Congreso asociación XXY 2026
Nuevas terapias experimentales

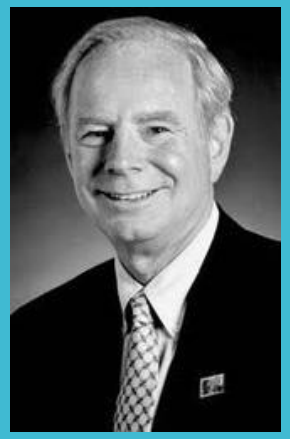
Guillermo Galdón MD PhD

- → Licenciado en Medicina por la Universitat Autónoma de Barcelona
- → Research Fellow at Wake Forest Institute for Regenerative Medicine
- → Doctor en Medicina por la Universitat de Barcelona: SSC en SK
- → Residente de Urología en el Complejo Hospitalario Universitario de Ferrol
- → Andrology Fellow en Men's Health Melbourne

Asociación Española del Síndrome de Klinefelter

MHM MEN'S HEALTH MELBOURNE
CENTRE FOR SPECIALIST MEN'S HEALTH, UROLOGY AND FERTILITY

Síndrome Klinefelter (SK)



Harry F. Klinefelter, MD

- Aneuploidia Sexual , **47 XXY**
  - → **10% Mosaicismo**
- **1/500-1000** nacidos varones
- Variedad de signos y síntomas descritos
  - → **Baja sensibilidad**
- > 90% permanecen asintomáticos hasta la edad adulta
  - → **50-75% Nunca diagnosticados**
- **Fibrosis testicular progresiva** a partir de la adolescencia
- **Diagnóstico temprano esencial** optimizar seguimiento y tratamiento para reducir comorbilidades.

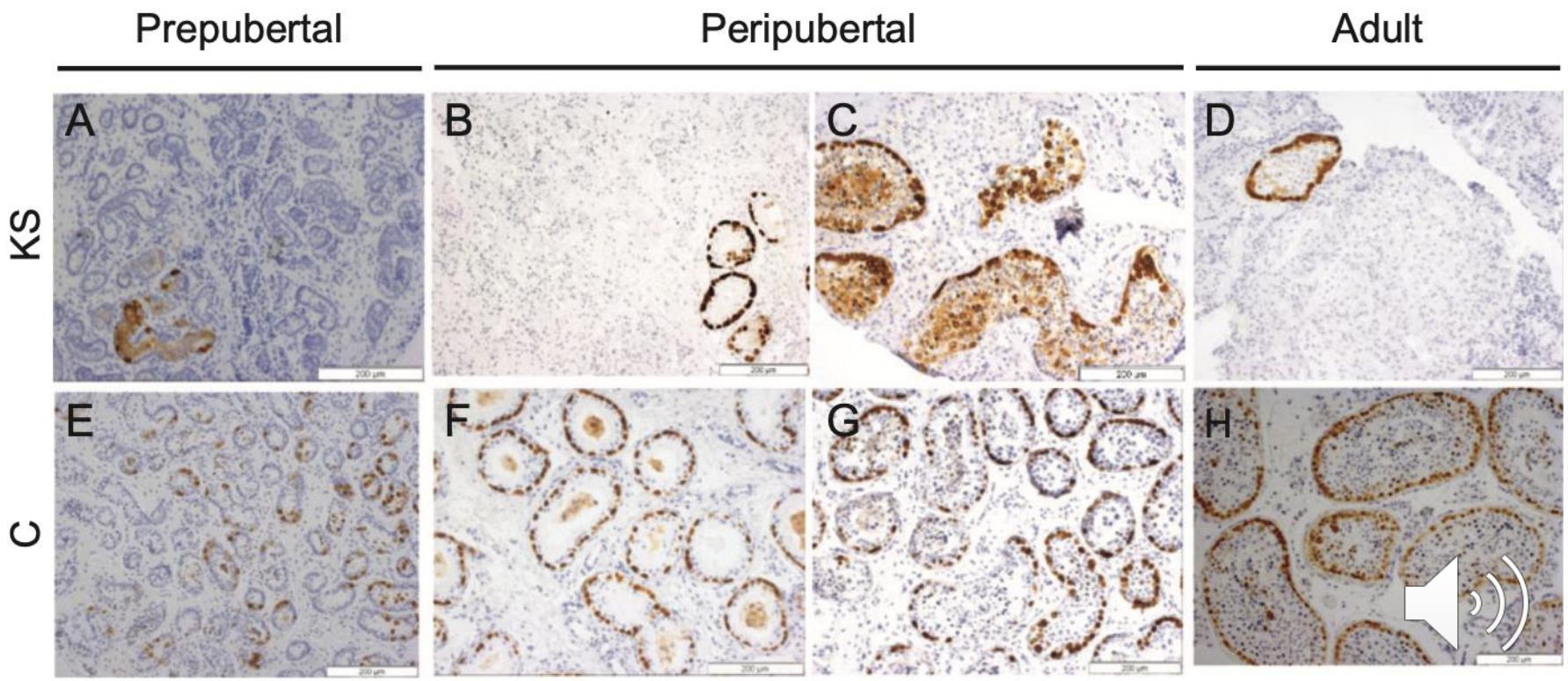
TABLE 1. Abnormalities associated with KS and their tentative frequencies[a]

Feature	Frequency (%)
Infertility (adults) (8, 57)	91–99[b]
Small testes (bi-testicular size <6 ml) (8)	>95
Increased gonadotropin levels (57)	>95
Azoospermia (adults) (57)	>95
Learning disabilities (children) (74)	>75
Decreased testosterone levels (57)	63–85
Decreased facial hair (adults) (57)	60–80
Decreased pubic hair (adults) (57)	30–60
Gynecomastia (adolescents, adults) (8, 33, 74)	38–75
Delay of speech development (children) (74)	40
Increased height (prepubertal, adults) (74, 123)	30
Abdominal adiposity (adults) (36)	~50
Metabolic syndrome (adults) (36)	46
Osteopenia (adults) (51, 124)	5–40
Type 2 diabetes (adults) (19, 36)	10–39
Cryptorchidism (8, 74)	27–37
Decreased penile size (children) (74)	10–25
Psychiatric disturbances (children) (74)	25
Congenital malformations, cleft palate, inguinal hernia (125)	~18
Osteoporosis (adults) (124)	10
Mitral valve prolapse (adults) (126, 127)	0–55
Breast cancer (adults) (16, 128)	Increased risk (~50 fold)
Mediastinal cancers (children) (22)	increased risk (~500 fold)
Fractures (17, 18)	Increased risk (2–40 fold)

Lanfranco et al, 2004; Groth et al 2013

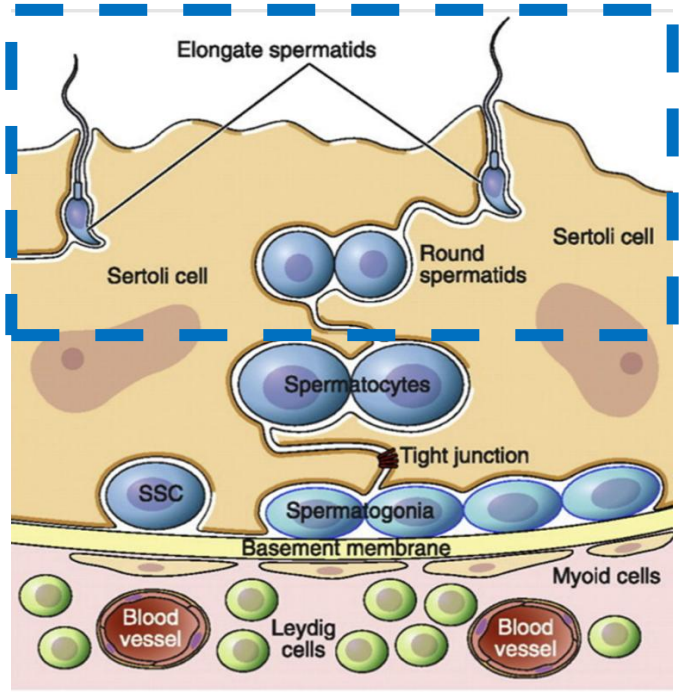
Fertilidad y SK

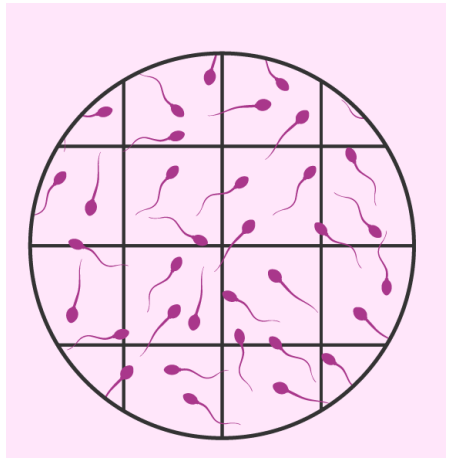
- Adultos SK **>90%** presentan **Azoospermia** < 1 million spermatozoa/mL
  - → **Causa genética** de infertilidad masculina **más frecuente**
  - → **10% de todos** los hombres con **Azoospermia NO Obstructiva**
- Fibrosis testicular progresiva **<u>acelerada durante la pubertad</u>**
  - → Posibles **focos de espermatogenesis** preservados en adulto

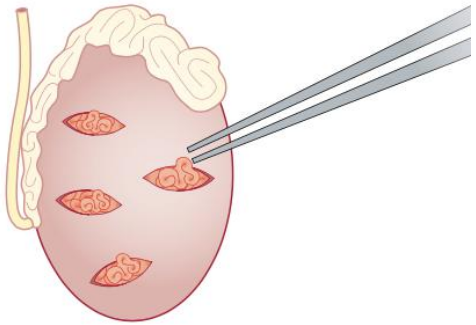


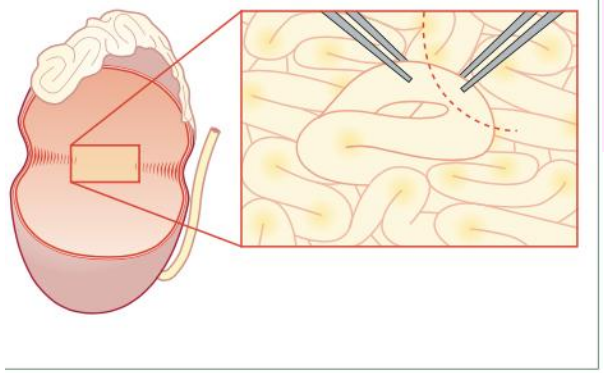
*Van Saen et al 2018

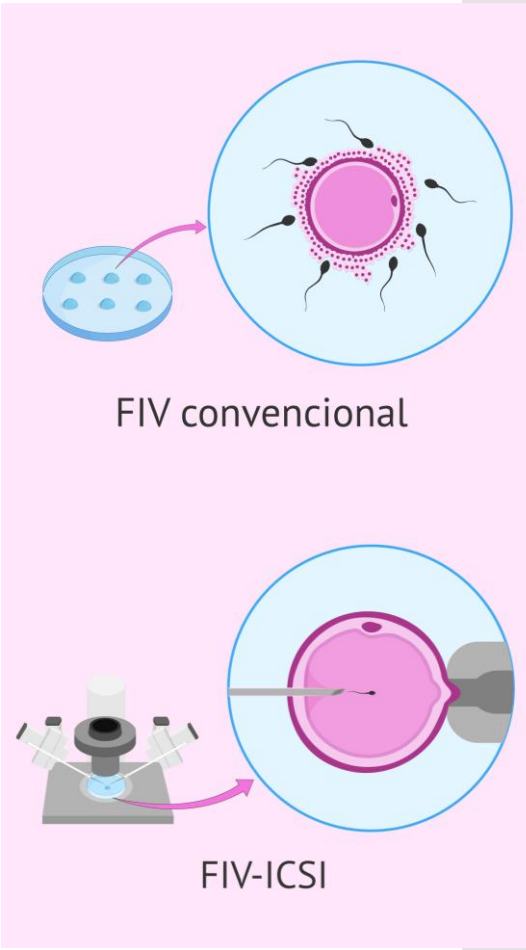
Estrategias de tratamientos de fertilidad







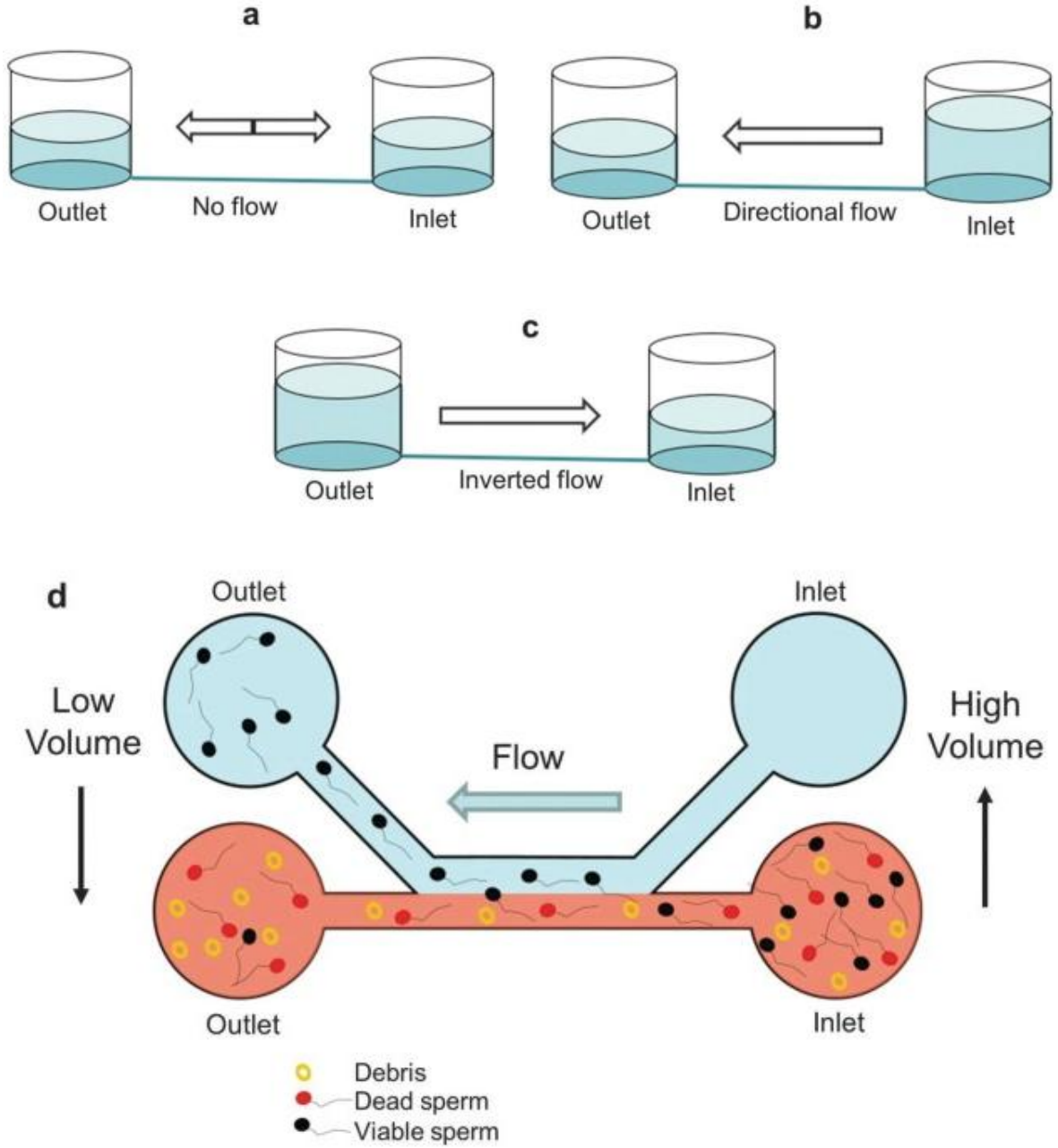




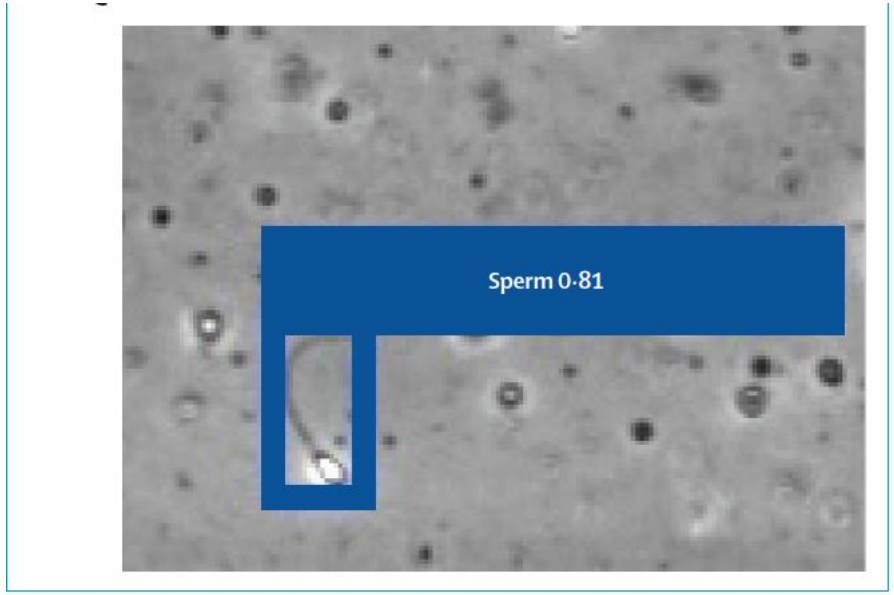
** Adaptado de Oatley et al 2012*

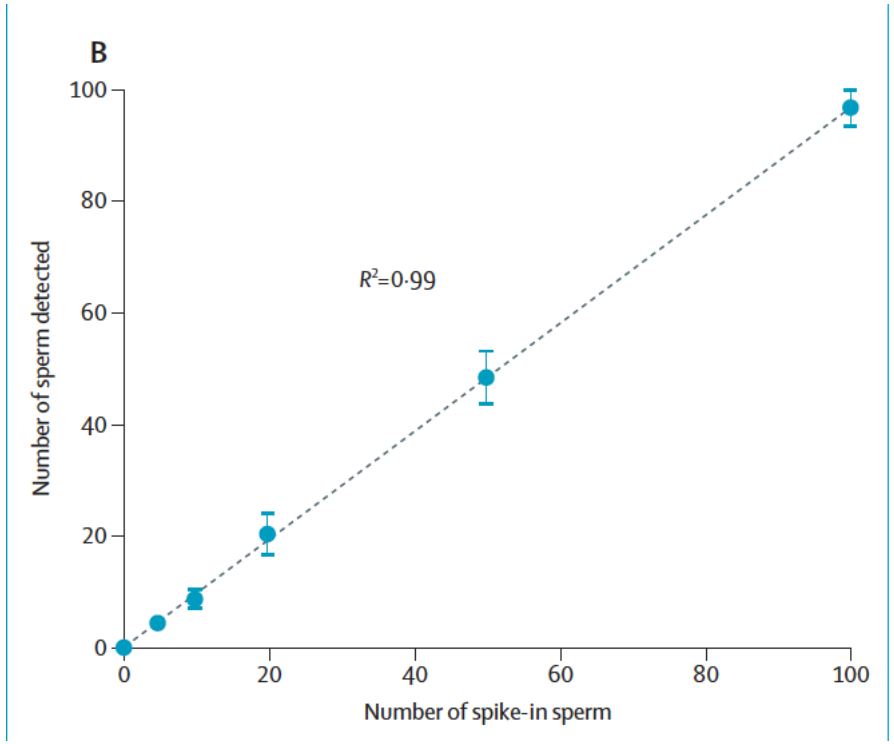
** Imágenes de https://www.reproduccionasistida.org

Nuevos Analisis seminales: **IA y microfluidica**

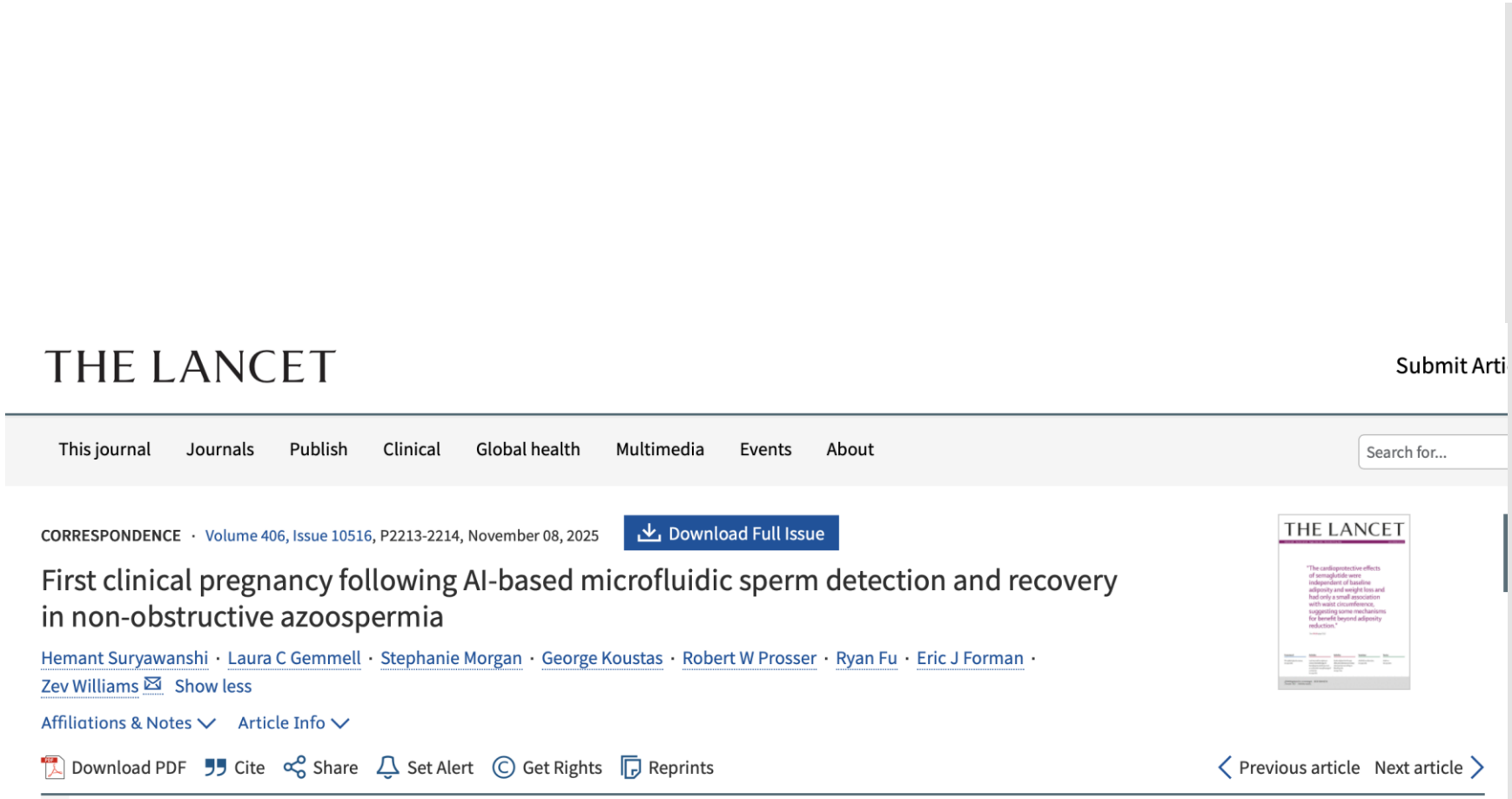


Nuevos Analisis seminales: **IA y microfluidica**

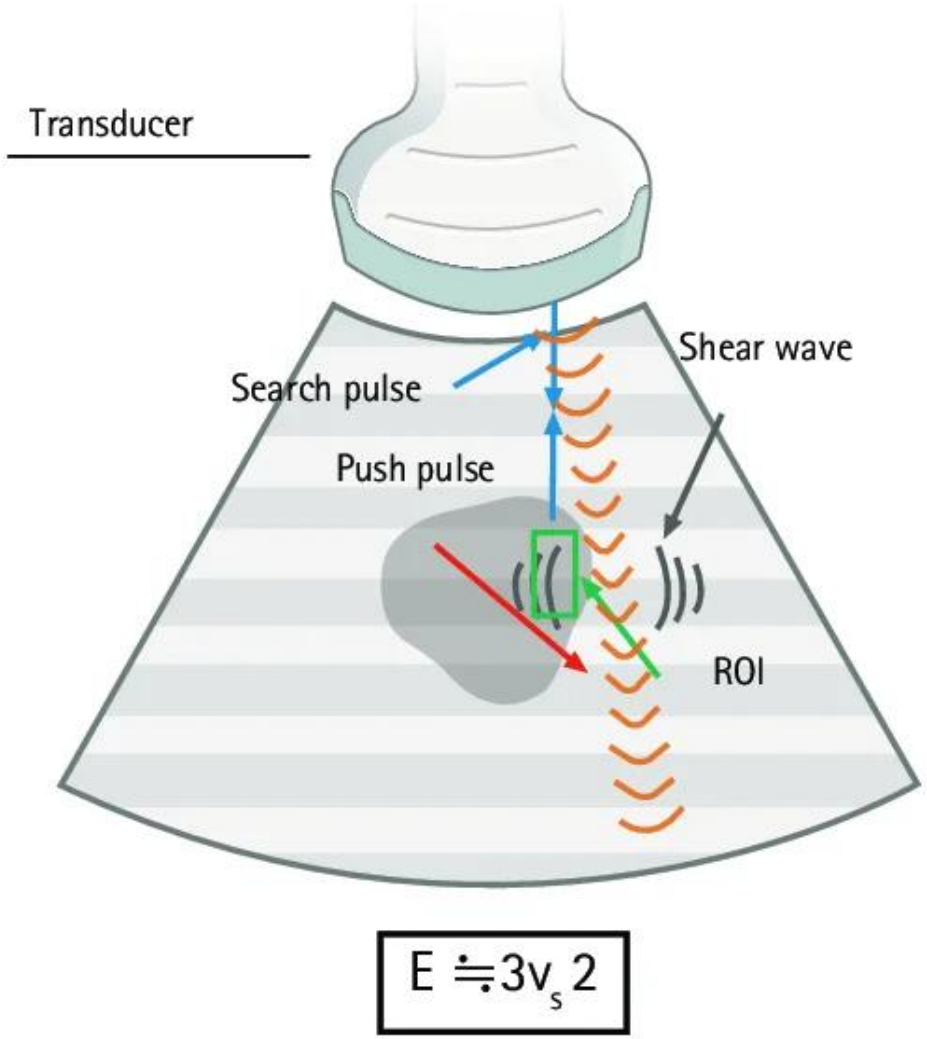




Nuevos Analisis seminales: **IA y microfluidica**



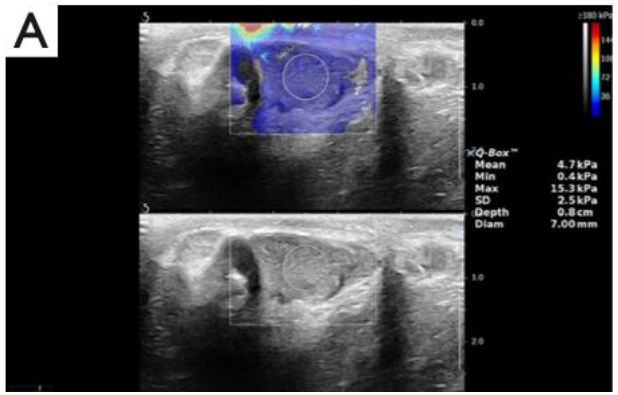
Nuevas pruebas de Imagen: **Elastografia**

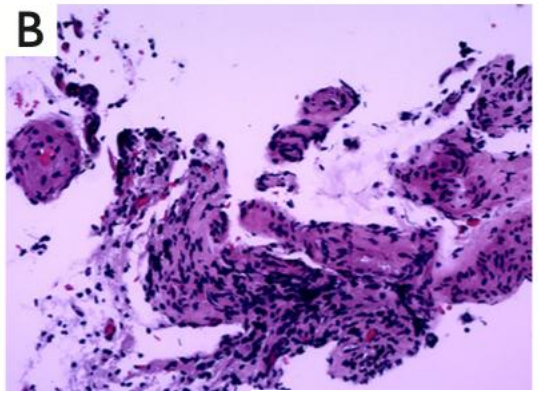


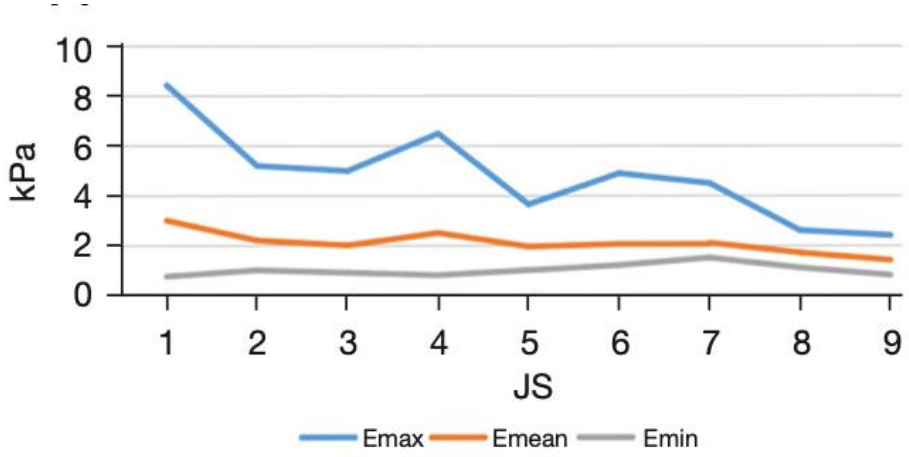
Nuevas pruebas de Imagen: **Elastografia**

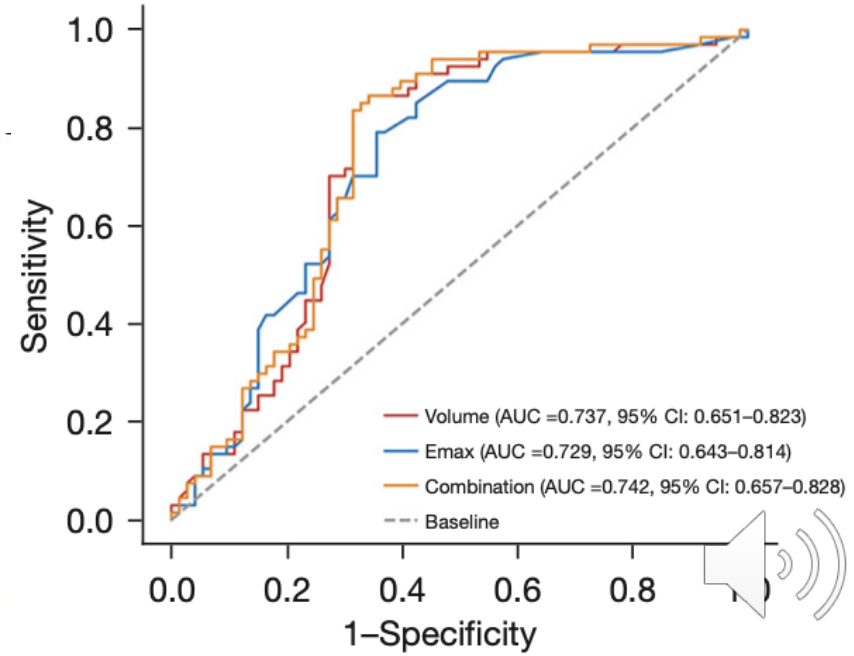
The relationship of testicular stiffness with Johnsen score and sperm retrieval outcome in men with non-obstructive azoospermia

Wei Fu[1]^, Jun Cui[2]^, Shaoshan Tang[1]^









Nuevas pruebas de Imagen: **Elastografia**

PD49-07

UTILITY OF TESTICULAR SHEAR-WAVE ELASTOGRAPHY IN THE EVALUATION OF PEDIATRIC PATIENTS WITH KLINEFELTER SYNDROME

Megan Escott, Abinav Udaiyar, Robert R. Wilson, Janmejay Hingu, Stanley Kogan, Marc Colaco, Marshal Schwartz, Steve Hodges, Anthony Atala, David Childs, Hooman Sadri-Ardekani, Winston Salem, NC*

INTRODUCTION AND OBJECTIVE: Shear-wave elastography (SWE) uses sonography to quantify tissue elasticity non-invasively. Prior research has investigated its utility in various pediatric testicular pathologies, including varicoceles, hydroceles, and pediatric microlithiasis. In patients with Klinefelter syndrome (KS), the testes undergo hyalinization and fibrosis that begins in adolescence. Still, the only prior study on testicular elastography in patients with KS was done in an adult male population with an average age of 33. Since there have been no studies on testicular elastography in pediatric patients with KS, we investigated the utility of SWE in evaluating pediatric patients with a known diagnosis of KS.

METHODS: Patients younger than 18 and diagnosed with KS underwent routine B-mode sonography and simultaneous multi-frame shear-wave elastography for their initial evaluation and follow-up. Elastography measurements (kPa and m/s) were acquired at each testicle's superior, center, and inferior poles. Average elastography measurements in the two age cohorts (below ten years old and 10–18 years old) were compared using two-tailed t-tests to a similar cohort of patients with no history of testicular pathology.

RESULTS: Forty-two imaging studies were completed in pediatric patients with KS. Elastography measurements in patients with KS under ten years old ($n=10$) were not significantly different from the testicular stiffness measurements of normal patients. However, elastography studies of patients with KS age ten and older ($n=74$) demonstrated statistically significant differences in testicular stiffness when compared to pubertal patients with no history of testicular pathology (2.99 kPa vs. 4.02 kPa, $p<0.001$ and 0.96 m/s vs. 1.12 m/s, $p<0.0001$).

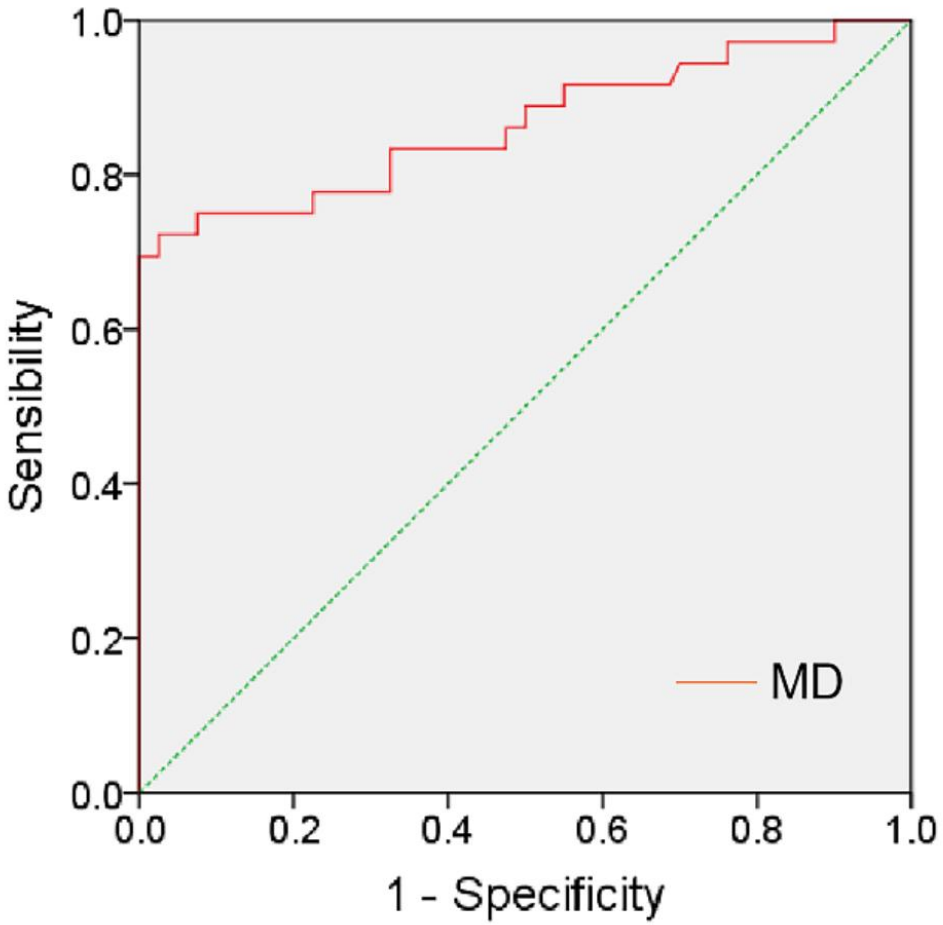
CONCLUSIONS: No work has been published on applying SWE to pediatric patients with KS. Here, we demonstrated that SWE detects a statistically significant difference in the testicular stiffness in pediatric patients with KS. This statistically significant difference between the ages of 10 and 18 likely reflects the onset of testicular fibrosis. Future work must validate SWE as a primary diagnostic tool for certain testicular disorders and develop its potential to replace biopsies and exploratory surgical procedures.

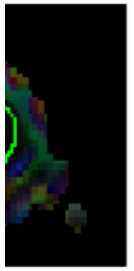
Source of Funding: Institutional (Internal) Funding

Nuevas pruebas de Imagen: **RMN DFI**

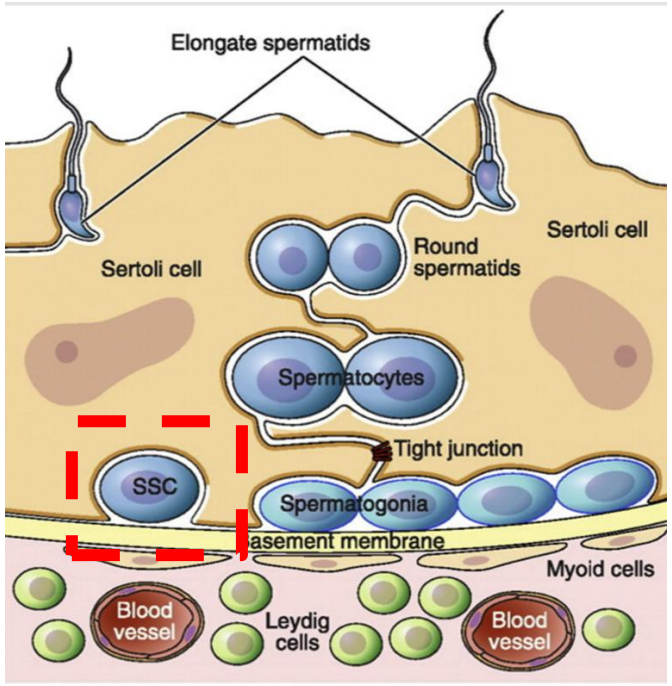
Noninvasive Prediction of Sperm Retrieval Using Diffusion Tensor Imaging in Patients with Nonobstructive Azoospermia

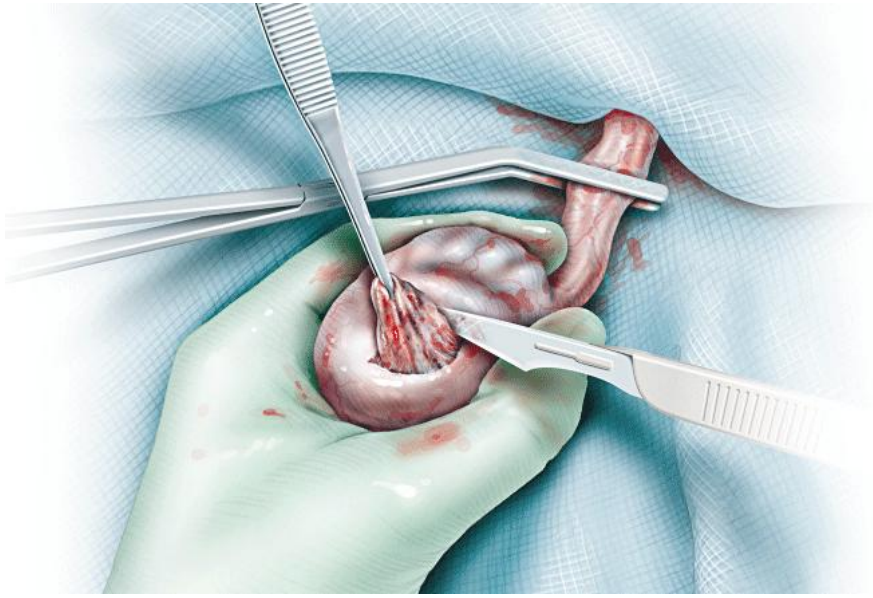
Sikang Gao [1], Jun Yang [2], Dong Chen [3], Xiangde Min [1], Chanyuan Fan [1], Peipei Zhang [1], Qiuxia Wang [1], Zhen Li [1], Wei Cai [1]





Estrategias **EXPERIMENTAL** de tratamientos de fertilidad





SSC: células madre germinales con la capacidad de **autorenovación, colonización** de los túbulos seminíferos y **establecimiento de espermatogénesis**.

→ Pueden haber SSC presentes en tejido testicular sin células diferenciadas.

→ **Nueva diana** de tratamiento de fertilidad experimental

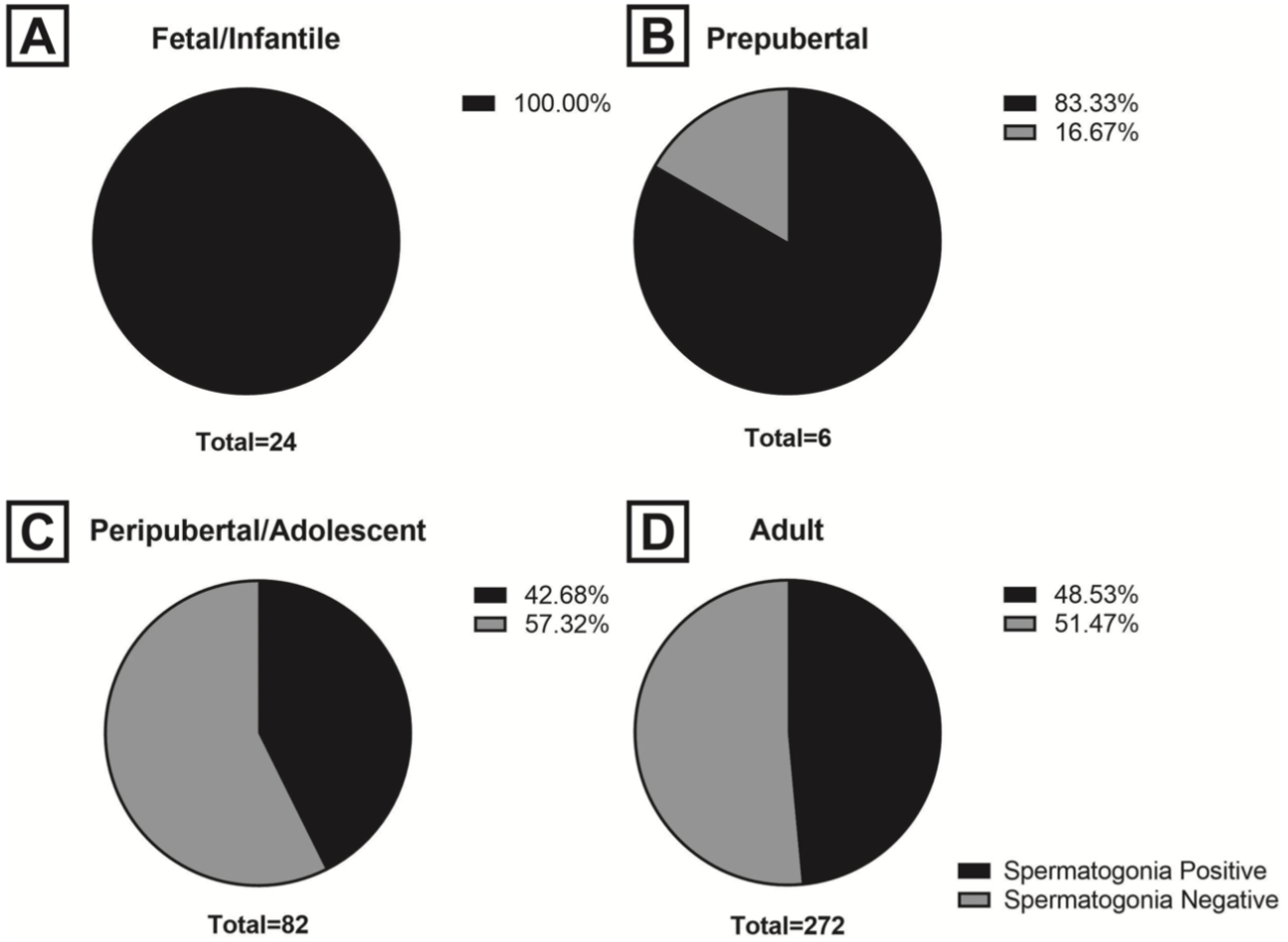
* *Adaptado de Oatley et al 2012*

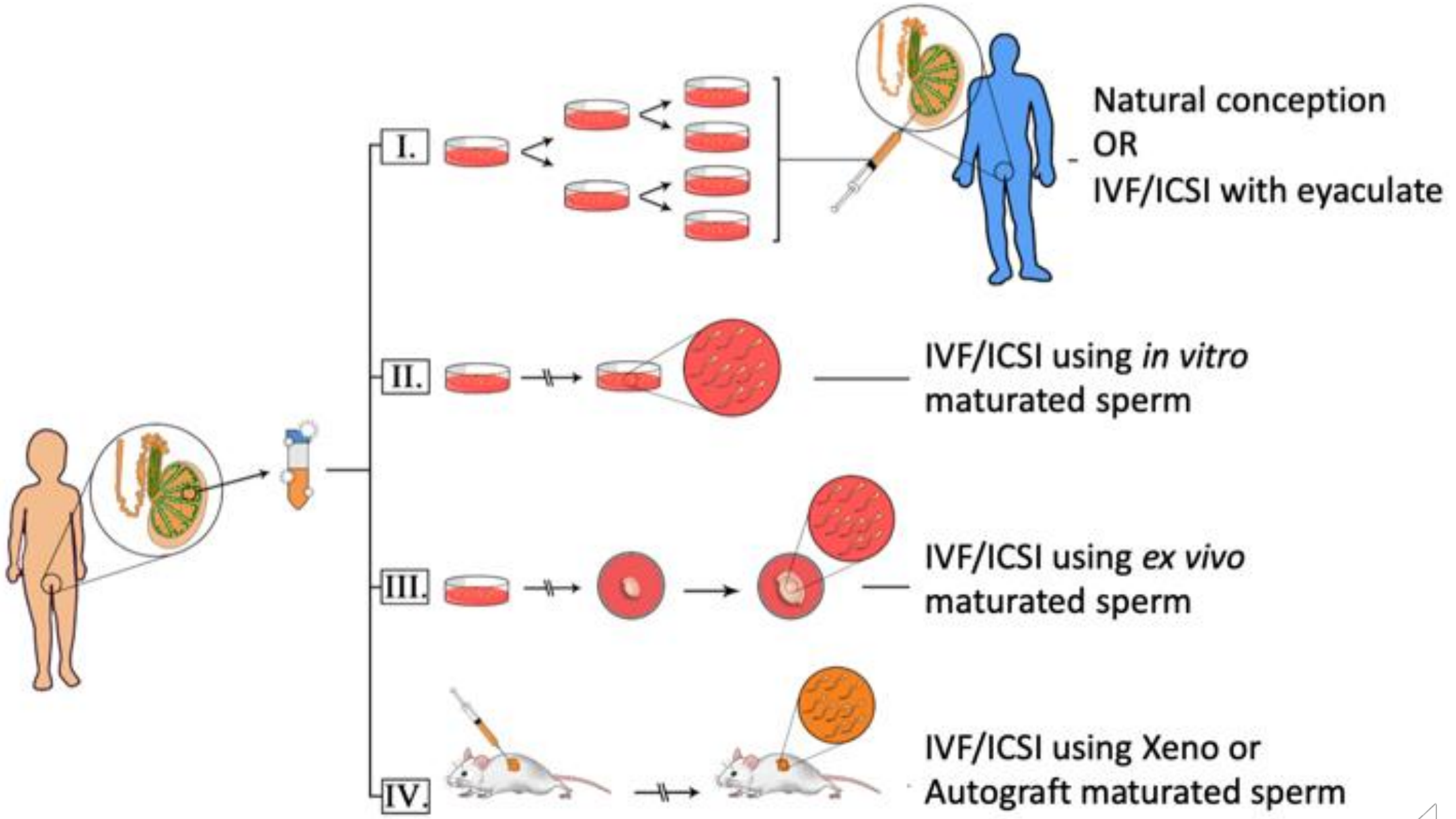
** Imágenes de https://www.reproduccionasistida.org

Presencia de espermatogonia

Age-related presence of spermatogonia in patients with Klinefelter syndrome: a systematic review and meta-analysis

Nicholas A. Deebel[1,2], Guillermo Galdon[2], Nima Pourhabibi Zarandi[2], Kimberly Stogner-Underwood[3], Stuart Howards[1], James Lovato[4], Stanley Kogan[1,2], Anthony Atala[1,2], Yanhe Lue[5], and Hooman Sadri-Ardekani[1,2,*]





**Adaptado de Zarandi et al, Stem cell and cloning, 2018*

Aislamiento y propagación *in vitro* de SSC Humanas

*Galdon et al 2022

JAMA®

Online article and related content current as of November 17, 2009.

Propagation of Human Spermatogonial Stem Cells In Vitro

Hooman Sadri-Ardekani; Sefika C. Mizrak; Saskia K. M. van Daalen; et al.

JAMA. 2009;302(19):2127-2134 (doi:10.1001/jama.2009.1689)

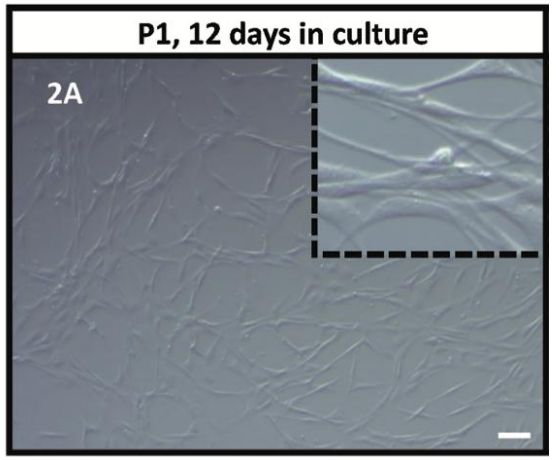
http://jama.ama-assn.org/cgi/content/full/302/19/2127

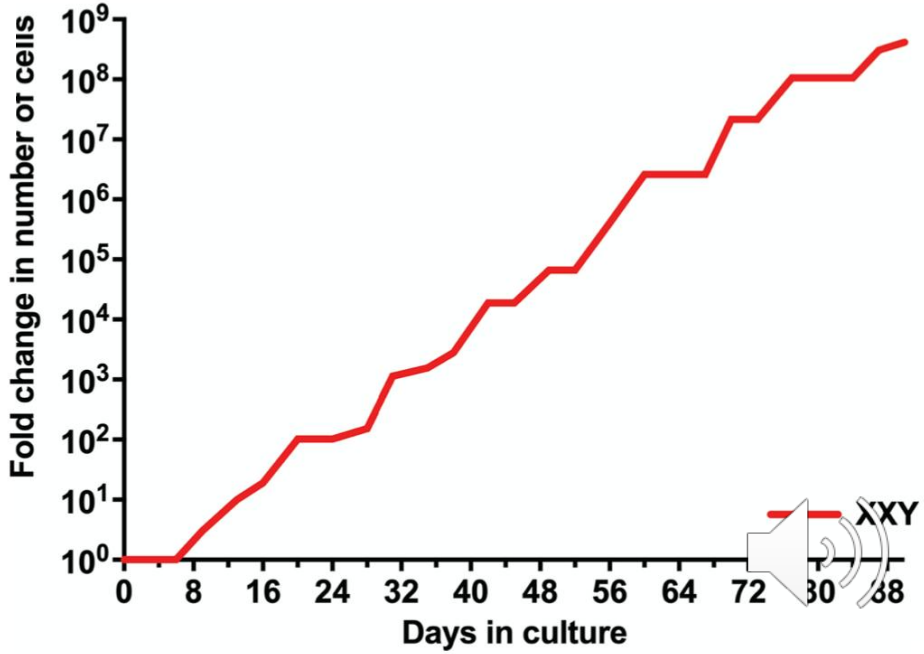
RESEARCH LETTER

Methods 99 (2016) 120–127

In Vitro Propagation of Human Prepubertal Spermatogonial Stem Cells

In vitro propagation of XXY human Klinefelter spermatogonial stem cells: A step towards new fertility opportunities



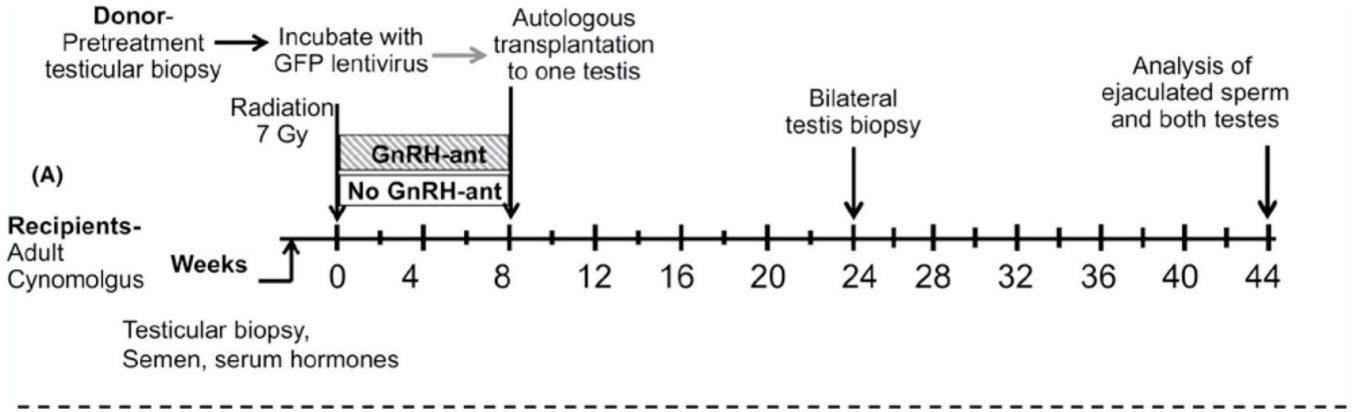


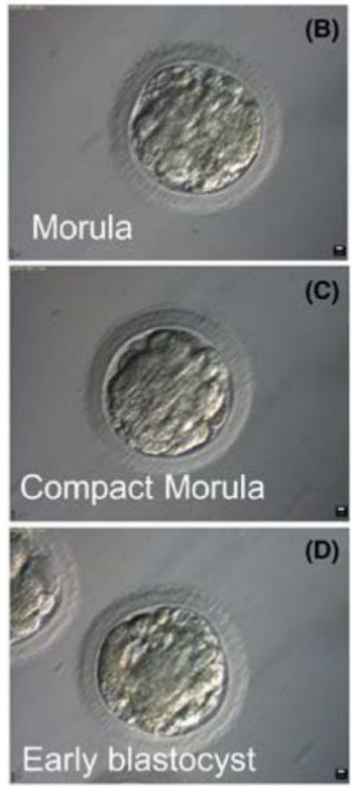
Trasplante de SSC primates

*Shetty et al 2020 and 2021

Restoration of functional sperm production in irradiated pubertal rhesus monkeys by spermatogonial stem cell transplantation

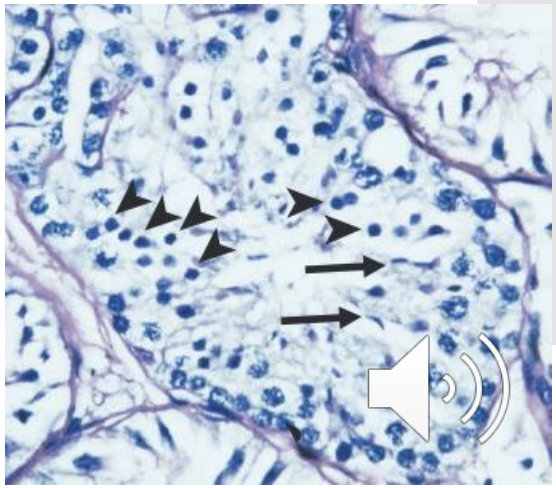
Gunapala Shetty[1], Jennifer M. Mitchell[2], Jennifer M. Meyer[2], Zhuang Wu[1], Truong N.A. Lam[1], Thien T. Phan[1], Jie Zhang[1], Lorraine Hill[2], Ramesh C. Tailor[3], Karen A. Peters[6], Maria C. Penedo[4], Carol Hanna[5], Kyle E. Orwig[6], Marvin L. Meistrich[1]





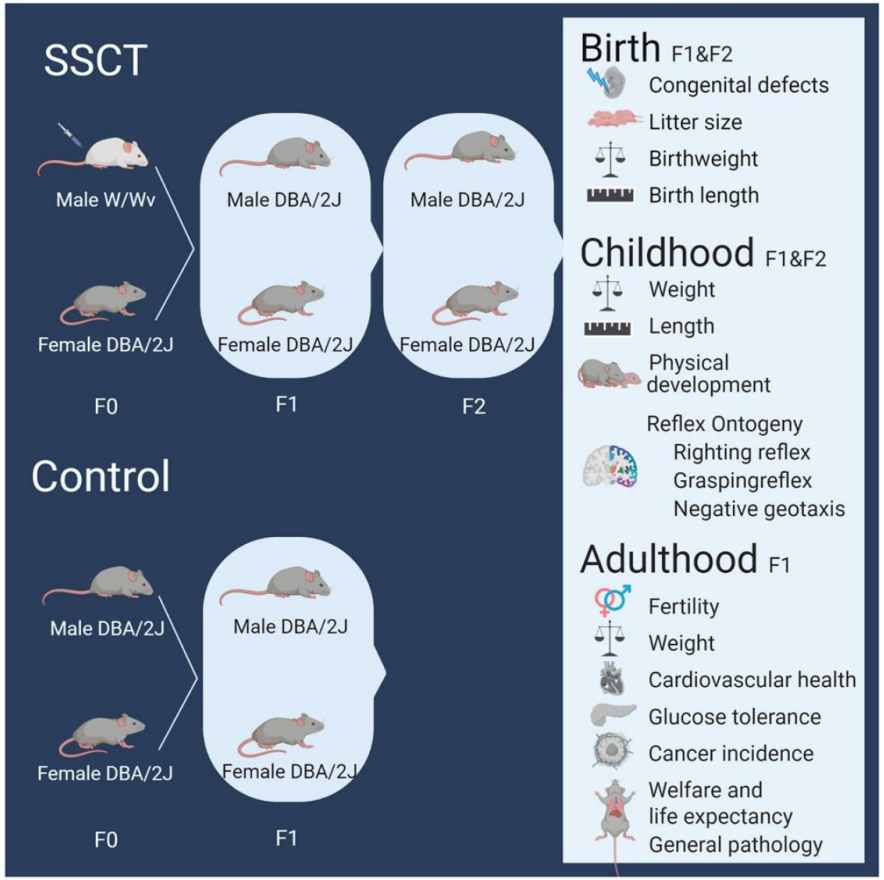
Postpubertal spermatogonial stem cell transplantation restores functional sperm production in rhesus monkeys irradiated before and after puberty

Gunapala Shetty [1], Jennifer M Mitchell [2], Truong N A Lam [1], Thien T Phan [1], Jie Zhang [1], Ramesh C Tailor [3], Karen A Peters [4], Maria Cecilia Penedo [5], Carol B Hanna [6], Amander T Clark [7], Kyle E Orwig [4], Marvin L Meistrich [1]



Dos generaciones sanas tras Trasplante de SSC murinas

Impact of restoring male fertility with transplantation of in vitro propagated spermatogonial stem cells on the health of their offspring throughout life



genesis. In this blinded preclinical study, the long-term health of SSCT-derived offspring was assessed for the first time, using a systematic blueprint testing throughout life. No major differences in health outcomes between mice born after SSCT in two consecutive generations (first generation [F1] and second generation [F2]) and control were found, thereby providing crucial evidence that SSCT is a safe procedure.

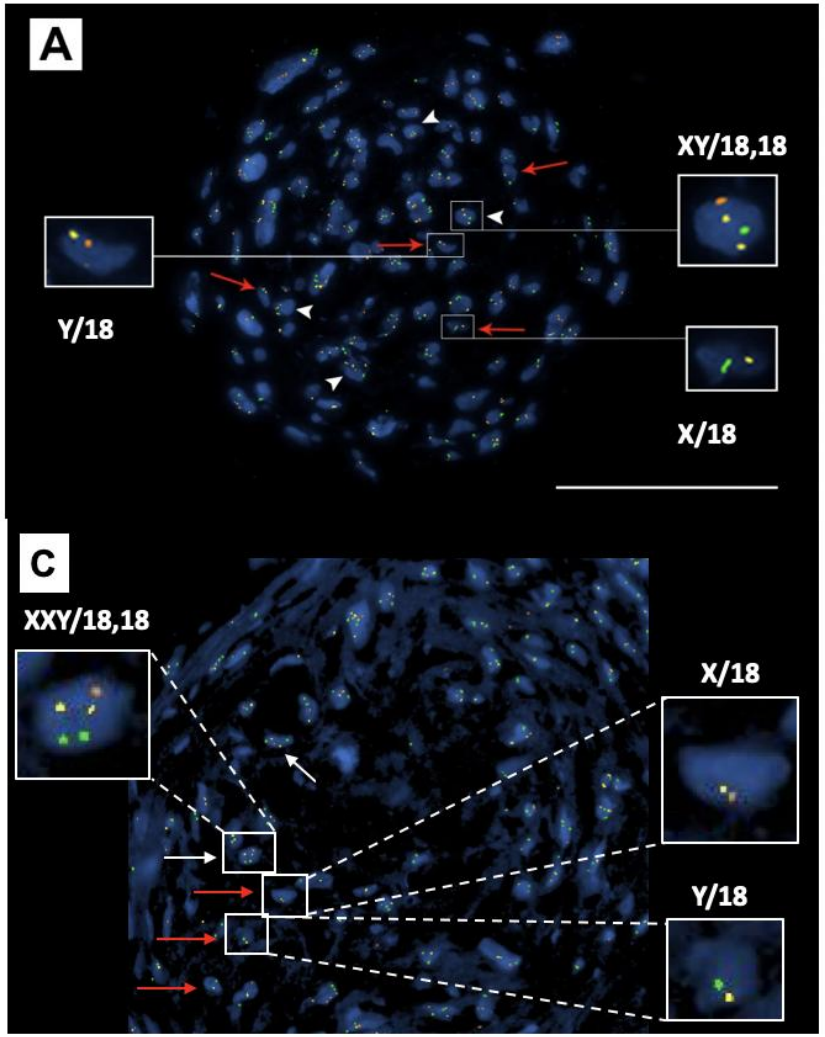
*Serrano et al 2014

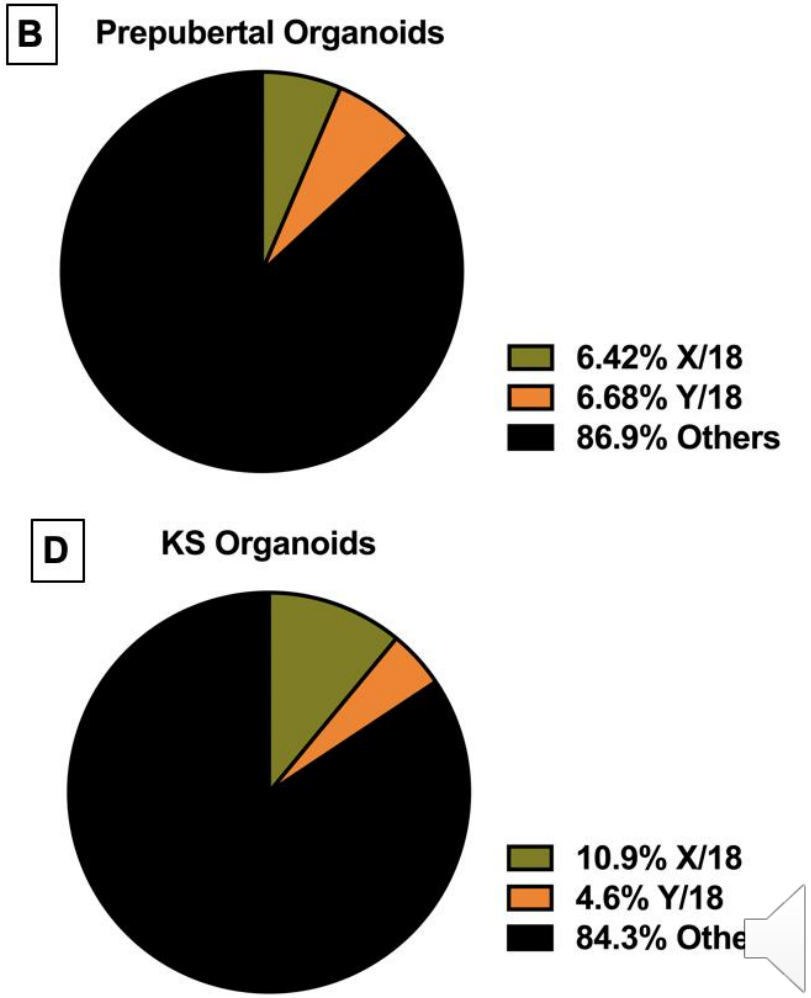
Spermato-genesis *in vitro*

*Galdon et al 2024

In vitro Generation of Haploid Germ Cells from Human XY and XXY Immature Testes

Guillermo Galdon[1-2*], Nima Pourhabibi Zarandi[1], Nicholas A. Deebel[1,3], Sue Zhang[1], Olivia Cornett[1], Mark J. Pettenati[4], Thomas D. Shupe[1], Stanley J. Kogan[1], Colin Bishop[1], Anthony Atala [1,3] and Hooman Sadri-Ardekani [1,3**]



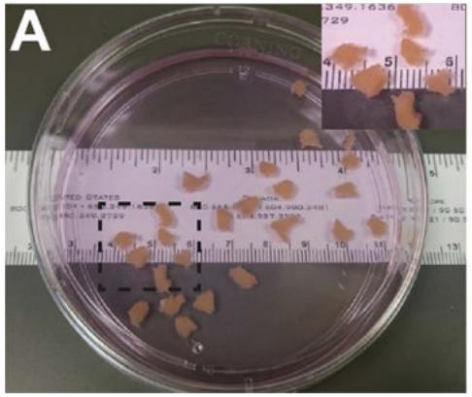


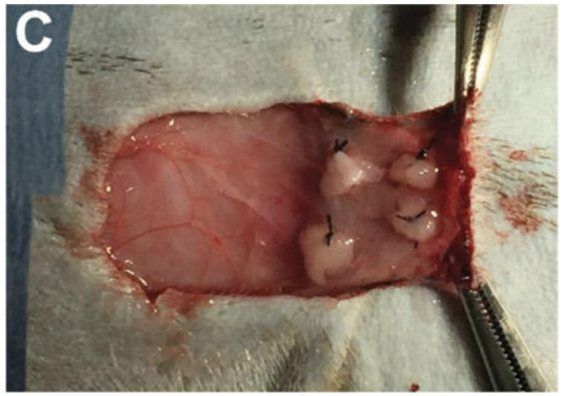
Injerto Testicular Autólogo Primates

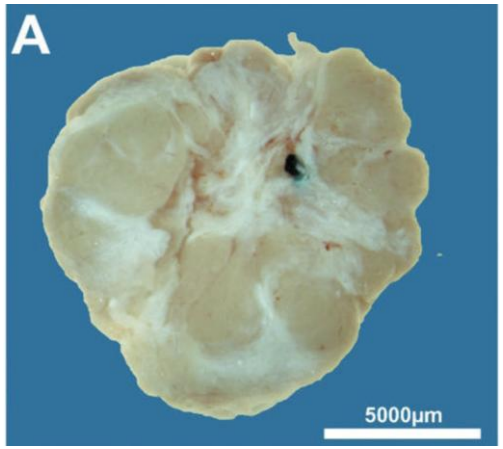
*Fayomi et al 2021

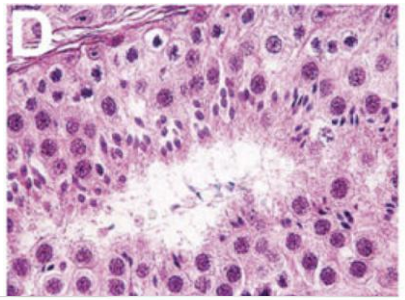
Autologous grafting of cryopreserved prepubertal rhesus testis produces sperm and offspring

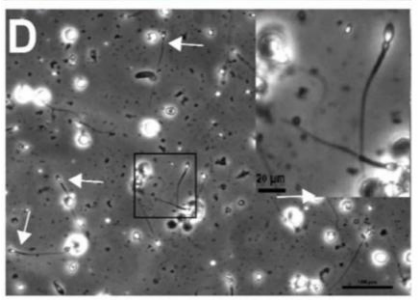
Adetunji P Fayomi [1 2 3], Karen Peters [3], Meena Sukhwani [3], Hanna Valli-Pulaski [2 3], Gunapala Shetty [4], Marvin L Meistrich [4], Lisa Houser [5], Nicola Robertson [5], Victoria Roberts [5], Cathy Ramsey [5], Carol Hanna [5], Jon D Hennebold [5], Ina Dobrinski [6], Kyle E Orwig [7 2 3]





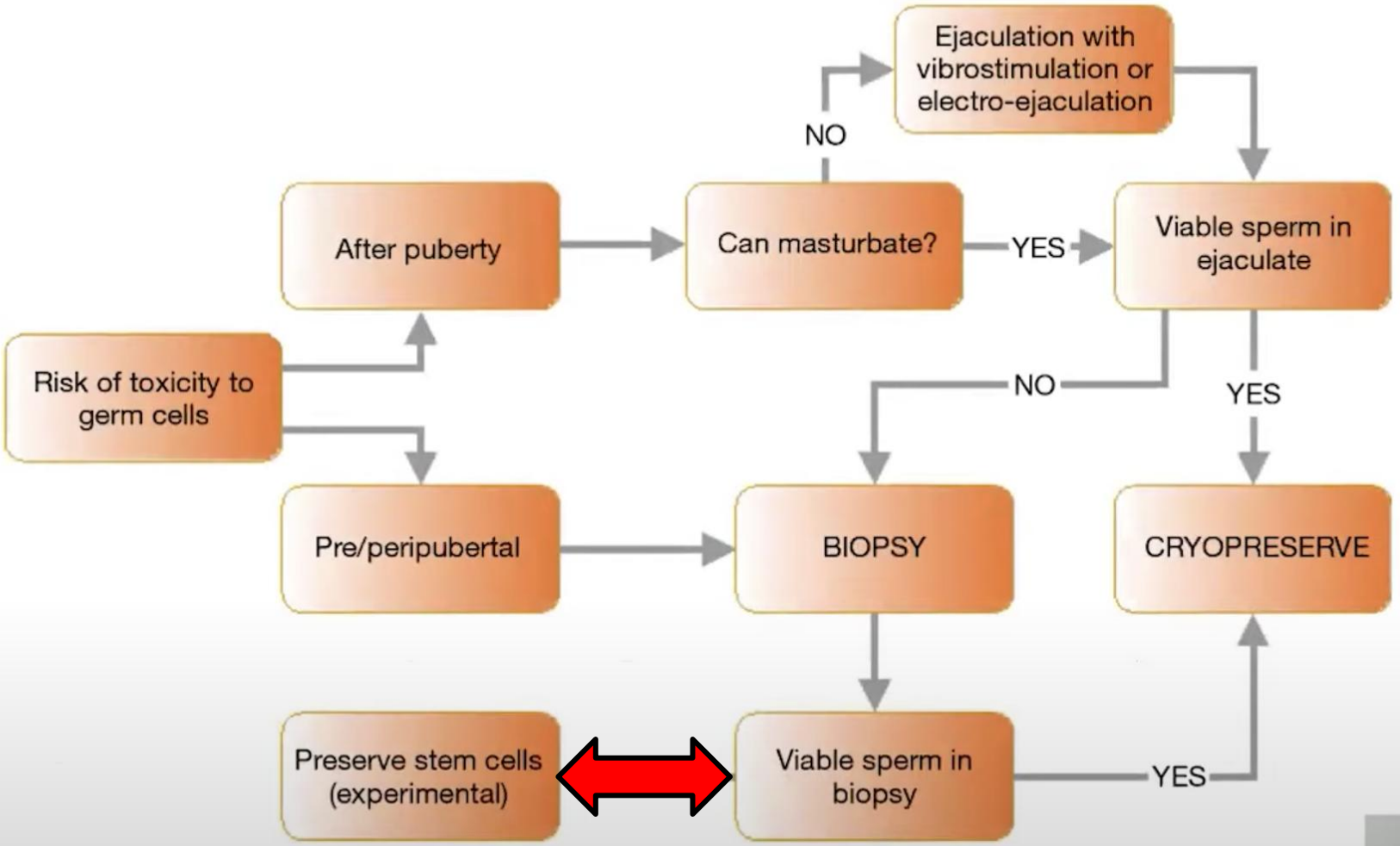






Webinar EAU Latest Update Male Infertility Aug 2023

**Dr Kopa presentation*



*Valli-Pulaski et al 2019, modified

Futuro Experimental

PROGRAMA NACIONAL EXPERIMENTAL DE PRESERVACION DE FERTILIDAD EN NIÑOS PREPUBERES CON CANCER O SINDROMES GENETICOS EN OSAKIDETZA

Centro Vasco de Transfusión y Tejidos Humanos
Dra. Cristina Eguizabal, Responsable Unidad Investigación.
Myriam Martin, investigadora
Dra. Silvia Santos, Responsable Banco de Tejidos
Dra. Clara Rodriguez
Dr. Miguel Angel Vesga
Dra. Lara Herrera del Val

Contacto: **cristina.eguizabalargaiz@osakidetza.eus**

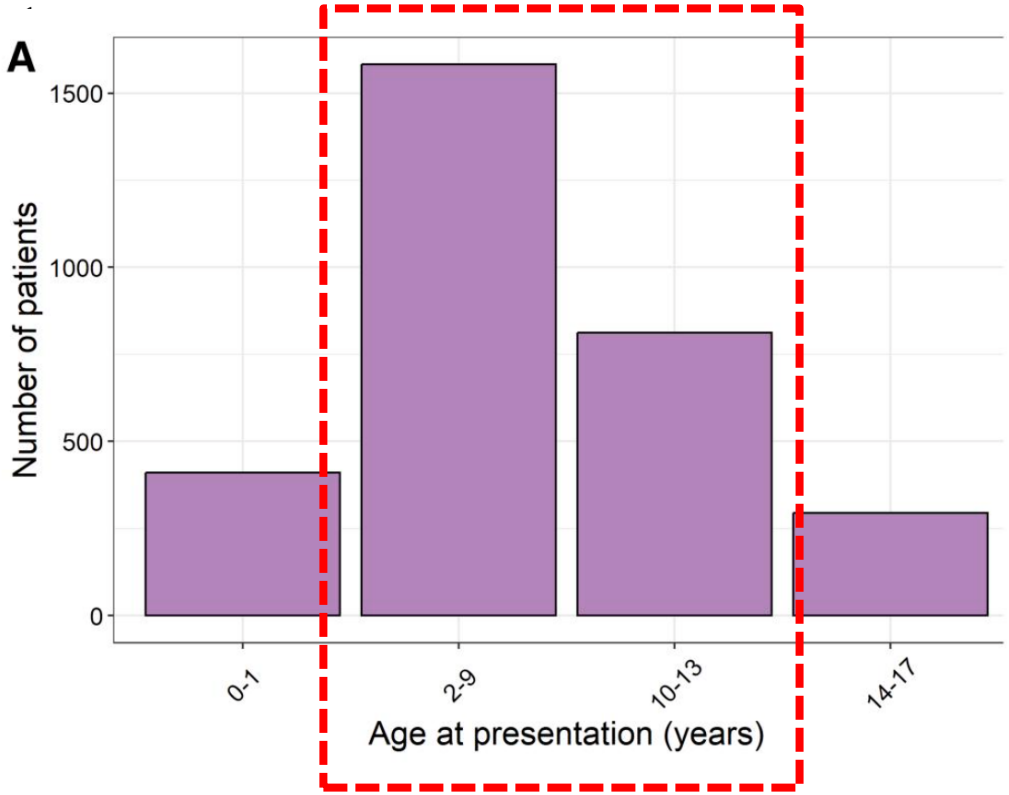
Hospital Universitario Cruces
Unidad de Reproducción Asistida
Dr. Roberto Matorras y Dra. Begoña Prieto
Servicio de Pediatria
Dr. Ricardo Lopez Almaráz
Dra. Estibaliz Solorzano

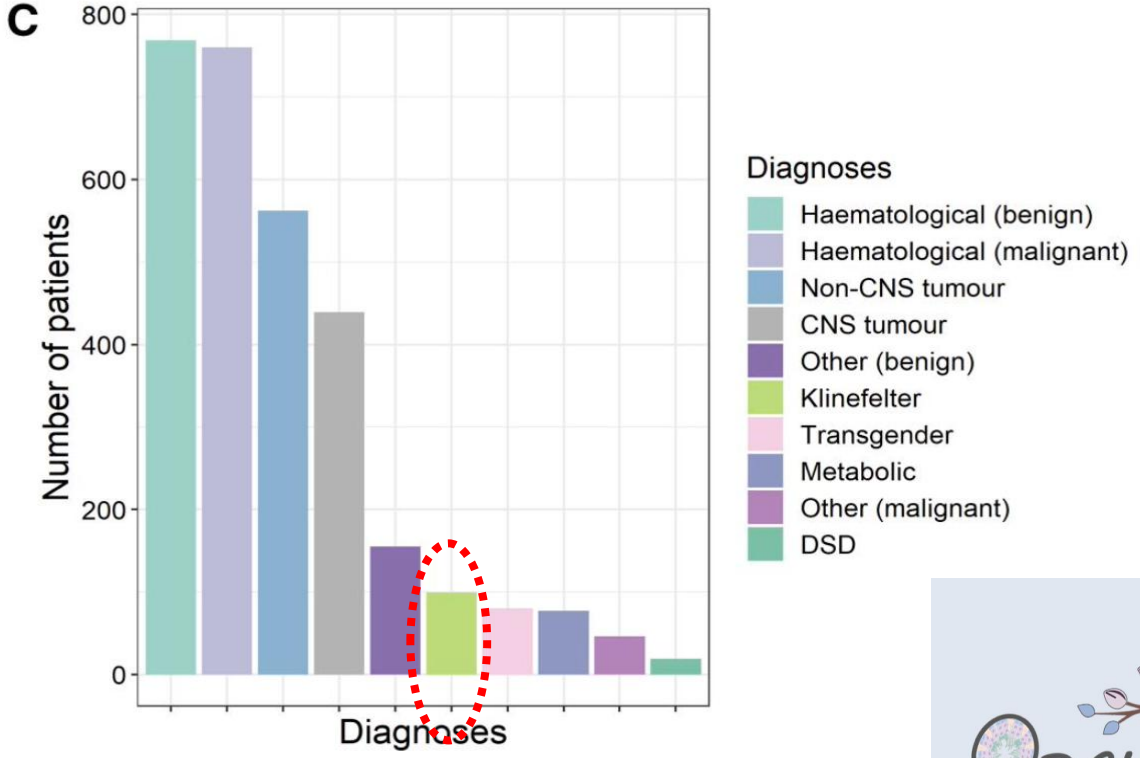
Hospital Universitario Puerta del Mar
Endoncrinologia Pediatrica
Dr. Jesus Dominguez

Hospital Universitario Ferrol
Servicio de Urologia
Dr. Gillermo Galdón

A 20-year overview of fertility preservation in boys: new insights gained through a comprehensive international survey

Kathleen Duffin [1,†], Nina Neuhaus [2,†], Claus Yding Andersen[3], Virginie Barraud-Lange [4,5], Aude Braye[6], Cristina Eguizabal [7,8], Aurélie Feraille [9], Jill P. Ginsberg[10], Debra Gook[11,12], Ellen Goossens [6], Kirsi Jahnukainen[13,14], Yasmin Jayasinghe[12,15], Victoria Keros[16,17], Sabine Kliesch[2], Sheila Lane[18], Callista L. Mulder [19,20], Kyle E. Orwig [21], Ans M.M. van Pelt [19,20], Catherine Poirot [22,23], Michael P. Rimmer [24], Nathalie Rives [9], Hooman Sadri-Ardekani [25,26], Myriam Safrai [21,27], Stefan Schlatt [2], Jan-Bernd Stukenborg [13], Marianne D. van de Wetering[28], Christine Wyns [29], and Rod T. Mitchell [24,30,*]





Opinión de expertos

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Check for updates

Is the time right for transplanting immature testicular tissue or cells to restore male fertility? Expert perspectives on clinical implementation of autotransplantation of cryopreserved testicular tissue or cells for fertility restoration

Myriam Safrai [a], Ellen Goossens [b], Rod T. Mitchell [c,d,*], Kyle E. Orwig [e], Callista L. Mulder [f,g], Ans M.M. van Pelt [f,g], Debra A. Gook [h,i], Aurélie Feraille [j], Emily Delgouffe [b], Jill P. Ginsberg [k], Jan-Bernd Stukenborg [l,m], Kathleen Duffin [c,d], Kirsi Jahnukainen [l,n], Claus Yding Andersen [o], Marianne D. van de Wetering [p], Michael P. Rimmer [c], Virginie Barraud-Lange [q,r], Nina Neuhaus [s], Sheila Lane [t], Hooman Sadri-Ardekani [u], Nathalie Rives [j,**,1], Christine Wyns [v,***,1]

Ensayos clínicos en curso: **Injerto Testicular**

Recruiting

Fertility Restoration With Autografting of Cryopreserved Immature Testicular Tissue (TESTIGRAFT)

ClinicalTrials.gov ID NCT07542626

Sponsor Cliniques universitaires Saint-Luc- Université Catholique de Louvain

Information provided by Cliniques universitaires Saint-Luc- Université Catholique de Louvain (Responsible Party)

Last Update Posted 2026-04-21

Recruiting

Autologous Testicular Tissue Transplantation

ClinicalTrials.gov ID NCT05414045

Sponsor Universitair Ziekenhuis Brussel

Information provided by Universitair Ziekenhuis Brussel (Responsible Party)

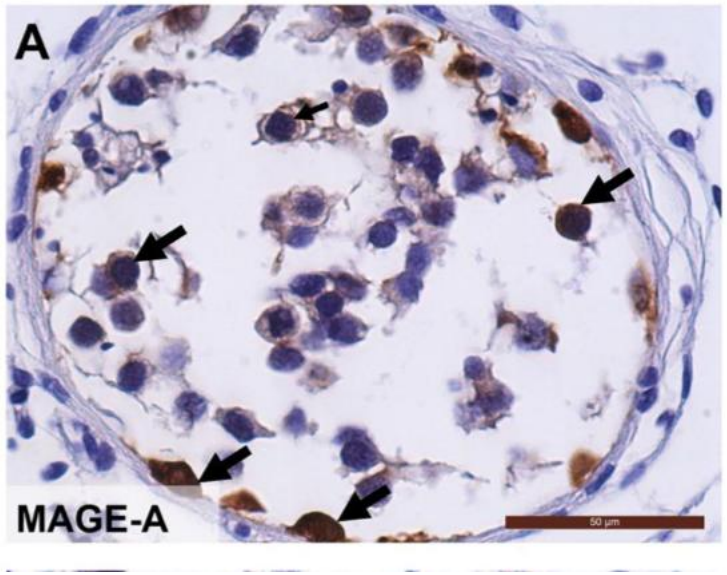
Last Update Posted 2026-04-23

Ensayos clínicos en curso: **Injerto Testicular**

Andrology

Results from the first autologous grafting of adult human testis tissue: a case report

Christian Fuglesang S. Jensen [1,2,*], Linn Salto Mamsen [3], Danyang Wang [2,3], Mikkel Fode [1,2], Aleksander Giwercman [4], Niels Jørgensen [5], Dana A. Ohl [6], Jens Fedder [7], Eva R. Hoffmann [8], Claus Yding Andersen [2,3], and Jens Sønksen [1,2]



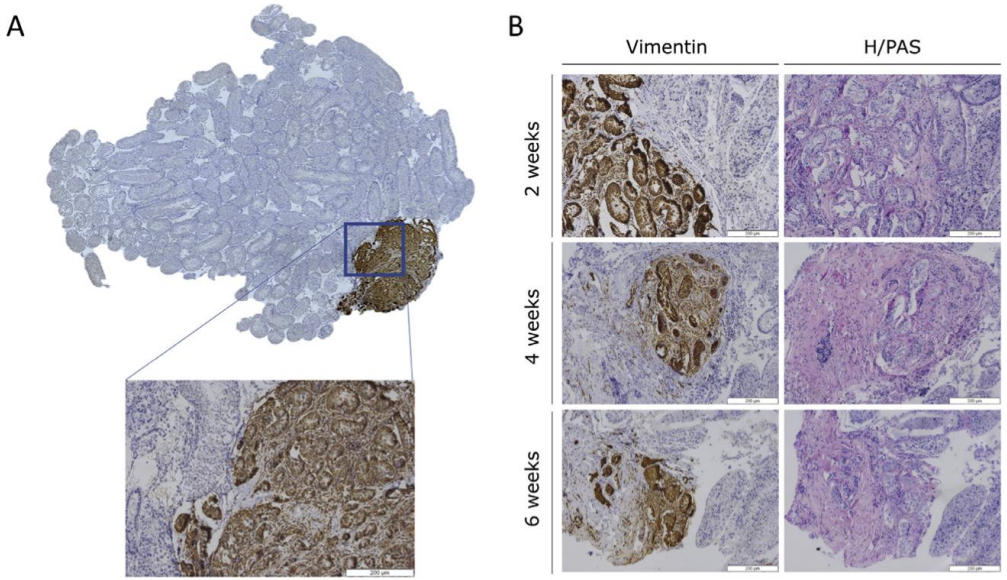
Ensayos clínicos en curso: **Injerto Testicular**

Intratesticular xenografting of Klinefelter pre-pubertal testis tissue as potential model to study testicular fibrosis

BIOGRAPHY

Margo Willems obtained her degree in biomedical sciences from Vrije Universiteit Brussel in 2019 and began her PhD thereafter at the Biology of the Testis laboratory, studying Klinefelter syndrome. She published her first manuscript in 2020 on the immune cells and vasculature in men with Klinefelter syndrome.

Margo Willems[1,*], Pia Seβenhausen[1], Inge Gies[2,3], Veerle Vloeberghs[4], Herman Tournaye[1,4,5], Dorien Van Saen[1], Ellen Goossens[1]



Ensayos clínicos en curso: **Injerto Testicular**

First successful transplant of human immature testicular tissue after gonadotoxic therapy during childhood: complete spermatogenesis in intra-testicular grafts

E. Goossens, PhD[1§*], V. Vloeberghs, MD[2§], E. De Beer, MSc[1], E. Delgouffe, PhD[1], I. Mateizel, PhD[2], C. Ernst, PhD[3], W. Waelput, PhD[4,5], I. Gies, PhD[6], H. Tournaye, PhD[1,2]

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Campus, Laarbeeklaan 101, 1090 Brussels, Belgium

Ensayos clínicos en curso: **Trasplante de SSC**

ClinicalTrials.gov

RECRUITING

Spermatogonial Stem Cell (SSC) Transplant and Testicular Tissue Grafting

ClinicalTrials.gov ID NCT04452305

Sponsor University of Pittsburgh

Information provided by Kyle Orwig, University of Pittsburgh (Responsible Party)

Last Update Posted 2024-01-09

Ensayos clínicos en curso: **Spermatogenesis in vitro**

ClinicalTrials.gov

Recruiting

Spermatogonial Differentiation Via Testicular Organoid (SDTO)

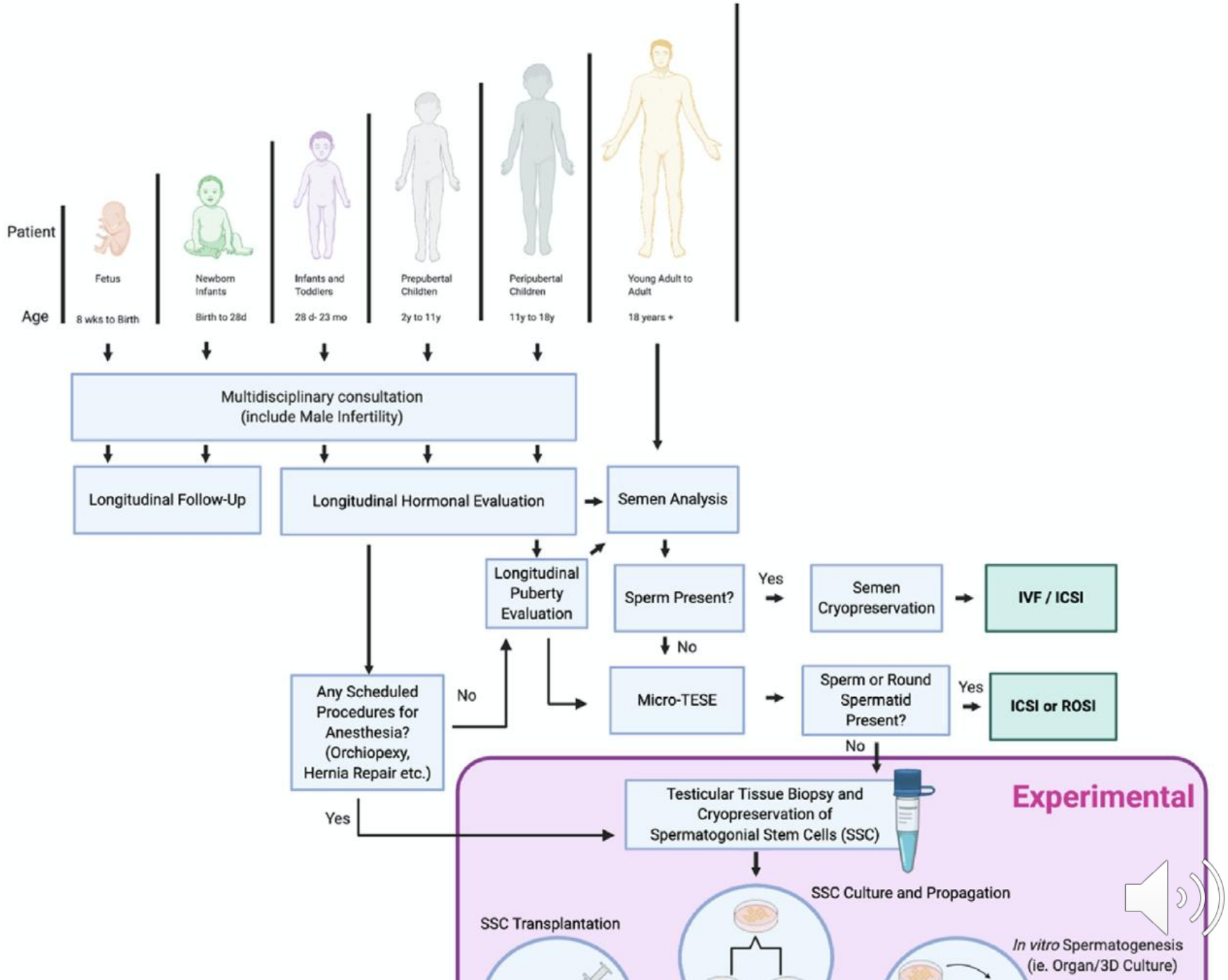
ClinicalTrials.gov ID NCT06841861

Sponsor CellARTs Inc.

Information provided by CellARTs Inc. (Responsible Party)

Last Update Posted 2025-02-24

Tratamiento de Fertilidad Futuro



Adaptado de Deebel et al 2021

Take-Home messages

- La introducción de avances tecnológicos son esenciales para **optimizar las posibilidades** de concepción en el paciente SK.
- La **criopreservación de tejido testicular** es un prometedor procedimiento **experimental** cada vez más cerca de la clínica. Esperamos que las **terapias de fertilidad basadas en SSC** aportarán nuevas opciones para pacientes SK. La **edad** de criopreservación debe **individualizarse** según características y preferencias del paciente y familia.
- La **continua evolución del manejo multidisciplinar** del SK permitirá minimizar su impacto en la calidad de vida.

Gracias

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