

CENTER FOR RECONSTRUCTIVE URETHRAL SURGERY



GUIDO BARBAGLI, M.D.
Arezzo - Italy

e-mail: info@urethralcenter.it

Websites: www.uretra.it
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INTERNATIONAL CONFERENCE

Urogenital Reconstructive Surgery



Moscow – Russia
June 15 – 16, 2017



Centro Chirurgico Toscano **Arezzo – Italy**

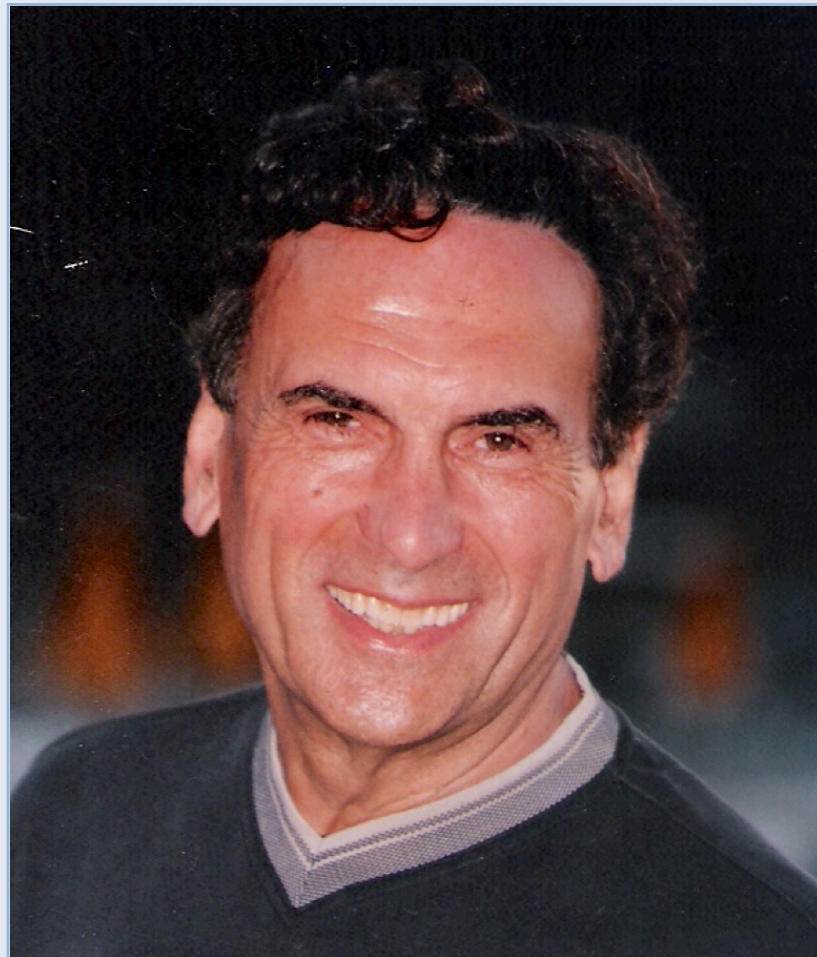
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**Urethral Reconstruction
Using Tissue Engineered
Material: State of the Art**



Prof. Sava Perovic - Belgrade - Serbia

The discussion I have prepared for today is on a difficult topic as it is **impossible** to provide you definitive guidelines.

In any case, I sincerely hope to provide you with useful information on the problems of this complex topic.



available at www.sciencedirect.com
journal homepage: www.europeanurology.com



European Association of Urology



Platinum Opinion

Clinical Experience with Urethral Reconstruction Using Tissue-engineered Oral Mucosa: A Quiet Revolution

Guido Barbagli^a, Massimo Lazzeri^{b,}*

^a Centro Chirurgico Toscano, Arezzo, Italy; ^b Department of Urology, Humanitas Clinical and Research Centre, Humanitas University, Rozzano (Milan), Italy

Eur Urol 2015, 68: 917-918

The number of publications referring to stem cells increased from 4.402 in 1996 to 21.193 in 2012, representing an annual growth rate of 7.0%.

Only, 5 articles have been published from 1990 to 2016 about the clinical use of tissue engineered material for urethral reconstruction in humans.

1° PROBLEM:

The gap between laboratory and patient bed !

TREATMENT OF POSTERIOR HYPOSPADIAS BY THE AUTOLOGOUS GRAFT OF CULTURED URETHRAL EPITHELIUM

GIUSEPPE ROMAGNOLI, M.D.,

MICHELE DE LUCA, M.D., FABIO FARANDA, M.D.,

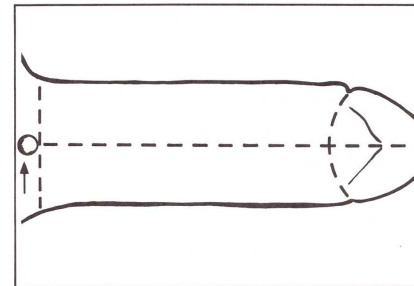
ROBERTO BANDELLONI, M.D.,

ADRIANO TITO FRANZI, M.D.,

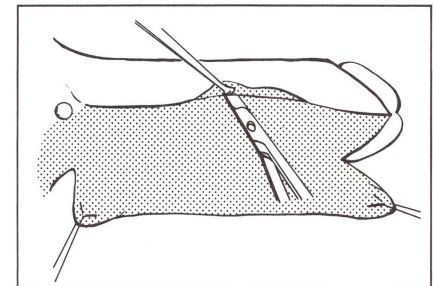
FERDINANDO CATALIOTTI, M.D.,

AND RANIERI CANCEDDA, M.D.

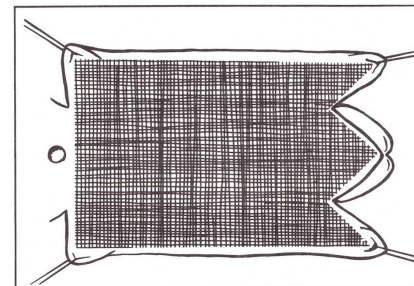
2 PATIENTS: 2 (100%) success



A



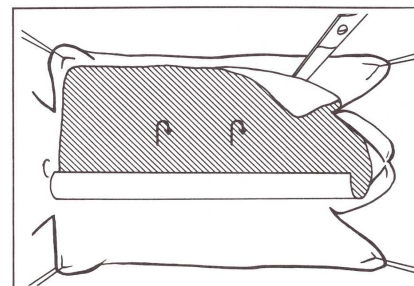
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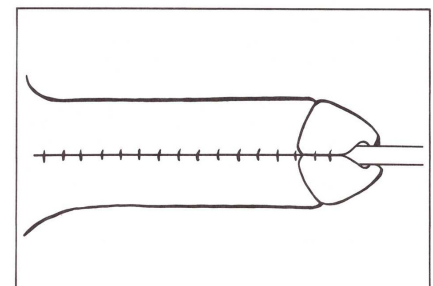
C



D



E



F

New England Journal of Medicine **1990**, 323: 527-530

ONE-STEP TREATMENT OF PROXIMAL HYPOSPADIAS BY THE AUTOLOGOUS GRAFT OF CULTURED URETHRAL EPITHELIUM

GIUSEPPE ROMAGNOLI, MICHELE DE LUCA, FABIO FARANDA, ADRIANO TITO FRANZI AND
RANIERI CANCEDDA

*From the Divisione di Chirurgia e Urologia Pediatrica, Ospedali Galliera, Istituto di Anatomia Umana Normale, Università di Genova and
Istituto Nazionale per la Ricerca sul Cancro, Genoa, Italy*

5 PATIENTS: 5 (100%)

J Urol 1993, 53: 1263-1271

Reconstructive Urology

Tissue-Engineered Buccal Mucosa Urethroplasty—Clinical Outcomes

Saurabh Bhargava ^{a,b}, Jacob M. Patterson ^{a,b}, Richard D. Inman ^a,
Sheila MacNeil ^b, Christopher R. Chapple ^{a,*}

^a Section of Reconstruction, Urodynamics and Female Urology, Royal Hallamshire Hospital, Sheffield, UK

^b Department of Engineering Materials and Division of Biomedical Sciences and Medicine, The Kroto Research Institute, North Campus, University of Sheffield, Sheffield, UK

5 PATIENTS: 5 (100%) failures

Eur Urol 2008, 150: 1204-1207

Tissue-engineered autologous urethras for patients who need reconstruction: an observational study

Atlantida Raya-Rivera, Diego R Esquiliano, James J Yoo, Esther Lopez-Bayghen, Shay Soker, Anthony Atala



**6 PATIENTS:
5 (%) success
1 (%) failure**

The Lancet 2011, 377: 1175-1182



Contents lists available at ScienceDirect

Advanced Drug Delivery Reviews

journal homepage: www.elsevier.com/locate/addr



Regulatory challenges for autologous tissue engineered products on their way from bench to bedside in Europe[☆]



Gouya Ram-Liebig^{a,*}, Juergen Bednarz^a, Burkard Stuerzebecher^b, Dirk Fahlenkamp^c, Guido Barbagli^d, Giuseppe Romano^e, Ulf Balsmeyer^c, Maria-Elsa Spiegel^b, Soeren Liebig^a, Helmut Knispel^b

^a UroTiss GmbH, Dresden, Germany

^b St. Hedwig Hospital, Department of Urology, Berlin, Germany

^c Zeisigwald Clinics Bethanien, Department of Urology, Chemnitz, Germany

^d Centro Chirurgico Toscano, Arezzo, Italy

^e Urology Unit, Ospedale del Valturno, Santa Maria alla Croce, Monteverdi-Arezzo, Italy

**21 PATIENTS:
17 (80.9%) success
4 (19.1%) failures**

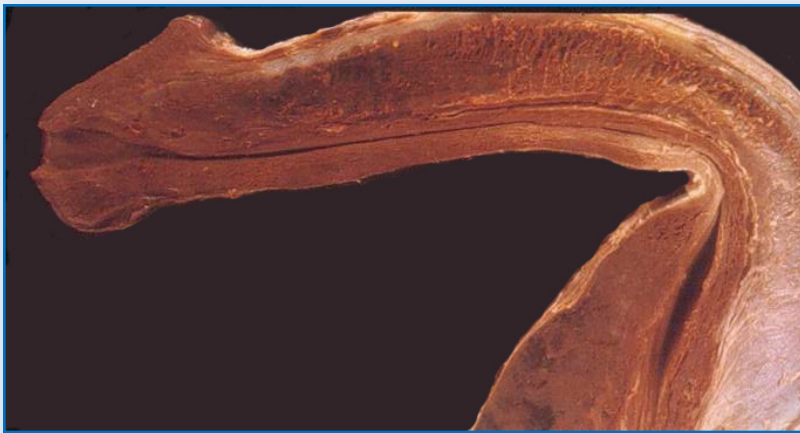
Advanced Drug Delivery Reviews 2015, 82-83: 181-191

To produce a certified tissue-engineered material for all the European Countries you need GMP laboratory, arrange a trial-study involving ± 200 patients and register your product to EMA.



2° PROBLEM:
The cost !

The people working in the laboratory on tissue engineered material don't know what normal urethra is, what is urethral pathology, what is urethral surgery !
They don't know what we need !



3° PROBLEM:
The expertise !

The use of tissue-engineered material is justified only when the current surgical therapy don't provide satisfactory and acceptable results.

At present, the current surgical therapy of urethral strictures provide us about 80% success rate.

**4° PROBLEM:
Which product for
which stricture ?**

Which product for which stricture ?



Lichen sclerosus

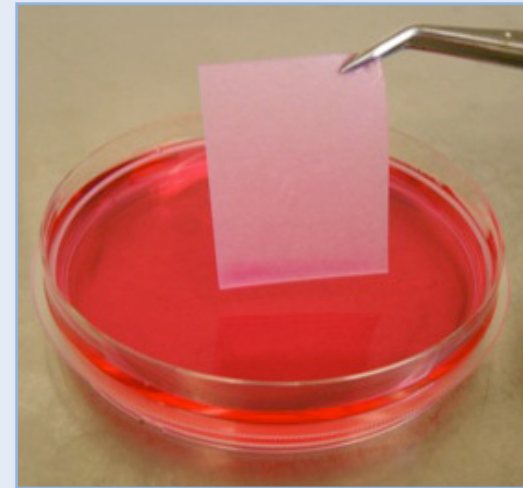
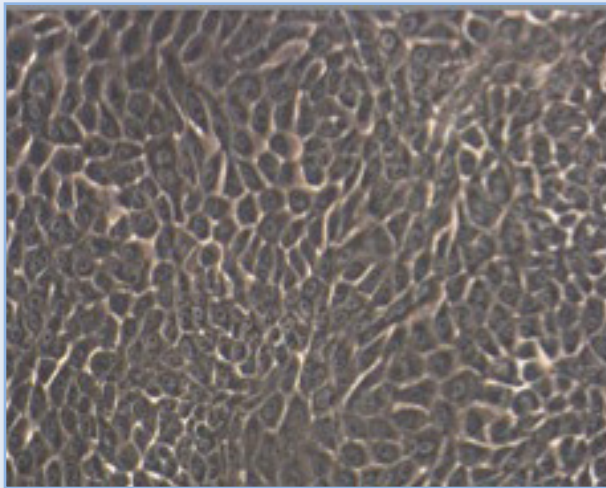
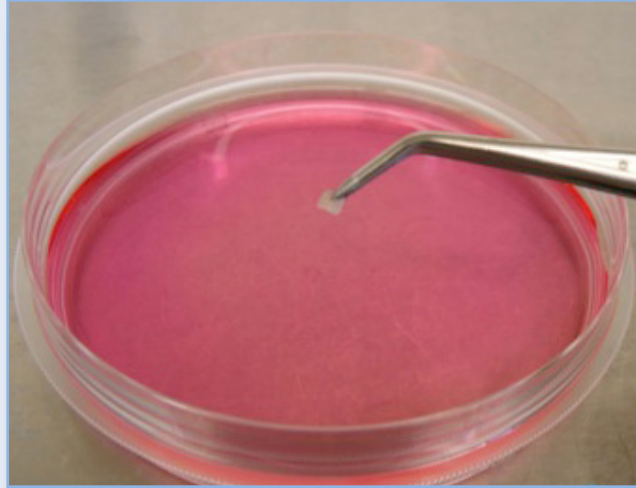


**Failed
hypospadias**



Panurethral stricture

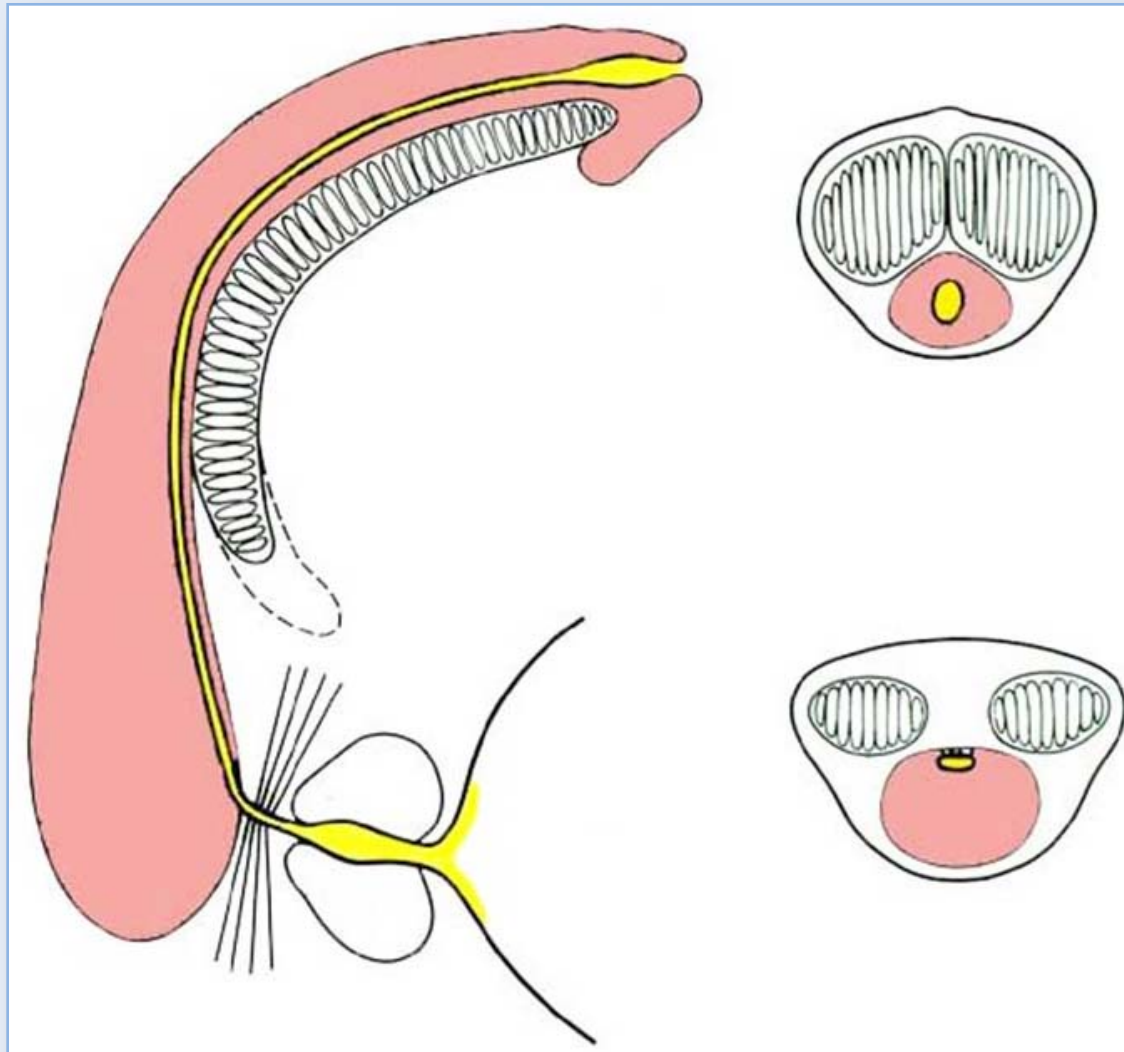
Which product for which stricture ?





5° PROBLEM:
**No spongiosum tissue
available!**

Tissue Engineered Material



?

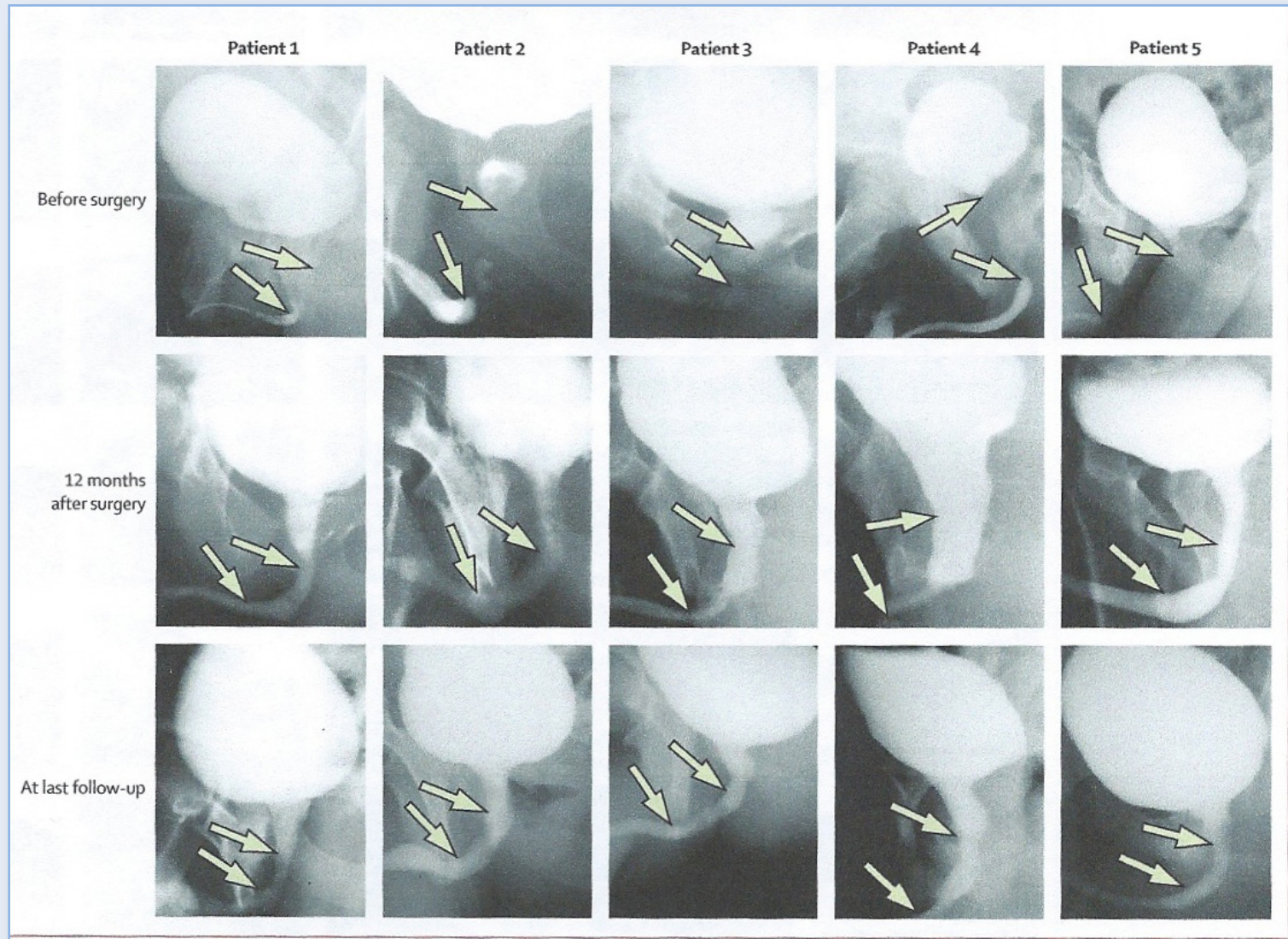
Tissue-engineered autologous urethras for patients who need reconstruction: an observational study

Atlantida Raya-Rivera, Diego R Esquiliano, James J Yoo, Esther Lopez-Bayghen, Shay Soker, Anthony Atala



Muscle and epithelial cells from the bladder were expanded and seeded onto tubularized polyglycolic acid scaffold.

The Lancet 2011, 377: 1175-1182



6° PROBLEM:

No spongiosum tissue available using a tissue engineering material: there are different solutions?

Human urethra transplant

Penis transplant

Cryopreserved Human Urethra Transplant

Human urethra transplants

*V Muruamendiaraz, J Cuervo, D Castaño, M Rivas del Fresno,
J M Pello*

The Principality of Asturias, Spain, has the highest rate of organ donors in the country and one of the highest in Europe. Our Tissue Cryopreservation Bank preserves artery, bone, tendon, skin and cardiac valve tissues.¹⁻³ Cadaver urethra extractions were begun in 1994. Histological studies of normal and cryopreserved human urethras revealed practically no differences before and after cryopreservation. After evaluating the results of experimental surgery on sows, the first procedure in a human being was carried out.

The patient was a 49-year-old man with a 1-2 cm bulbar urethral stenosis, who had previously undergone two internal Sachse urethrotomies. A cryopreserved donor urethral patch

was put in place in June, 1996. No complications occurred intraoperatively, nor in the postoperative period. The patient was discharged after 15 days. Three more transplants procedures were done during July and August. A cryopreserved urethral patch was placed in the first two cases, and a complete portion of urethra of about 4-5 cm was grafted in the third patient. All transplants have survived and the patients are urinating normally.

We believe that use of cryopreserved urethra may offer a new treatment for urethral stenosis.

- 1 Hansen TN, Dawson PE, Brockbank KGM. Effects of hypothermia upon endothelial cells: mechanisms and clinical importance. *Cryobiology* 1994; 31: 101-06.
- 2 Boren CH, Roon AJ, Moore WS. Maintenance of viable arterial allografts by cryopreservation. *Surgery* 1978; 83: 382-91.
- 3 Hunt CJ, Song YC, Bateson EAJ, Pegg DE. Fractures in cryopreserved arteries. *Cryobiology* 1994; 31: 506-15.

Department of Urology, Hospital de Cabueñes, Cabueñes, 33204 Gijón, Asturias, Spain (V Muruamendiaraz)

The Lancet 1997, 349: 326

Penis Transplant

Health

South Africans perform first 'successful' penis transplant

By James Gallagher
Health editor, BBC News website

13 March 2015 | Health



The world's first successful penis transplant has been reported by a surgical team in South Africa.

The 21-year-old recipient, whose identity is being protected, lost his penis in a botched circumcision.

March 13, 2015

Penis Transplant

Baltimore Doctors to Perform First Penis Transplant in the U.S. on a Soldier Injured in Afghanistan

4.9k
SHARES



Surgeons in an Operating Room

OWEN FRANKEN/GETTY

July 12, 2015

Penis Transplant

NEWS : HEALTH SYSTEMS

Johns Hopkins Set to Begin Penis Transplant Program



by Martha Kempner

December 11, 2015 - 2:46 pm

Officials from the Baltimore-based Johns Hopkins University School of Medicine said that within the next year it will begin offering penis transplants, specifically for wounded soldiers. The surgery will use an organ from a deceased donor and doctors believe that within months, the patients should start to regain urinary function, sensation, and ultimately sexual function.

rhrc.us/1mflNml

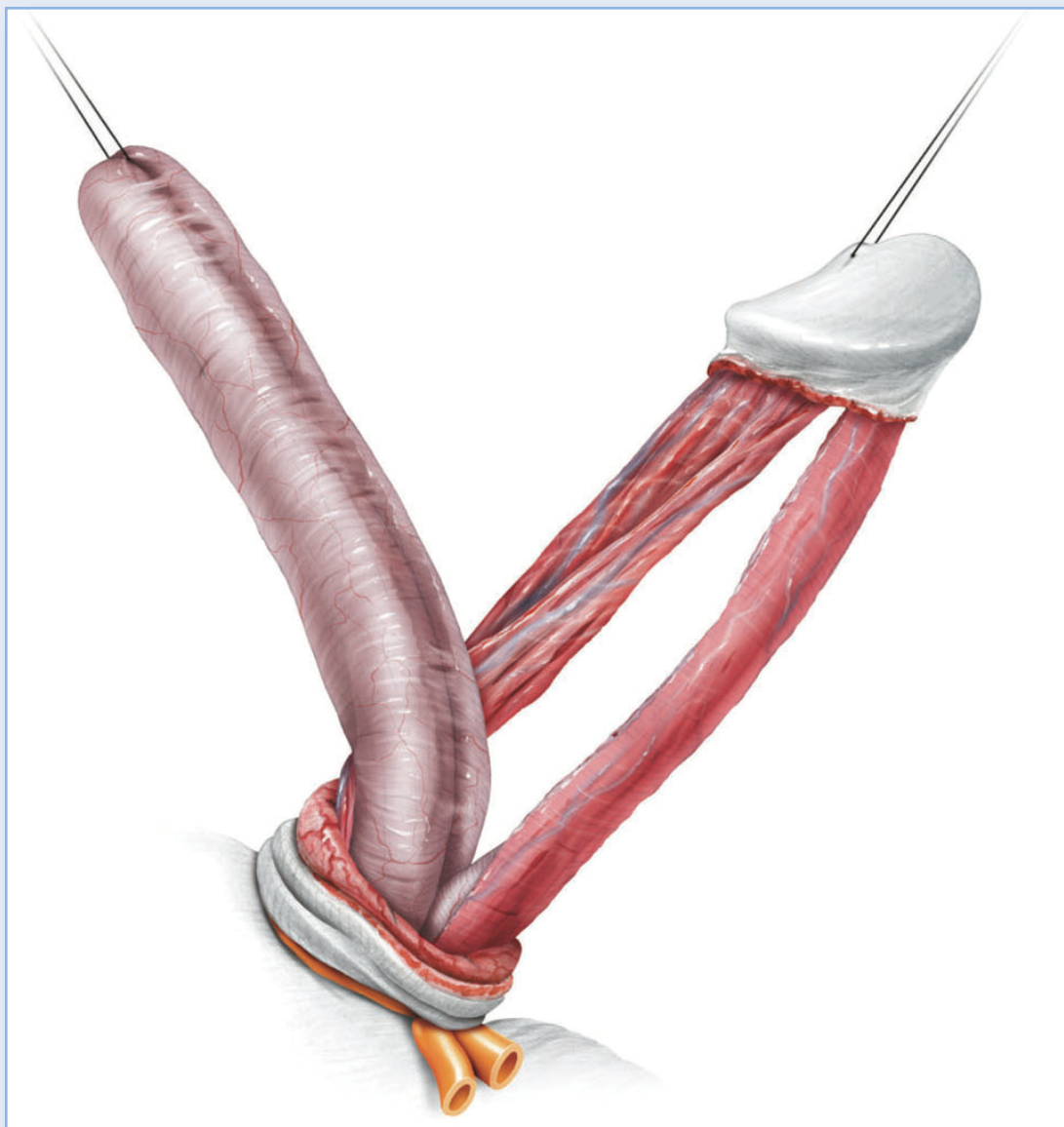
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December 11, 2015



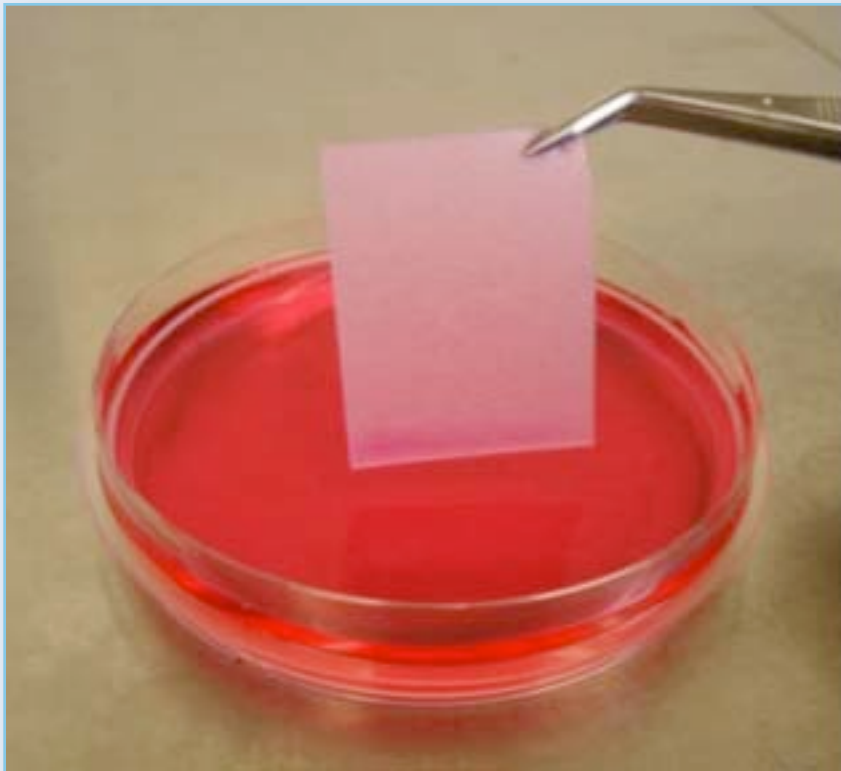




1987



2016



Next future

Tissue Engineered Material

Platinum Opinion

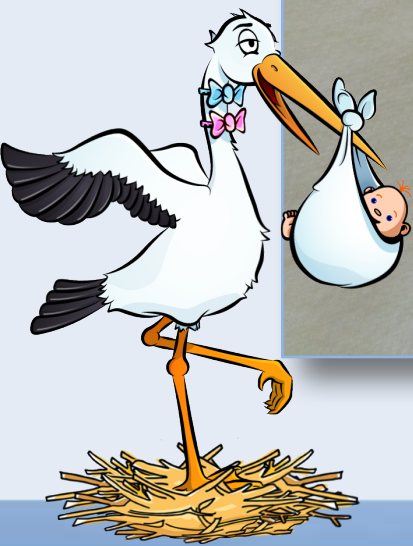
Clinical Experience with Urethral Reconstruction Using Tissue-engineered Oral Mucosa: A Quiet Revolution

Guido Barbagli^a, Massimo Lazzeri^{b,}*

^a Centro Chirurgico Toscano, Arezzo, Italy; ^b Department of Urology, Humanitas Clinical and Research Centre, Humanitas University, Rozzano (Milan), Italy

“ However, the realization of these projects represents a very difficult challenge and we must take care to not deceive our patients into thinking that this “quiet revolution” in urethral reconstruction will be available soon for all urethral conditions (congenital or acquired) requiring surgery.”

Eur Urol **2015**, 68: 917-918



William Barbagli

e-mail: info@urethralcenter.it

www.uretra.it

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