A step-by-step tutorial on PD surgery: Incision and Grafting

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PD Treatment Options

• Spontaneous resolution
• Oral therapy
• Intralesional injection therapy
  – Calcium channel blockers (Verapamil)
  – Interferon (IFN) α2b
  – Xiaflex (collagenase, Auxilium, Malvern, PA)
• Surgical options
  1. Plication of contralateral corpora (Nesbit principle)
  2. Incision & grafting (I & G) procedures
  3. Prosthesis option with modeling or ancillary procedures
Prerequisites for Surgical Correction of PD

• Stabilization of acute inflammatory phase (≥12 months)
• Failure of medical/intralesional therapy
• Patient psychologically ready & has realistic expectations about surgery
• Has anatomic deformity that precludes sexual intercourse, e.g. severe curvature, indentation, dyspareunia
• If ED (vascular insufficiency) – penile straightening procedure ± prosthesis implantation
Pre-op Evaluation of Peyronie’s Disease

History
• Medical causes, psychological status, familial trait
• Previous penile trauma or surgery, medications
• Mode of onset (gradual or sudden), progression
• Penile rigidity, pain, ability to have intercourse

Physical
• Penile dimensions (record flaccid & stretched length)
• Plaque size, location and number
• Penile erection to evaluate anatomical deformity (intracavernous injection, home photograph)
Preoperative Assessment (PD)

- Assessment of penile vascular (erectile) status allows for optimal surgical approach

- Penile duplex Doppler U/S: assesses structure of corpus cavernosum, tunica albuginea (plaque) & penile vascular function (collateral communications)
Surgical Approaches for PD

1. Tunical Shortening – Reconstructive procedure on convex side (opposite to the plaque)

2. Penile Lengthening – Reconstructive procedure on concave side (same side as plaque) - incision & grafting

3. Penile Prosthesis - (manual modeling, multiple tunical incisions, incision/excision ± grafting)
Dear Sirs: I am returning the remaining portion of your "GROW-A-FOOT" penis creme.
Tunical Lengthening (I&G) Procedures

- Indications: Severe curvature (>60 degrees) or deformity, marked penile shortening (or short penis), or narrowing/waisting/instability

- Incision/excision of plaque and graft placement

- Drawbacks – Sensory deficit, urethral injury, residual or recurrence of curvature, progressive ED
Grafting Materials for PD

• **Autografts** — Tissue harvested by surgeon from patient at time of surgery (additional time factor)
  e.g.: dermis, dura mater, tunica vaginalis, dorsal penile or saphenous vein, temporalis fascia, crura, fascia lata,

• **Synthetic Inert Substances**
  e.g.: Dacron, Gortex, silicone with silastic borders

• **Allografts or Xenografts** — Tissue harvested from another person or species (time saver)
  1. Human cadaveric pericardium (Tutoplast, Biodynamics, Parsippany, NJ)
  2. SIS (porcine small intestinal submucosa) (Cook, Indianapolis, IN)
Surgical Procedure

- Plaque incision preferred over excision of the tunical defect

- Standard circumcision incision with de-gloving of the penis

- Buck’s fascia entered just lateral to the urethra; care taken to dissect the neurovascular bundle free from dorsal plaque and the urethra from ventral plaque

- Alternative; dorsal approach remove the dorsal vein and dissect neurovascular bundle off laterally to expose long, thin plaque
Ventral Plaque
Strategy for Dorsal Plaque

Microdissect under dorsal A’s & nerves

H-Incision

Y-Incision
H type incision
Y- Incision and Grafting Technique
Complications of Grafting for PD

- Hematoma
- Wound infection
- Urinary retention or urethral injury
- Distal sensory numbness of glans (neuropraxia)
- Diminished distal rigidity (venous leak ?)
- Graft contraction
- Erectile dysfunction
Grafting – Long Term Results

• Kalsi et al (2005 BJU) >5 y F/U
  N= 40; ED- 22.5%
  ↓ length- 35%

• Montorsi et al (2004 AUA) > 5y F/U
  N= 50; Curve recurs/persists 12% ; Length lost -100%
  ED- 22%
  ↓ orgasm- 41%
  Satisfaction- 60%

• Levine & Taylor (2007 AUA) x 58 months
  N=111; Curve recurs- 8%  Length lost- SPL 47%, Subjective  65%
  ED- 24%
  ↓ sensation- 31% (89% + orgasm)
  Satisfaction 76%
Post-Straightening Rehabilitation

• Begin penile massage & stretching
  - 2 wks post-op with cocoa butter
    Devine, C- personal communication

• PDE5 i qhs post-op to enhance nocturnal erections
  Levine et al J Urol 2005

• Penile Extender Rx ~ 2-3wks post-op x 3-6 months
  Moncada et al, AUA 2007, 750A
Managing Penile Shortening after PD Surgery

- Trial of penile extender (Andro-Penis®) to prevent length loss after plication or grafting procedures
- 40 men - mean 58 yrs – 12 grafting & 28 plication procedures
  20 Rx’d w/extender 2-3 wks post-op 8-12h/day x 4 months vs 20 controls

- Results
  Overall shortening 0.5-4cm – less w/graft (NS)
  Extender use ↑ length 1-3cm & ∞ hours use
  SF – 36 ↑↑ for extender vs control

Conclusion – post-op penile stretching safe/effective way to minimize length loss

Moncada et al 750A AUA 2007
TAP vs PEG +/- Traction

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<th>SPL (cm)</th>
<th>TAP TT+</th>
<th>TAP TT-</th>
<th>PEG TT+</th>
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Adipose derived-stem cells (ADSCs)

- Repair damaged tissue
- Augment cellular differentiation
- Stimulate release of multiple growth factors
Adipose derived-stem cells (ADSCs)

There is a growing interest in tissue-engineered products.

Porcine small intestinal submucosa (SIS, Cook Urological) used in repair of various tissues & organs, because of properties of incorporation, biodegradability & mechanical strength.

The aim of this rat study was to assess the feasibility and overall success of seeding ADSCs onto SIS during tunica albuginea surgery.

PNAS, 2012
Methods and Results

- Male SD rats were divided into the following groups:
  
  1) control group – no surgery (n=8)
  2) sham operated group (n=8)
  3) rat tunica albuginea I & G with SIS (n=8)
  4) rat tunica albuginea I & G with stem cell-seeded SIS (n=8)

- All rats had terminal surgery 8 wks after first stage surgery, which involved erectile pressure readings with CNS, penile morphometric measurements & tissue collection for histological evaluation, real-time-PCR, Western blot & immunostaining analyses
A. Methyl violet staining of ADSCs (100×)

B. Flow cytometry analysis of rat ADSCs within 3–5 passages showed that cells were CD29 (97.62%), CD90 (92.21%) and CD105 (15.87%) positive. There was no significant expression of CD45 (4.37%).

C. The 3rd passage of ADSCs was incubated with BrdU at 20 μmol/L for 48 hours. Immunofluorescence was performed to calculate the labelling index (positive rate). The nuclei of ADSCs showed green fluorescence and the labeling rate exceeded 95%.
H&E staining of SIS & rADSCs-SIS complexes

A. Four-layer SIS showed non-directed fibers which were completely acellular.

B. rADSCs-graft complexes were cultured on the cell culture inserts (Falcon®) at the interface between the culture medium and a CO₂ rich environment. After 1 week, H&E staining demonstrated that rADSCs grew well and formed multiple layers on the scaffolds.
Tunica albuginea reconstructive surgery in the rat penis

A: The 2nd, 3rd & 4th groups underwent first stage surgery with a 5-mm incision (arrows) on both sides of the tunica albuginea.

B & C: A 10 mm² SIS or stem cell seeded SIS graft (arrow) was interpositioned and sutured with 8-0 nylon for the 3rd & 4th groups.

D: Both sides of the penile tunica albuginea underwent an operative procedure.

PNAS, 2012
Evaluation of erectile function response to cavernosal nerve electrostimulation (CNS)

- The cavernosal nerve identified posterolateral to the prostate on one side, and an electrical stimulator with a stainless-steel bipolar hook placed around it.

- CNS performed using 15 Hz of different voltages (2.5v, 5.0v, 7.5v) for 60 seconds and then given a rest period of 3 minutes in between each stimulation to allow for sufficient recovery time of intracellular pathways.
• Total erectile response (using ICP) was determined by measuring the area under the curve (AUC) in mmHg/second from the beginning of CNS until ICP returned to baseline or pre-stimulation pressure.

• The ratio of maximal ICP-to-MAP was determined relative to controls for variations in systemic blood pressure.

• Statistics show maximal increase in ICP, ICP/MAP and total ICP values in response to CNS with different voltage settings (2.5v, 5.0v, 7.5v) for 1 minute in all groups. Excluding the 2.5V stimulation setting, all measurements in rats with the SIS graft were significantly lower than in sham operated rats (p < 0.05).

• Seeding ADSCs on SIS grafts produced a significant restoration of erectile response compared to the SIS graft only group (p < 0.05). Maximal increase in ICP, ICP/MAP & total ICP responses were not statistically different between sham operated and SIS+ADSCs treated (p > 0.05).

\[ \triangle P > 0.05; \quad * P < 0.05, \quad ** * < 0.01 \]

PNAS, 2012
rADSC label and its survival

- In the frozen section of the penis after grafting by rADSCs seeded SIS, still able to detect faint BrdU signal (arrows) on the surface of the graft through anti-BrdU immunofluorescence

- Also found sporadic BrdU-labelled cells in the corpus cavernosum

PNAS, 2012
Masson’s trichrome

- Masson’s trichrome staining indicated the tunica albuginea of control (A) and sham operated rats (B) after 8 weeks showing numerous collagen bundles orientated in two directions with an abundance of elastic fibers.

- In the SIS graft group (C) there was moderate fibrosis under the graft and a mild foreign-body reaction around the suture.

- In the ADSCs-seeded SIS graft group (D), only mild fibrosis was present around the graft, and the elastic fibers of the graft were orientated in two layers, similar to the adjacent tunica albuginea.

** Open arrows indicate SIS graft, curved arrows the suture, solid arrows the normal tunica albuginea, and lined arrows the fibrosis.

PNAS, 2012
Real-time pcr of erectile related genes in corpus cavernosum

- Compared with control & sham groups, TGF-β1 (A) & iNOS (F) mRNA expression increased significantly in the SIS graft group, while seeding rADSCs on the SIS graft reduced their expression.

- FGF-2 mRNA (B) had lower expression level in the control than in the other surgery groups.

- Compared with both the control and sham groups, mRNA levels of the eNOS (D), nNOS (E) and VEGF (C) decreased significantly in the SIS graft group. However, seeding with rADSCs on the SIS graft resulted in significant restoration of their expression.

1-control; 2-sham; 3-SIS group; 4-SIS+rADSCs group. △ > 0.05; * < 0.05; * * < 0.01

PNAS, 2012
IMMUNOFLUORESCENCE FOR eNOS, nNOS AND iNOS IN THE CORPUS CAVERNOSUM

- Immunofluorescent staining for eNOS (A) and nNOS (B) showed diffuse and marked immunoreactivity for the molecule in the corpus cavernosum of the control, sham operated and ADSCs-seeded SIS graft groups. eNOS and nNOS expression demonstrated weak signaling in rats from the SIS graft group.

- Diminished immunofluorescence staining for nNOS was detected in the dorsal nerves (C) of the SIS graft group compared with the other groups.

- iNOS (D) protein was weakly stained in the control corpus cavernosum. Its expression was apparently strong in the other 3 operative groups, and the SIS graft group had the highest immunoreactivity.
Conclusions: Stem cells in TA surgery

- ADSCs successfully engrafted in rat study
- ADSCs accelerate recovery of TA & underlying CC function by inhibiting fibrosis & up-regulating expression of VEGF
- ADSCs mediate a rehabilitative effect on erectile function in rats undergoing TA surgery by increasing eNOS & nNOS and decreasing iNOS
- ADSC seeded on grafting material may play an important role in future reconstructive surgeries involving TA

PNAS, 2012
Algorithm Treatment of PD

Observation/Med Rx

Minimally Invasive (ILI) Rx

Doppler U/S Evaluation

Cav inflow > 30cc/s
No venous leak

- Plication or Incision & grafting
  - May require future intervention (e.g. oral Rx, VED, prosthesis, etc)

Cav inflow < 25cc/s
Distal softness

- Penile prosthesis +/- modeling
  - Consider incision/excision +/- graft if:
    - Curvature > 60 degrees
    - Plaque size > 4-5 cm
    - Ventral plaque
Incision and Grafting for PD: Conclusions

- Treatment tailored to patient and his complaints
- Medical or minimally invasive Rx for first year (acute phase)
- After curvature, plaque, & pain stabilize, and if pt unable to penetrate - perform penile duplex Doppler before surgery
- Surgical: incision/excision and grafting procedure
  - Curvature > 60-70 degrees
  - Complex abnormality (waisting, hinge, instability, etc.)
  - Plaque size > 4-5 cm
- Grafting materials: human pericardium, SIS, ADSC option in future
Need to fit the surgery (incision and grafting procedure) for the right indications