249	2066	450/2066 (21.8)	341/431 (79.1)	7/249 (2.8) 4/246 (1.6)

[a]Patients with previous late spermatids/sperm in ejaculates.

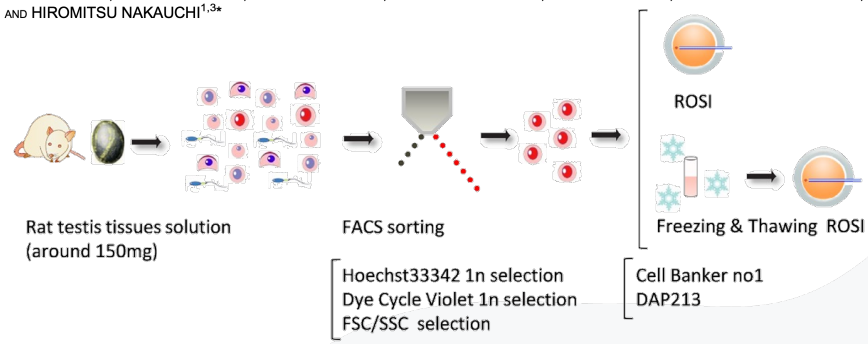
[b]Patients without previous late spermatids/sperm in ejaculates/diagnostic testicular biopsy.

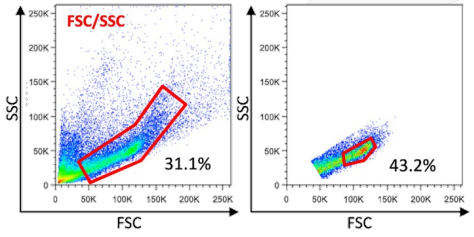
Round spermatid injection

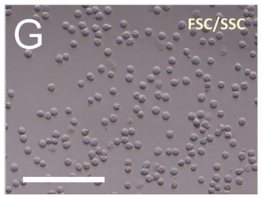
Are we injecting round spermatids ?

Practical Selection Methods for Rat and Mouse Round Spermatids Without DNA Staining by Flow Cytometric Cell Sorting

TOMONARI HAYAMA,[1†] TOMOYUKI YAMAGUCHI,[1*] MEGUMI KATO-ITOH,[1] YUMIKO ISHII,[1] NAOAKI MIZUNO,[1] AYUMI UMINO,[1] HIDEYUKI SATO,[1] MAKOTO SANBO,[2] SANAE HAMANAKA,[1] HIDEKI MASAKI,[1] MASUMI HIRABAYASHI[2], AND HIROMITSU NAKAUCHI[1,3*]







Scale bar = 100um

Fourteen babies born after round spermatid injection into human oocytes

Atsushi Tanaka[a,1], Motoi Nagayoshi[a], Youichi Takemoto[a], Izumi Tanaka[a], Hiroshi Kusunoki[b], Seiji Watanabe[c], Keiji Kuroda[d], Satoru Takeda[d], Masahiko Ito[e], and Ryuzo Yanagimachi[f,1]

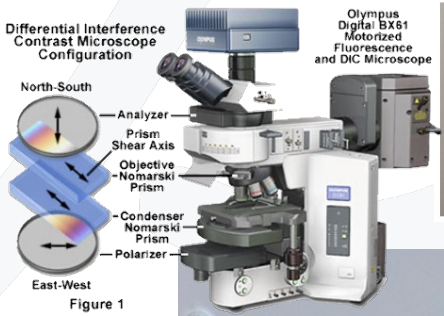
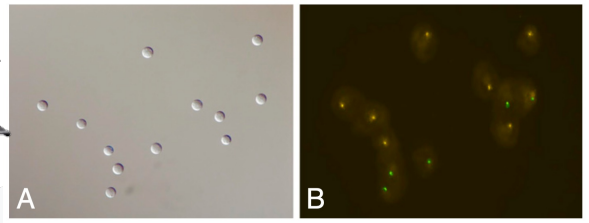
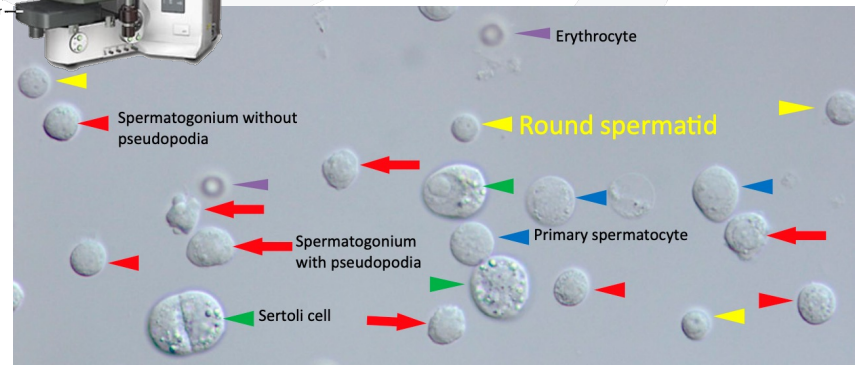
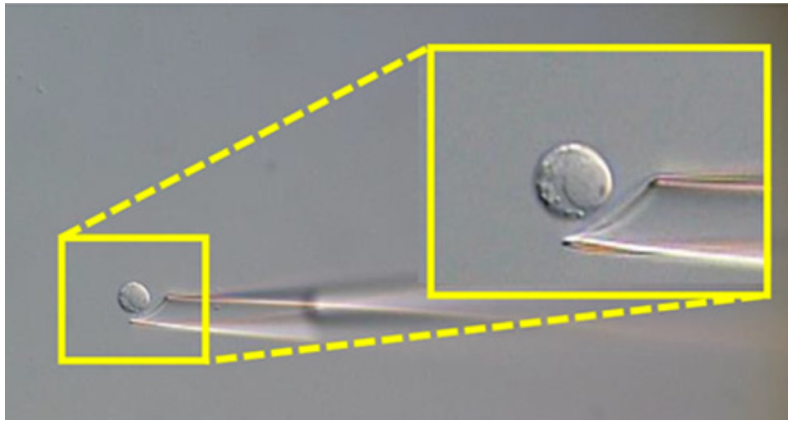


Figure 1





Round spermatid injection
An efficient strategy?



Ninety babies born after round spermatid injection into oocytes: survey of their development from fertilization to 2 years of age

Atsushi Tanaka, M.D., Ph.D.,[a] Kohta Suzuki, M.D., Ph.D., M.P.H.,[b] Motoi Nagayoshi, M.D.,[a] Akihiro Tanaka, M.B.I.T.,[a] Youichi Takemoto,[a] Seiji Watanabe, Ph.D.,[c] Satoru Takeda, M.D., Ph.D.,[d] Minoru Irahara, M.D., Ph.D.,[e] Naoaki Kuji, M.D., Ph.D.,[f] Zentaro Yamagata, M.D., Ph.D.,[g] and Ryuzo Yanagimachi, Ph.D.[h]

Fertility and Sterility® Vol. 110, No. 3, August 2018 0015-0282

- mTESE in 721 non-obstructive azoospermic men with no sperm recovered
- 84 deliveries on 2 657 ROSI: 3,1% delivery rate per cycle (ITT)

What if no spermatozoa?

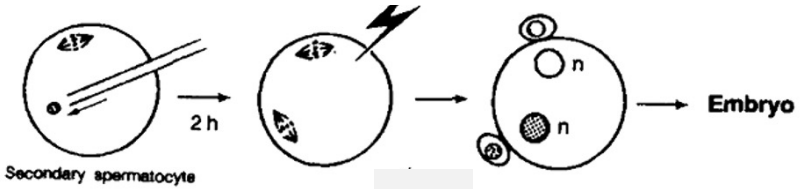
Other options?

Development of Normal Mice from Oocytes Injected with Secondary Spermatocyte Nuclei[1]

Yasuyuki Kimura and R. Yanagimachi[2]

Department of Anatomy and Reproductive Biology
University of Hawaii School of Medicine, Honolulu, Hawaii 96822

BIOLOGY OF REPRODUCTION **53,** 855–862 (1995)



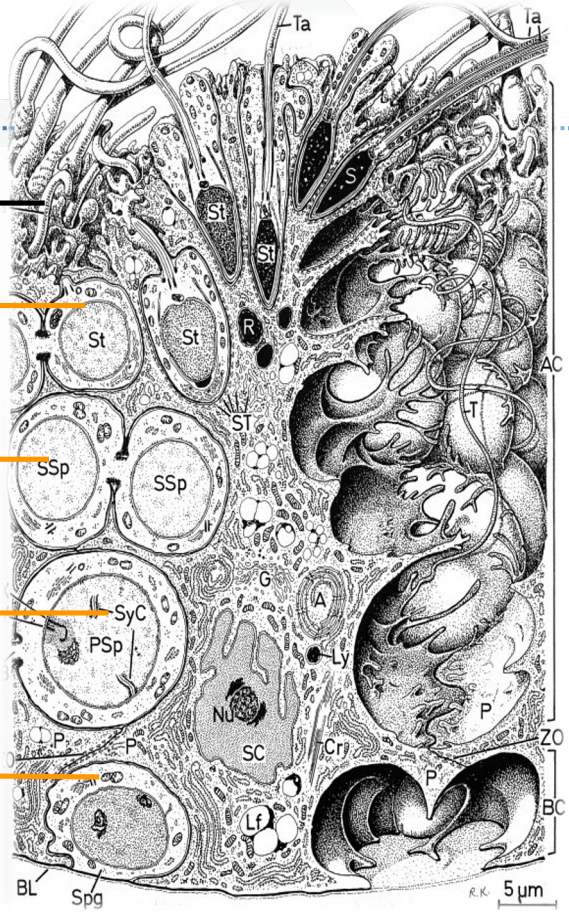
Spermatozoa
Elongated spermatids

Round spermatids (incl. ejaculated)
Tesarik et al., 1995

Secondary spermatocytes
Sofikitis et al., Lancet 1998

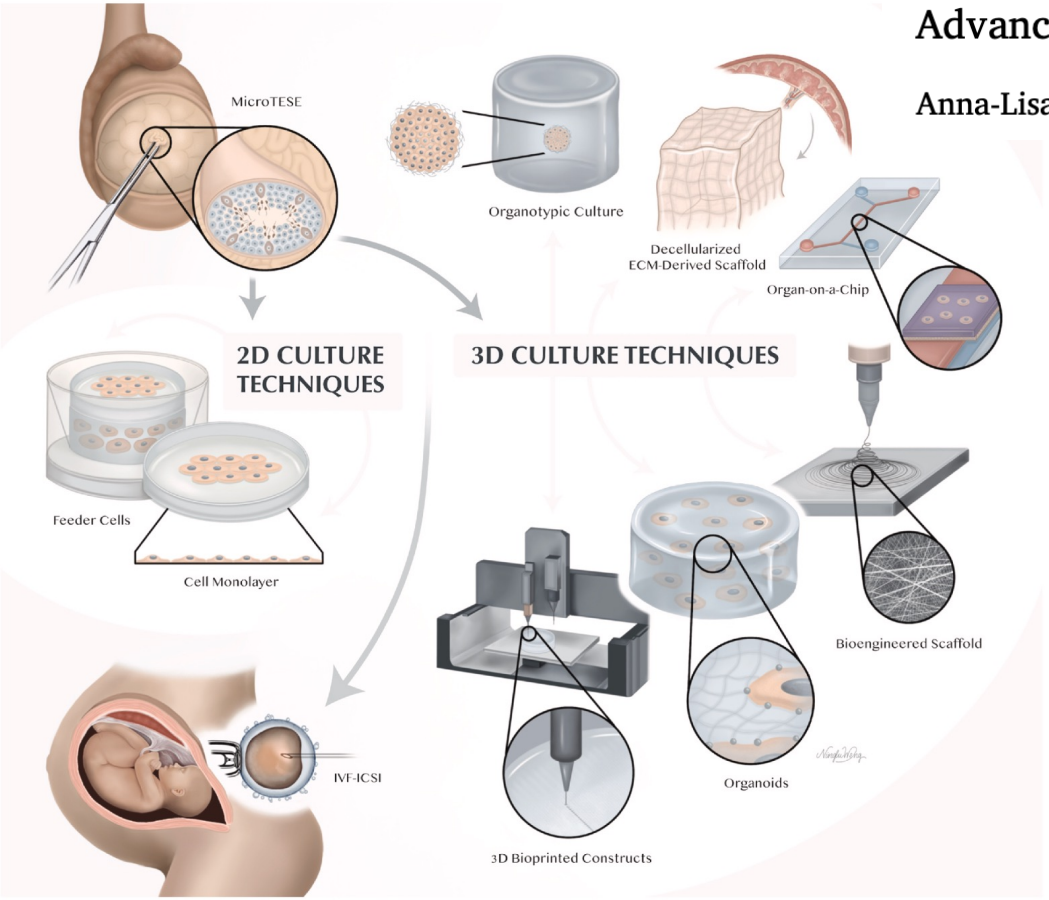
IVM primary spermatocytes
Tesarik et al. 1998

xenotransplanted spermatogonia
Sofikitis et al. 1999 (abstract)



What if no spermatozoa?

Other options?



Advances in human *In vitro spermatogenesis*: A review

Anna-Lisa V. Nguyen [a], Sania Julian [b,c], Ninglu Weng [d], Ryan Flannigan [c,e,*]

Molecular Aspects of Medicine 100 (2024) 101320

The Evolutionary Route of in vitro Human Spermatogenesis: What is the Next Destination?

Merve Gizer[1,2] · Selin Önen[2] · Petek Korkusuz[2,3]

Stem Cell Reviews and Reports (2024) 20:1406–1419

What if no spermatozoa?

Other options?

FERTILITY AND STERILITY

PREGNANCY AFTER TESTICULAR TRANSPLANT: IMPORTANCE OF TREATING THE COUPLE

SHERMAN J. SILBER, M.D.*
LOUIS J. RODRIGUEZ-RIGAU, M.D.†

the first successful human testicular transplant in 1978 on an anorchid man, using a testis from his genetically identical twin brother. The recipient experienced a successful outcome, with his serum testosterone levels normalizing and sperm production resuming, even leading to fathering five children

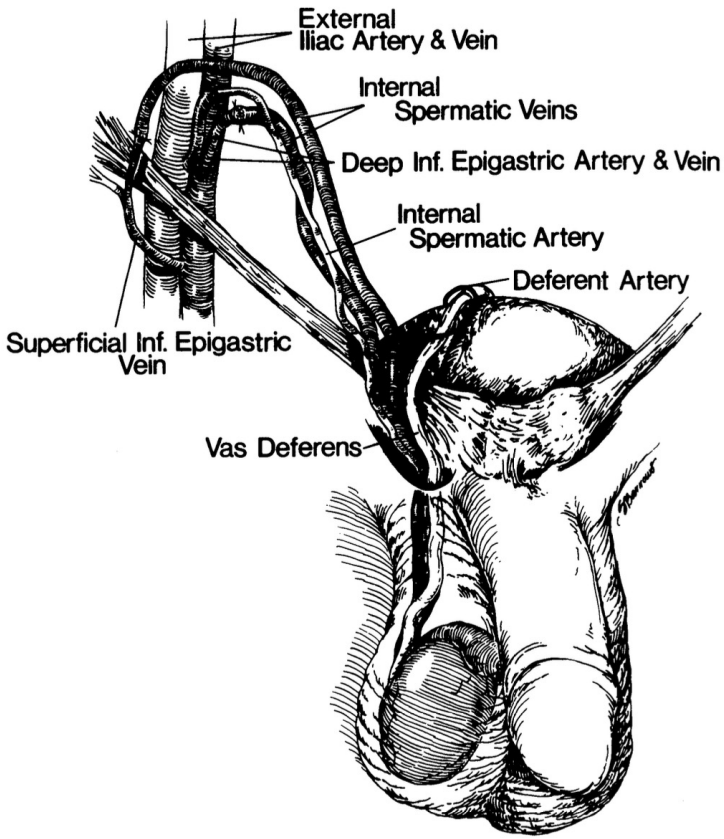


FIG. 1. Vascular anastomosis for testis transplant. (Reprinted with permission from Microsurgery, Edited by S. J. Silber. Baltimore, Williams & Wilkins Co., 1979.)