



# Biopsie testiculaire sous microscope (microTESE)

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# PLAN

- Introduction
- **Historique**
- Cadre nosologique
- **Histopathologie de l'azoospermie non obstructive**
- Technique chirurgicale
- **Complication de la microTESE**
- Facteurs prédictifs d'extraction de spermatozoïdes
- **Thérapie adjuvante avec microTESE ?**
- Resultats de la microTESE
- **Conclusion**

# INTRODUCTION

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- Azoospermie = absence de spz dans l'éjaculat
- 15% des hommes infertiles
- AZOO = **NOA** (Azoo Non Obstructive) + OA (Azoo obstructive)
- **NOA = 60% cas d'azoospermie**

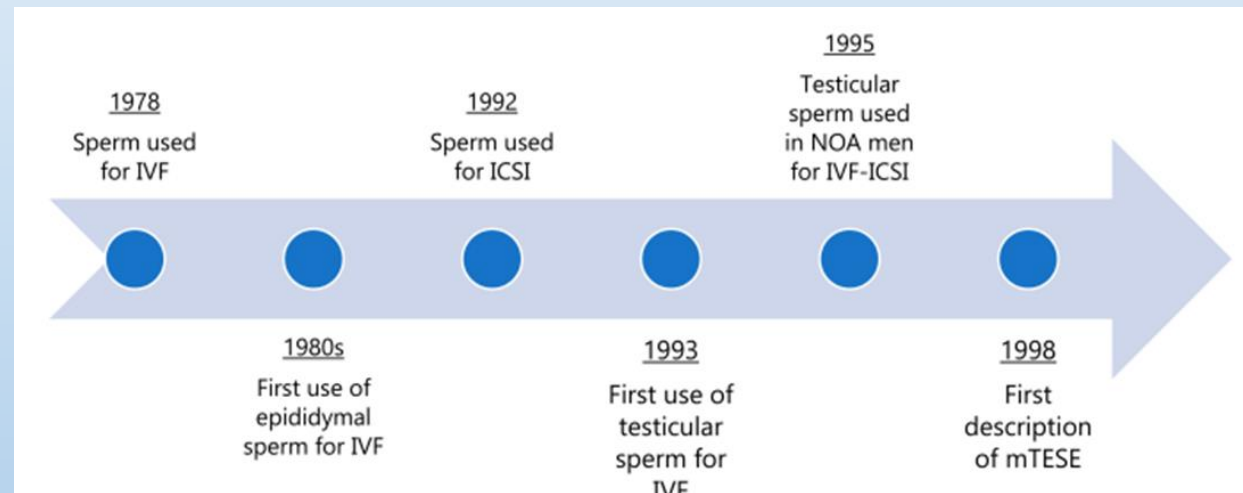
L'extraction chirurgicale de spz avec ICSI demeure l'unique option pour les patient souffrant de NOA.

# HISTORIQUE

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- **1995:** DEVROEY a été le premier à décrire la TESE conventionnelle

Devroey P et al. (1995) *Pregnancies after testicular sperm extraction and intracytoplasmic sperm injection in non-obstructive azoospermia*. Human Reprod 10(6):1457–1460.



- **1998:** SCHLEGEL a introduit la microTESE dans l'optique d'augmenter le taux d'extraction de spz et de diminuer les lésions testiculaires

Schlegel PN (1999) *Testicular sperm extraction: microdissection improves sperm yield with minimal tissue excision*. Human Reprod (Oxford, England) 14(1):131–135

# ETIOLOGIES NOA

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- **ETIOLOGIES TESTICULAIRES:**
  - Genétiques (Klinefelter, Microdéletions ChrY)
  - Congenitales (cryptorchidie)
  - Radiothérapie, Chimiothérapie
  - Traumatiques
  - Infectieuses (orchite ourlienne)
  
- **ETIOLOGIES PRE TESTICULAIRES:**
  - Hypogonadisme hypogonadotrope
  
- **AUTRES ETIOLOGIES: 15%**
  - Idiopathique

# CADRE NOSOLOGIQUE et HISTOLOGIE

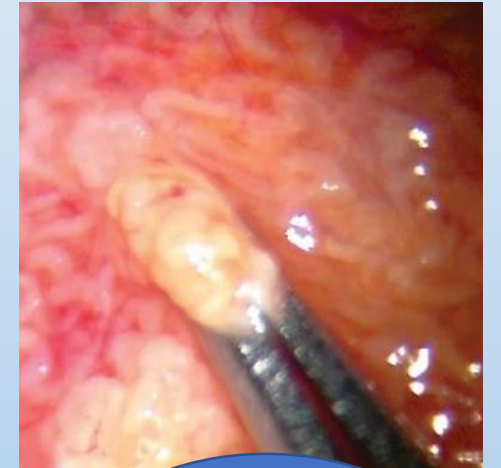
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- Hypotrophie testiculaire + FSH élevée
- Insuffisance testiculaire avec production faible (pas de spz dans l'éjaculat)
- **Production de SPZ hétérogène +++**
  - 600 à 800 tubes séminifères / testicule
  - 1 seule foyer de production est nécessaire au recueil de SPZ pour ICSI



## OBJECTIF

Identifier un foyer de spermatogenèse et recueillir des SPZ pour ICSI

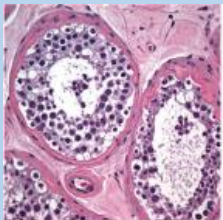
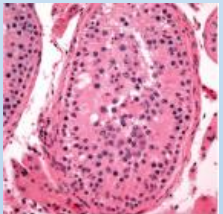
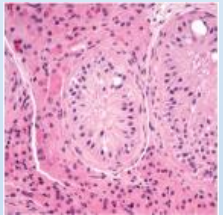
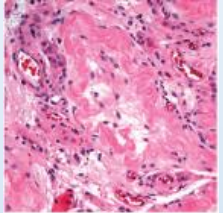


Localisation géographique imprévisible

# HISTOPATHOLOGIE: NOA

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- 4 formes histologiques sont décrites:
  - **seminiferous tubular hyalinization:** hyalinisation tubulaire ou absence de tubes seminiferes
  - **sertoli cell-only syndrome:** absence de cellules germinales
  - **maturation arrest:** incomplete par arret à un stade particuliers,
  - **Hypospermatogenesis:** reduction du nombre de cellules germinales avec tous les stades présents



➤ Chacune de ces formes histologiques peut exister seule, mais le plus souvent , plusieurs types co-existent\*


# HISTOPATHOLOGIE: NOA



AUGUST 01 2010

## A Practical Approach to Testicular Biopsy Interpretation for Male Infertility

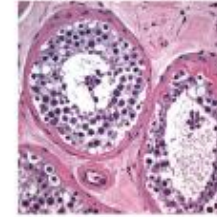


Lisa A. Cerilli, MD ; Wayne Kuang, MD; David Rogers, MD

*Arch Pathol Lab Med* (2010) 134 (8): 1197–1204.

<https://doi.org/10.5858/2009-0379-RA.1> [Article history](#) 

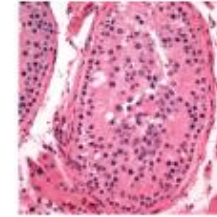
Hypospermatogenesis



All stages of spermatogenesis present but reduced to a varying degree. This includes the mixed pattern with some tubules showing Sertoli cells only or hyaline sclerosis with other tubules containing complete spermatogenesis.

In a series of 39 patients with hypospermatogenesis on testicular biopsy, MicroTESE was successful in retrieving sperm in **79%** of these men.<sup>9</sup>

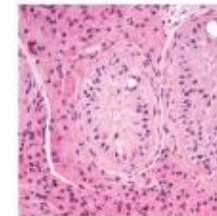
Maturation arrest



Complete arrest at a particular stage, most often at the spermatogonial or primary spermatocyte stage. If rare spermatids are present focally, the lesion is best classified as severe hypospermatogenesis, rather than arrest.

In a series of 61 patients with maturation-arrest on testicular biopsy, testicular exploration can successfully identify sperm in these men. For men with pure early MA (maturation up to the level of the primary spermatocyte), the retrieval rate was **14.3%**. For men with late MA (maturation from the secondary spermatocyte to immature spermatids), the retrieval rate was 46.1%. The retrieval rate for men with a mixed pattern (early and late MA or SCO with MA), the retrieval rates ranged from **26.7% to 47.5%**.<sup>9, 10</sup>

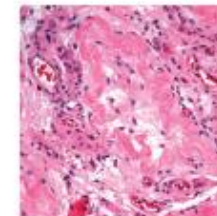
SCO



Tubules contain only Sertoli cells, and there is complete absence of germ cells.

In a series of 373 patients with SCO on testicular biopsy, MicroTESE was successful in retrieving sperm in **45%** of these men. Pregnancy rates with IVF/ICSI were approximately 50%.<sup>11</sup>

Seminiferous tubule hyalinization



Thickening of the peritubular membranes due to fibrosis and basement membrane-like material, with absence of intratubular germ cells and Sertoli cells.

The reproductive prognosis of patients with uniform seminiferous tubule hyalinization is **very poor**.

# MicroTESE: Objectifs

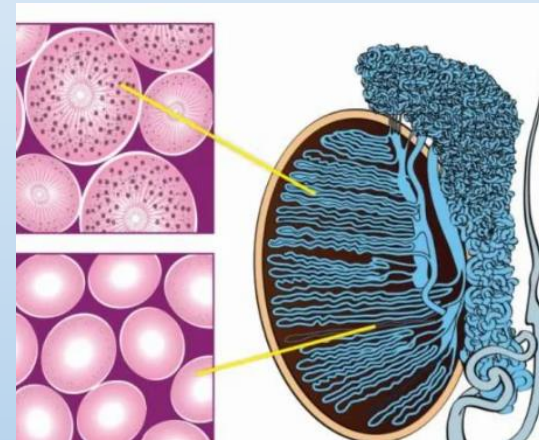
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- Identification des foyers de spermatogenese
- Préservation de la vascularisation testiculaire
- Minimisation de la quantité de parenchyme prelevé

# Identification des foyers de spermatogenese

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- Localisation de ces foyers de production **hétérogène** et **imprévisible**



# Préservation de la vascularisation testiculaire

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- L'incision équatoriale puis la microdissection permet de **reperer** et **d'épargner** la vascularisation du testicule

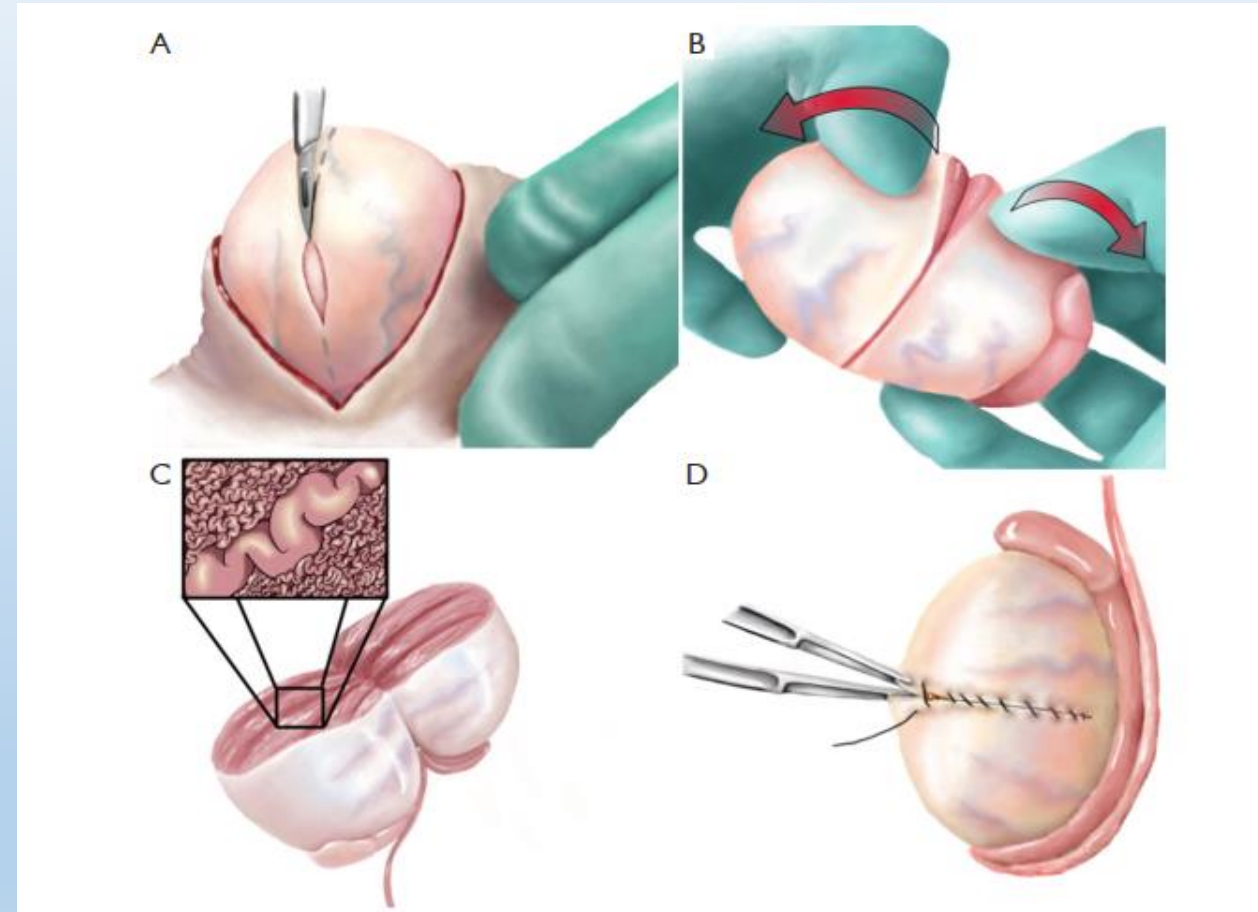


# Minimisation de la quantité de parenchyme prélevé



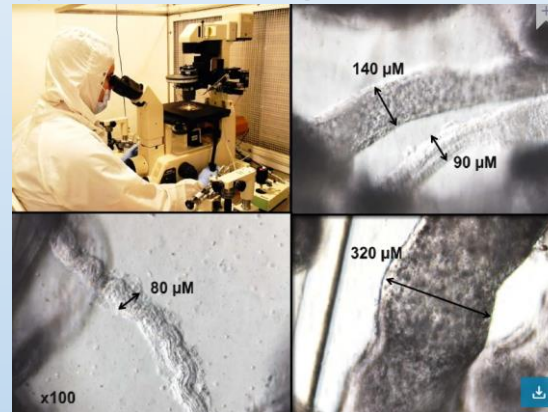
# mTESE: technique chirurgicale

- Extériorisation du testicule
- Incision équatoriale de l'albuginée
- Examen au microscope \*10-25
- Identification des sites de production
- Excision du tissu



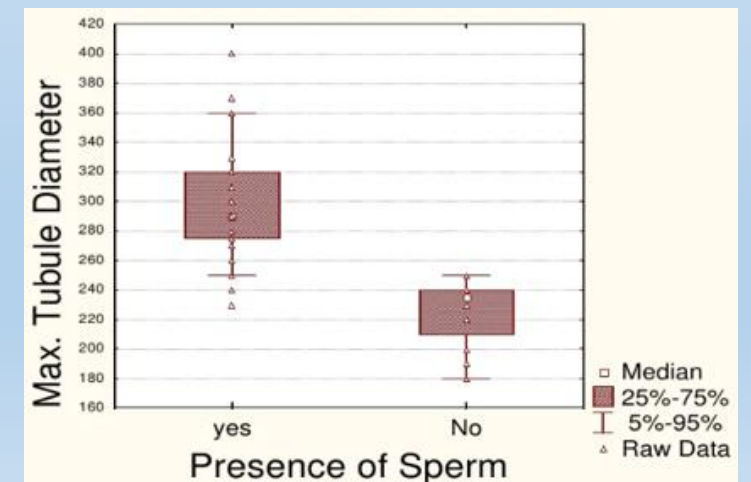
# MicroTESE: technique chirurgicale

- **Enjeu:** identifier les foyers de spermatogenese, en se basant sur :
  - diametre des tubes séminiferes
  - microvascularisation



- Melleur cut off de diametre de tube seminifere pour le recueil de spz = 110  $\mu\text{m}$  (Se=86%, Spe=74.4%)\*
- Lorsque le diametre est sup à 300  $\mu\text{m}$  = 1 seul tube séminifère est suffisant pour ICSI ou freezing\*

\*M Amer et al. 2008



# Facteurs prédictif d'extraction de SPZ : NOA

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## MARQUEURS CLINIQUES:

- Syndrome de Klinefelter
- Cryptorchidie
- Age paternel
- Volume testiculaire (cut off 12 cc)

## MARQUEURS BIOLOGIQUES:

- FSH
- Inhibine B
- **Microdeletions chromosome Y**



## AUTRES FACTEURS:

- Technique chirurgicale

## MARQUEURS HISTOLOGIQUES:

- **Histopathologie testiculaire**

# Facteurs prédictif d'extraction de SPZ : NOA

Fertility  
and Sterility 

MODERN TRENDS | VOLUME 91, ISSUE 4, P963-970, APRIL 01, 2009

## Controversies in the management of nonobstructive azoospermia

Angelo Carpi, M.D.   • Edmund Sabanegh, M.D. • Jeffrey Mechanick, M.D.

Published: March 23, 2009 • DOI: <https://doi.org/10.1016/j.fertnstert.2009.01.083>

### Accuracy values of noninvasive tests or techniques proposed for predicting sperm retrieval after testicular biopsy in nonobstructive azoospermia.

Parameter or exam	Reference	Sensitivity, %	Specificity, %	Overall predictive value, %
Testicular volume	15	7.6–50	6.7–71	
FSH	15	9–71	40–90	
Inhibin B	23	44.6	63.4	
FSH, total T, inhibin B	10	71	71.4	
Testicular volume + hormones	11			80.8
Doppler ultrasound imaging	31	47.3	89	

Carpi. Controversies in nonobstructive azoospermia. Fertil Steril 2009.

# Facteurs prédictif d'extraction de SPZ : NOA

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- Ces marqueurs donnent un reflet global de la spermatogenese
- Mais ne sont pas corrélés à la présence ou à la localisation d'éventuels foyers de spermatogenese
- **Bilan génétique** et l'**histologie testiculaire** semblent etre les marqueurs les mieux corrélés au SRR
- Pas de marqueur idéal à ce jour: plus d'études sont nécessaires

# COMPLICATIONS

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## **PERTURBATION DE LA TESTOSTERONEMIE**

- Retour à la normale en 03 à 06 mois
- Inf à la TESE

## **MODIFICATIONS ULTRASTRUCTURALES TESTICULAIRES**

- Rares et rapidement résolutive

Deruyver Y, Vanderschueren D, Van der Aa F. Outcome of microdissection TESE compared with conventional TESE in non-obstructive azoospermia: a systematic review. *Andrology* 2014;2:20-4

Ramasamy R, Yagan N, Schlegel PN. Structural and functional changes to the testis after conventional versus microdissection testicular sperm extraction. *Urology* 2005;65:1190-4.

Amer M, Ateyah A, Hany R, et al. Prospective comparative study between microsurgical and conventional testicular sperm extraction in non-obstructive azoospermia: followup by serial ultrasound examinations. *Hum Reprod* 2000;15:653-6.

Schlegel PN, Su LM. Physiological consequences of testicular sperm extraction. *Hum Reprod* 1997;12:1688-92

# RESULTATS DE LA mTESE

- Quantité de parenchyme recueillie NOA
  - La microTESE fait toujours mieux que la TESE avec un SRR supérieur\*

\*Pantke et al. 2008

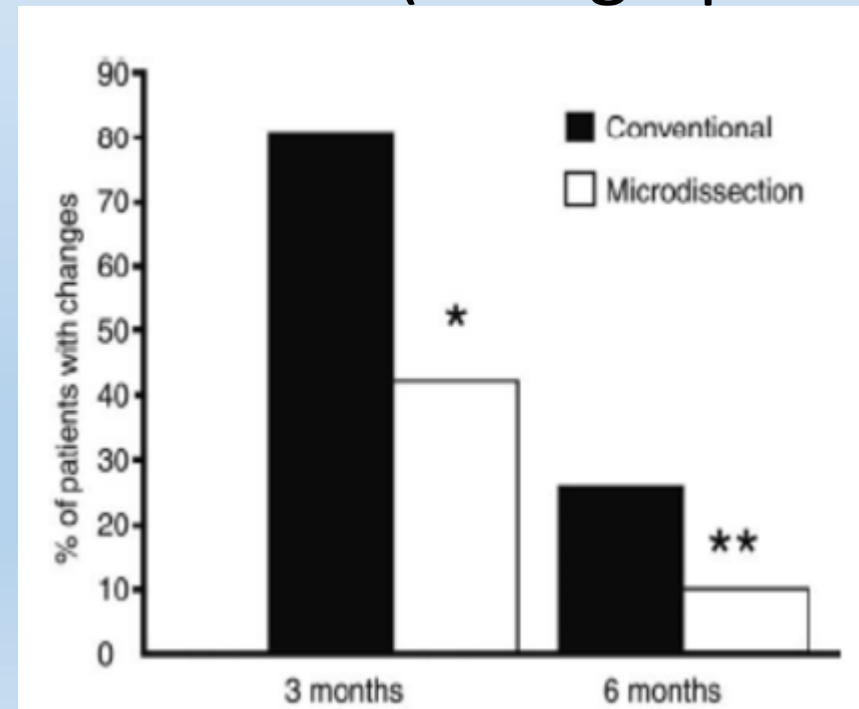
n TESE/M-TESE	SRR TESE (amount of tissue removed)	SRR M-TESE (amount of tissue removed)	Advantage M-TESE	Reference
37/56	35% (-3 x 50 mg)	43% ( $\geq 3 \times 10$ -15 mg)	+8%	[58]
100/100	30% (Unifocal $54 \pm 27$ mg)	47% ( $5 \pm 3$ mg)	+17%	[56]
22/27	45% (250-750 mg)	63% ( $\times 2$ -10 mg)	+18%	[55]
83/460	32% (-500 mg)	57% ( $\times 2$ -10 mg)	+25%	[57]
24/74	17% ( $\times 150$ mg)	45% (20-100 mg)	+28%	[59]
176/176	13% (Variable 1-4 biopsies)	50% ( $\times 2$ -10 mg)	+33% <sup>a</sup>	[60]
46/46	0% (failed TESE elsewhere)	46% ( $\times 10$ -15 mg)	+46% <sup>a</sup>	[61]

<sup>a</sup> Repeated sperm retrieval procedure: Advantage of M-TESE has to be corrected by SSR that would have been achieved with repetitive TESE.

# RESULTATS DE LA mTESE

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- Perturbations hormonales (testostérone, FSH et LH)
- Modifications du parenchyme testiculaire (échographie scrotale)



\*Ramasamy et al. 2005

# RESULTATS DE LA mTESE

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<b>Study</b>	<b>#Pts</b>	<b>%MicroTESE Success</b>	<b>%TESE Success</b>
<b>Amer et al 2000</b>	<b>100</b>	<b>45%</b>	<b>30%</b>
<b>Okada et al 2002</b>	<b>98</b>	<b>45%</b>	<b>17%</b>
<b>Okubu et al 2002</b>	<b>17</b>	<b>48%</b>	<b>24%</b>
<b>Tsujimura et al 2002</b>	<b>93</b>	<b>43%</b>	<b>35%</b>
<b>Ramon et al 2003</b>	<b>321</b>	<b>62%</b>	<b>58%</b>
		<b>49%</b>	<b>33%</b>

# RESULTATS DE LA mTESE

JOURNAL ARTICLE

## Prospective comparative study between microsurgical and conventional testicular sperm extraction in non-obstructive azoospermia: follow-up by serial ultrasound examinations FREE

Medhat Amer, Ahmed Ateyah, Ragab Hany, Wael Zohdy

*Human Reproduction*, Volume 15, Issue 3, 1 March 2000, Pages 653–656,

<https://doi.org/10.1093/humrep/15.3.653>

**Published:** 01 March 2000 **Article history** ▾

- **Methode** : 100 patients NOA avec histologie testiculaire identique
- 1 testicule = TESE et l'autre = mTESE
- Suivi echographique à 1 3 et 6 mois

**Table IV.** Intratesticular haematoma, fibrosis and segmental devascularization following microdissection and conventional TESE at 1, 3 and 6 months ( $n = 60$ )

Postoperative interval (months)	Microsurgical	Conventional	<i>P</i>
<b>Hypoechoic focal lesion (haematoma)</b>			
1	9 (15.0)	35 (58.3)	< 0.05
3	4 (6.7)	31 (51.7)	< 0.05
6	0	6 (10.0)	.....
<b>Focal echogenic lesion (fibrosis)</b>			
1	0	0	.....
3	0	2 (3.3)	.....
6	2 (3.3)	18 (30.0)	< 0.05
<b>Devascularization</b>			
1	2 (3.3)	7 (11.7)	NS
3	2 (3.3)	3 (5.0)	NS
6	0	0	.....

**Table II.** Sperm recovery rate (SRR%) and mean weight of testicular tissue (mg) taken from the two sides operated on by microsurgery and conventional surgery ( $n = 100$ )

	Microsurgery	Conventional	<i>P</i>
SRR (%)	47	30	<0.05
Weight of testicular tissue removed (mg)	4.65 ± 3.27	53.57 ± 27.45	<0.05

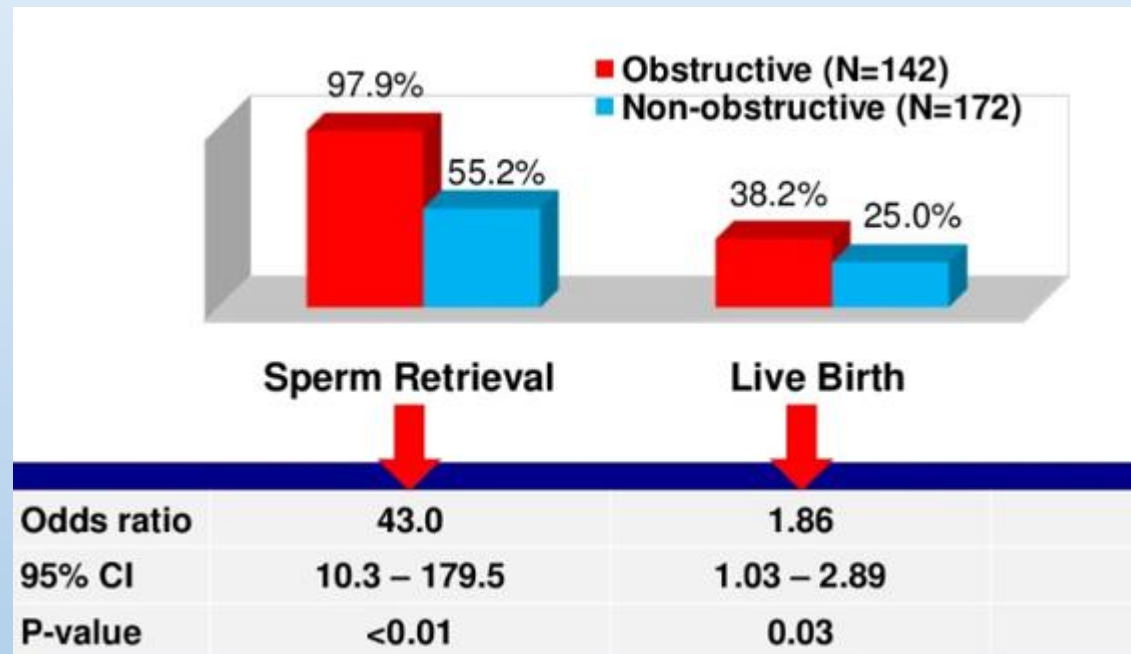
# Potentiel reproducteur en PMA des SPZ testiculaires des patient NOA

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ICSI	Ejaculated Sperm N=220	Testicular/ Epididymal Sperm (OA) N=39	Testicular Sperm NOA N=52	P-value*
%2PN Fertilization	70.0	73.6	<b>52.2*</b>	<b>0.01</b>
%TQE on Day 3	48.5	46.3	<b>35.7*</b>	<b>0.03</b>
%Clinical Pregnancy Rate	43.2	51.3	<b>25.9*</b>	<b>0.04</b>
Miscarriage (%)	12.1	20.0	14.3	NS

\*Esteves et al. 2008

# Potentiel reproducteur en PMA des SPZ testiculaires des patient NOA



# microTESE: faisable sans microscope ?

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Bouker et al. *Basic and Clinical Andrology* (2019) 29:11  
<https://doi.org/10.1186/s12610-019-0091-9>

Basic and Clinical Andrology

RESEARCH ARTICLE

Open Access

## Step-by-step loupes-mTESE in non-obstructive azoospermic men, a retrospective study



Amin Bouker\*, Lazhar Halouani, Mahmoud Kharouf, Habib Latrous, Mounir Makni, Ouafi Marrakchi, Raoudha Zouari and Salima Fourati

Résultats similaires (loupes avec grossissement \*6-10) en termes de **SRR** et de **complications**

# THERAPIE ADJUVANTE: optimiser le SRR ?

## • Varicocelectomie

- Interet pour l'optimisation du SRR
- Niveau de preuve faible (etudes de cohortes)

## • Stimulation hormonale

- Selon le profil hormonal du patient afin de « booster » les foyers de spermatogenese
- Niveau de preuve faible (pas de RCT)
- Meilleurs candidats : testostérone basse et histologie (arret de maturation tardifs ou hypospermatogenese)

**Table 9** Varicocele repair as a predictor of sperm retrieval success in men with non-obstructive azoospermia

Year	Author	Study type	No. patients	Predictors	Results
2004	Schlegel et al. [107]	Retrospective study	138 with NOA and varicocele (70 patients had undergone varicocelectomy whereas 68 served didn't undergo repair)	Semen parameters and SR rates by micro-TESE after varicocele repair	SR rate was 60% (42/70) in the treated group as compared to 60% (41/68) in the untreated group (NS) 7/31 (22%) patients with NOA had spermatozoa (motile or non-motile) reported on a postoperative semen analysis, at an average follow-up of 14.7 months
2009	Inci et al. [105]	Retrospective study	96	SR rates by micro-TESE after varicocele repair	SR rate was 53% in the treated group as compared to the 30% in the untreated group (OR: 2.63, 95% CI 1.05-6.60, $p=0.036$ )
2010	Haydardedeoglu et al. [106]	Retrospective cohort	269	SR rates by micro-TESE after varicocele repair	SR rate was 60.81% in the treated group as compared to the 38.46% in the untreated group ( $p=0.01$ )
2016	Esteves et al. [102]	Meta-analysis	468	SR rates by micro-TESE after varicocele repair	Relative to patients who had not undergone varicocele repair, the SR rate increased (OR: 2.65; 95% CI 1.69-4.14; $p < 0.001$ )

**Table 8** Adjuvant medical therapy as a predictor of sperm retrieval success in men with non-obstructive azoospermia

Year	Author	Study type	No. patients	Predictors	Results
2003	Aydos et al. [56]	Prospective cohort	108	Medical therapy	There was a significant improvement in SR rates among patients who had undergone treatment with FSH injections for three months before SR compared to untreated patients (64% vs. 33%) ( $p < 0.01$ )
2011	Moein et al. [98]	Prospective cohort	48	Medical therapy	After medical treatment with tamoxifen for three months, 6/32 (18.7%) patients were able to produce ejaculated sperm. Of those who remained azoospermic after treatment ( $n=26$ ), the SR rate was 50% (13/26), and it was higher than the non-treated cohort (31.3%; 5/16) ( $p=0.000$ )
2012	Shiraishi et al. [109]	Prospective cohort	48	Medical therapy	Successful SR by micro-TESE in 20% of patients ( $n=28$ ) after 6 months of medical treatment with daily subcutaneous hCG injections for 4-5 months, and 0% in non-treated controls ( $n=20$ ) ( $p < 0.05$ )
2012	Reifsnnyder et al. [100]	Retrospective cohort	1054	Medical therapy	Out of the 736 men whose preoperative data was available, 388 (53%) men had their baseline testosterone levels greater than 300 ng/dl before SR and were not treated. The SR rate in these men was 56% In the remaining 348 (43%) men with baseline testosterone levels less than 300 ng/dl, medical therapy (estrogen modulators, hCG) was given for 2-3 months before SR. The SR rate in this group of hypogonadal men was not significantly different (52%) than that of eugonadal men
2013	Hussein et al. [99]	Prospective cohort	612	Medical therapy	Sperm were found in the ejaculate of 10.9% patients (54/496) after medical treatment with clomiphene citrate or hCG A total of 442 patients remained azoospermic after medical treatment; the SR rate in this group was significantly higher (57%) than the control group comprised of 116 patients (33.6%; $p < 0.001$ )

Combien de temps ?  
1 à 2 cycles = 06  
mois



# CONCLUSION

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- microTESE permet:
  - Localisation précise des foyers de spermatogenese
  - Minimiser la quantité de parenchyme recueillie
  - Preserver la vascularisation testiculaire
- microTESE meilleure que TESE en terme de **SSR** et de **complications** = GOLD Standard
- Facteurs prédictifs: **Histologie** et **Microdeletions du chrY**
- Potentiel reproducteur en ICSI: NOA > OA

MERCI