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Futuristic Concept in Management of Female SUI: Permanent Repair Without Permanent Material

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1. Introduction

Stress urinary incontinence (SUI) is defined as the complaint of involuntary leakage of urine on exertion or on sneezing or coughing **(Abrams et al, 2002)**. Female SUI is a common distressing health problem, affecting large number of women worldwide, with prevalence rates ranging from 12.8% to 46.0% **(Botlero et al, 2008)**. SUI is considered the most common type of urinary incontinence among women and presents about 50 % of these populations, while mixed urinary incontinence presents 36 % and only 14 % are due to urge urinary incontinence **(Hannestad et al, 2000)**. SUI has a negative impact on women quality of life specially their social, physical, occupational, psychological, and sexual aspects of life.

SUI arises when the bladder pressure exceeds the urethral pressure, in the setting of sudden increases of intra-abdominal pressure (coughing, sneezing …etc). Most researchers now identify two main etiologic mechanisms for the development of SUI: urethral hypermobility due to loss of urethral support - the hammock-like supportive layer described by DeLancey **(DeLancey, 1994)**, and intrinsic sphincter deficiency (ISD), with most patients having elements of both disorders (Table 1).

There are several options for treatment of female SUI. Conservative treatment (pelvic floor muscle exercise) is usually advocated as a 1st line therapy since it carries minimal risks and studies have shown up to 70% improvement in symptoms of SUI following appropriately performed pelvic floor exercise **(Price, Dawood and Jackson, 2010)**. Conservative management strategies include:

1. Life style changes (weight reduction, smoking cessation, ↓ fluid intake, treatment of constipation …. etc).
2. Pelvic floor muscle training ± biofeedback.
3. Vaginal cones and electrical stimulation.

Regarding pharmacotherapy, no drug till now has been approved to be used by the Food and Drug Administration (FDA) for the treatment of female SUI. Duloxetine is a serotonin–norepinephrine reuptake inhibitor (SNRI) has been investigated, it can significantly improve the quality of life of patients with SUI, but it is unclear whether or not benefits are sustainable in addition it has a common side-effects **(Mariappan et al, 2007)**.

1- Bladder neck/urethral hypermobility (due to loss of urethral support):	- Vaginal delivery. - Aging. - Estrogen deficiency. - Connective tissue disorders.
2- Intrinsic sphincter deficiency (ISD):	- Multiple anti-incontinence procedures - Radical pelvic surgery - Radiation - Menopause - Urogenital atrophy
3- Other risk factors:	- Chronic ↑ in intra-abdominal pressure. - Constipation. - Smoking. - Physical inactivity. - Genetic predisposition.

Table 1. Show various etiological factors involved in the pathophysiology of SUI.

Surgical treatment for SUI should be undertaken for women with SUI who have failed conservative treatment strategies or if the patient wants definitive treatment from the start.

Over the past years, many surgical procedures have been used for the treatment of female SUI with varying degrees of success. Recently, a number of new minimally invasive surgical techniques have been developed for treatment of female SUI that aimed to decrease the morbidity, improved safety and improvement of the surgical outcomes, while maintaining the efficacy of traditional open incontinence surgery. The Tension free vaginal tape (TVT) procedure was first described and evaluated by Ulmsten et al in Sweden in 1996 **(Ulmsten et al, 1996)**, then the Transobturator tape (TOT) procedure was developed in 2001 by DeLorme to avoid the retropubic space **(DeLorme E, 2001)**. Midurethral slings (TVT and TOT) have the following advantages:

1. The ability to be performed under local anaesthesia in patients who are unfit for major surgery.
2. Better for young aged women due to better cosmetic appearance since there is now open wound such the old traditional surgical methods.
3. Lower costs, shorter hospital stay, early recovery time and less postoperative pain.

Further improvement in surgical procedures towards less invasive sling technique has led to the innovation of a mini-sling e.g. TVT Secur system, which is a surgical device requiring only a single suburethral incision to be inserted **(Neuman and Shaare-Zedek, 2007)**. Mini-slings have the following advantages over the ordinary midurethral slings (TVT and TOT):

1. The complications associated with suprapubic and groin incisions will be eliminated.
2. Cystoscopy will not be necessary.
3. Operative time will be shorter than with other midurethral sling techniques.

2. Midurethral slings for SUI treatment

2.1 Surgical principle of midurethral slings

Petros and Ulmsten proposed the integral or midurethral theory of the female pelvic floor and urethral closure mechanism **(Petros and Ulmsten, 1993)**, which has been the basis upon which many of the newer treatments for SUI have been developed. The idea that a loss of mid-urethral support is a causative factor in female SUI led to the use of synthetic midurethral tapes which became popular because of ease of placement and excellent outcomes. After their introduction by Ulmsten and Delorme, TVT and TOT gained a great popularity and rapid widespread and become now the gold standard treatment minimally invasive treatment of female SUI. Both techniques (TVT and TOT) aimed to recreating urethral support using a polypropylene mesh placed at midurethral without tension to create an artificial collagenous neoligament, using the foreign body reaction induced by the host defense mechanism. TVT acts as a pubourethral neoligament anchored suprapubically, which tightens around the urethra in the setting of increased intra-abdominal pressure. TOT had the following advantage over TVT by avoiding the blind trocar passage in the retropubic space by passing the trocar through the obturator muscles and membrane, thus decreasing the risk of major bladder, bowel perforation and vascular injury also decreasing the need for cystoscopy use after tape placement (figure 1 and 2).

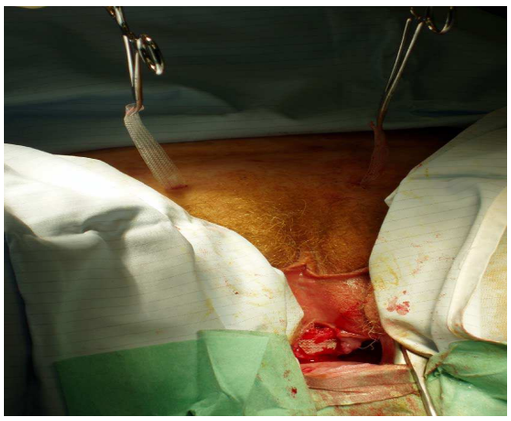

Fig. 1. TVT in position **(Morley and Nethercliffe, 2005)**.

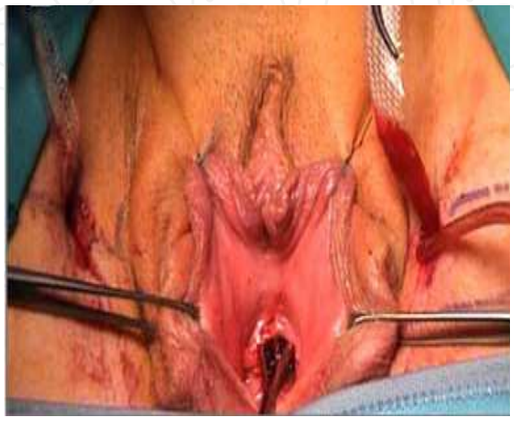

Fig. 2. TOT in position **(De Leval, 2003).**

2.2 Clinical results of midurethral slings

2.2.1 TVT surgical outcomes

TVT has undergone the most rigorous testing all over the years, and now it is considered the gold standard treatment option for female SUI. To date it is estimated that more than 1 million cases have been performed worldwide **(Deng et al, 2007)**. There are now many prospective studies in literature with a long-term follow-up showing great success of TVT for the treatment of female SUI with cure rate > 80 % as seen in (table 2) denoting the long term durability of this procedure. In 2008, Nilsson et al reported the longest follow-up (11 years) of TVT operation and demonstrated that (90% objective cure rate) of women treated without any significant late-onset adverse effects **(Nilsson et al, 2008)**. In another study with follow-up for 10 years. TVT showed satisfactory objective (84%) and subjective (57%) cure rates with (23%) improvement **(Aigmueller et al, 2011)**.

Author	Number of patients	Patient group	Duration of follow-up (years)	Treatment outcomes (subjective/objective) % cured
Villet et al, 2002	124	SUI	32.5 months	88.7%
Rezapour et al, 2001a	34	Recurrent SUI	4	82%
Rezapour et al, 2001b	80	Mixed urinary incontinence	4	85%
Rezapour et al, 2001c	49	SUI due to (ISD)	4	74%
Deffieux et al, 2007	51	SUI	6.9	80%
Nilsson et al, 2004	90	SUI	7	81.3%

Table 2. Long term results of TVT.

TVT has replaced the old gold standard Burch colposuspension. In a randomized control trial (RCT) conducted by Ward and Hilton who compared TVT with the open colposuspension on they reported equal efficacy with subjective cure rate 81% and 80% in TVT and Burch group respectively. The duration of hospitalization, operative time and the time taken to return to normal activity seem to be shorter in the TVT group. The authors concluded that the TVT procedure is as effective as the Burch colposuspension in urodynamically proven patients with SUI at a 2-year follow-up **(Ward and Hilton, 2004)**. The same authors have published their 5-year out comes in this study where they reported subjective cure in 81% in the TVT group and 90% in the colposuspension group. They stated that the effect of both procedures on cure and improvement in quality of life has been maintained for long time **(Ward and Hilton, 2008)**.

2.2.2 TOT surgical outcomes

Short-term data regarding the efficacy of the TOT suggest that this procedure perform as well as the TVT and may perhaps cause fewer complications. TOT has shown to be of equal

efficacy to TVT with cure rate > 80% (table 3), however, still long-term studies have yet to be done to evaluate the effectiveness and durability of the TOT procedure.

Author	Number of patients	Patient group	Duration of follow-up	Treatment outcomes (% cured)
Cindolo et al, 2004	80	SUI with urethral hypermobility	4 months	92
Grise et al, 2006	206	SUI	Mean (16 months)	79.1
Giberti et al, 2007	108	SUI due to urethral hypermobility	2 years	80
Roumeguere et al, 2005	120	Urodynamic SUI	1 year	80
Waltregny et al, 2008	91	SUI	3 year	88
Liapis, Bakas and Creatsas, 2010	74 (32 TVT-O and 41 TVT-O + ant. Colporrhaphy	SUI and Cystocele	4 year	82.4 and 80.5 % respectively

Table 3. Results of TOT.

2.2.3 TVT versus TOT outcomes

TVT and TOT since their introduction in the treatment of female SUI have gained a great popularity and wide spread use in a large number of studies. Both techniques showed nearly equal efficacy with more than 80% cure rate in the majority of studies as mentioned before (Table 2, table 3). Novara et al, in a large systematic review and meta-analysis showed that patients treated with TVT had slightly higher objective cure rates (OR: 0.8;CI: 0.65–0.99; p = 0.04) than those treated with TOT; however, subjective cure rates were similar in both technique **(Novara et al, 2010)**. In a long term follow-up after 5 years both TVT and TVT-O procedures were safe, with equivalent results (72.9% and 71% of patients objectively cured after TVT-O and TVT, respectively) **(Angioli et al, 2010)**.

2.3 Material used for midurethral slings

Over the past years there was a great evolution in the use of biological and synthetic materials in the treatment of different reconstructive pelvic surgery e.g. SUI and pelvic organ prolapse (POP) in an effort to improve surgical outcomes. However, the potential benefits of using grafts need to be carefully balanced against the risks of using foreign materials to the patient's body. Amid in 1997 published a classification for synthetic mesh used in abdominal hernia surgery based on the pore size (macroporous, microporous, submicro-porous) and fiber type (monofilaments or multifilament) of the synthetic mesh **(Amid, 1997)**. Synthetic grafts may be non-absorbable, absorbable, or a mixture of the two. The non-absorbable polypropylene mesh is the most common type used in reconstructive pelvic surgery. Synthetic tapes available in the market for urogynecological practice see (table 4).

The pore size and interstices distance between the fibers (figure 3) are important mesh characteristics that determine whether host inflammatory cell and fibroblasts can penetrate the mesh or not. The ideal synthetic tapes used for the treatment of SUI should have the following characters: made of polypropylene, low weight, macroporous, monofilament mesh, with an elasticity between 20 and 35%, as these tapes have a lower incidence of infection and tissue erosion **(Rosch et al, 2004; Deprest et al, 2006).**

Pore size classification	Component	Trade name	Fibre type
Type I: Totally macroporous (pore size of >75 µm)	Polypropylene	Prolene, Gynemesh, Gynemesh PS (Ethicon)	Monofilament
		Marlex, Pelvitex a (Bard)	Monofilament
	Polypropylene/ Polyglactin 910	Surgipro b SPMM (Tyco)	Mono-multifilament
	Polyglactin 910	Vypro (Ethicon)	multifilament
		Vicryl (Ethicon)	
Type II: Totally microporous (pore size of <10 µm)	Expanded PTFE	Gore-Tex (Gore)	multifilament
Type III: Micro or macro-micro	Polyethylene	Mersilene (Ethicon)	multifilament
	PTFE	Teflon (Gore)	multifilament
	Braided polypropylene	Surgipro b SPM (Tyco)	multifilament
	Braided polypropylene–open weave	Surgipro b SPMW (Tyco)	multifilament
	Perforated Expanded PTFE	Mycro-mesh (Gore)	
Type IV: Submicronic pore size (pore size of <1 µm)	Polypropylene sheet	Cellgard	Monofilament

PTFE: Polytetrafluoroethylene
a Collagen coated macroporous polypropylene materials.
b Several kinds of Surgipro (Tyco) materials are marketed under the same name and have different constructs.

Table 4. Classification and characteristics of synthetic implant materials marketed for urogynecologic indications **(Deprest et al, 2006).**

Type I macroporous mesh with (pore size >75 µm) allowing easier penetration of inflammatory cells such as leukocytes (9–15 µm), macrophages (16–20 µm), fibroblast and blood vessels into the graft to phagocytose bacteria (<1 µm) lowering the risk of infection, in addition host tissue in growth and incorporation is promoted resulting in good support. On the other hand, multifilament meshes have interstices that are <10 µm and bacteria (<1 µm) can replicate within these interstices. However, access to macrophages and ability to fight

bacterial colonisation within the interstices is impaired **(Winters et al, 2006)**. Monofilament mesh does not have small interstices and the risk of mesh infection and erosion is reduced with its use.

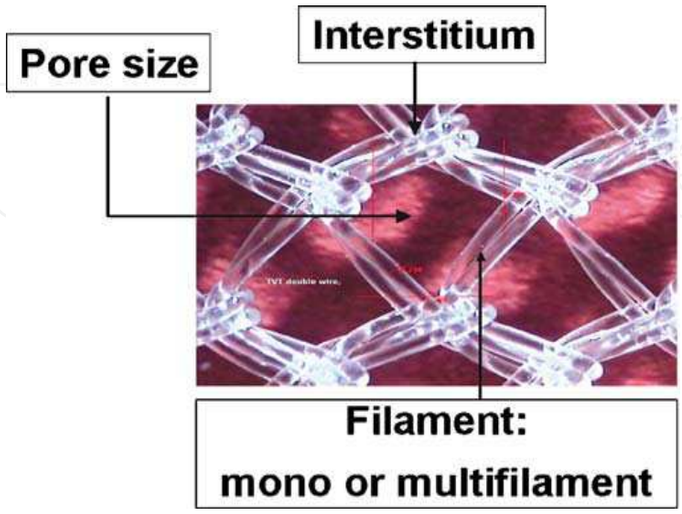

Fig. 3. Terminology used to classify synthetic implants. Magnified view of a part of a polypropylene tape as used for TVT procedure (Gynaecare, Johnson and Johnson) with identification of filament type, interstitium, and pore size **(Deprest et al, 2006).**

Biological implants have many sources; they may be an autologous graft (derived from the patient's own body tissue), allograft (derived from post-mortem tissue banks) or xenograft (derived from animals) **(Dwyer, 2006)**. Types of biologic implants available in the market that can be used in urogynecology practice (table 5):

Biological types	Component	Trade name
Autologous grafts	Rectus fascia Fascia lata Vaginal mucosa	
Allografts	Fascia lata Dura mater	Lyodura
Xenografts	Porcine non-cross-linked small intestine submucosal collagen Porcine non cross-linked dermal collagen Porcine dermal cross-linked collagen Fetal bovine skin derived collagen scaffold Bovine non-cross-linked pericardium	Surgisis (Cook) InteXen (AMS) Pelvicol, Pelvisoft, Pelvilace (Bard) Xenform (Boston Scientific) Veritas (Synovis)

Table 5. Classification of biologic implant materials marketed for urogynecologic indications **(Deprest et al, 2006).**

2.4 Complications of synthetic midurethral slings

Although midurethral slings are minimally invasive procedures with high efficacy, however they result in bothersome complications which should not be minimized. The reported complication rates for midurethral slings ranged from 4.3% to 75.1% for TVT and 10.5% to 31.3% for TOT **(Daneshgari et al, 2008).** Awareness of these complications should encourage improvements in patient counseling as well as further investigation of the underlying mechanisms. Summary of the complications of midurethral sling procedures (table 6):

a) Intraoperative complications:	- Major: Vascular lesions. Nerve injuries. Gut lesions. - Minor: Bladder injury. Urethral injury.
b) Early postoperative complications:	- Retropubic haematoma. - Blood loss > 200 ml. - Urinary tract infections. - Spondylitis.
c) Late postoperative complications:	- Transient urinary retention. - Permanent urinary retention. - Groin and thigh pain. - Genitourinary erosion. - De novo urgency. - Urethral obstruction. - Dyspareunia.

Table 6. Summary of the complications of midurethral sling procedures.

With regard to complications, most of the complications reported were intraoperative minor ones, with little or no disabling effects provided they are recognized and treated intraoperatively. A very limited number of major complications (e.g. bowel, vascular, and nerve injuries, necrotizing fasciitis, ischiorectal abscess, urethrovaginal fistulas, sepsis, and patient deaths) have been reported after placement of midurethral slings. Deng et al reported on the prevalence of major complications in the US Food and Drug Administration's Manufacturer and User Facility Device Experience database, identifying 32 cases of vascular injuries, 33 bowel injuries, and 8 patient deaths after TVT placement **(Deng et al, 2007)**.

A new terminology and classification system has been developed by the International Urogynecological Association (IUGA) and the International Continence Society (ICS) for full description of all possible physical complications related directly to the insertion of prostheses (meshes, implants, tapes) & grafts in female pelvic floor surgery (figure 4). A key advantage of a standardized classification is that all parties involved in female pelvic floor surgery including surgeons, physicians, nurses, allied health professionals and industry will be referring to the same clinical issue. It is anticipated that a category (C), time (T), and site (S) - (CTS) codified table of complications will be a necessary part of reports of surgical procedures relevant to this document. With a standardized classification in place, quicker assessment of adverse events will be achieved together with uniform reporting of prosthetic-related complications **(Haylen et al, 2011)**.

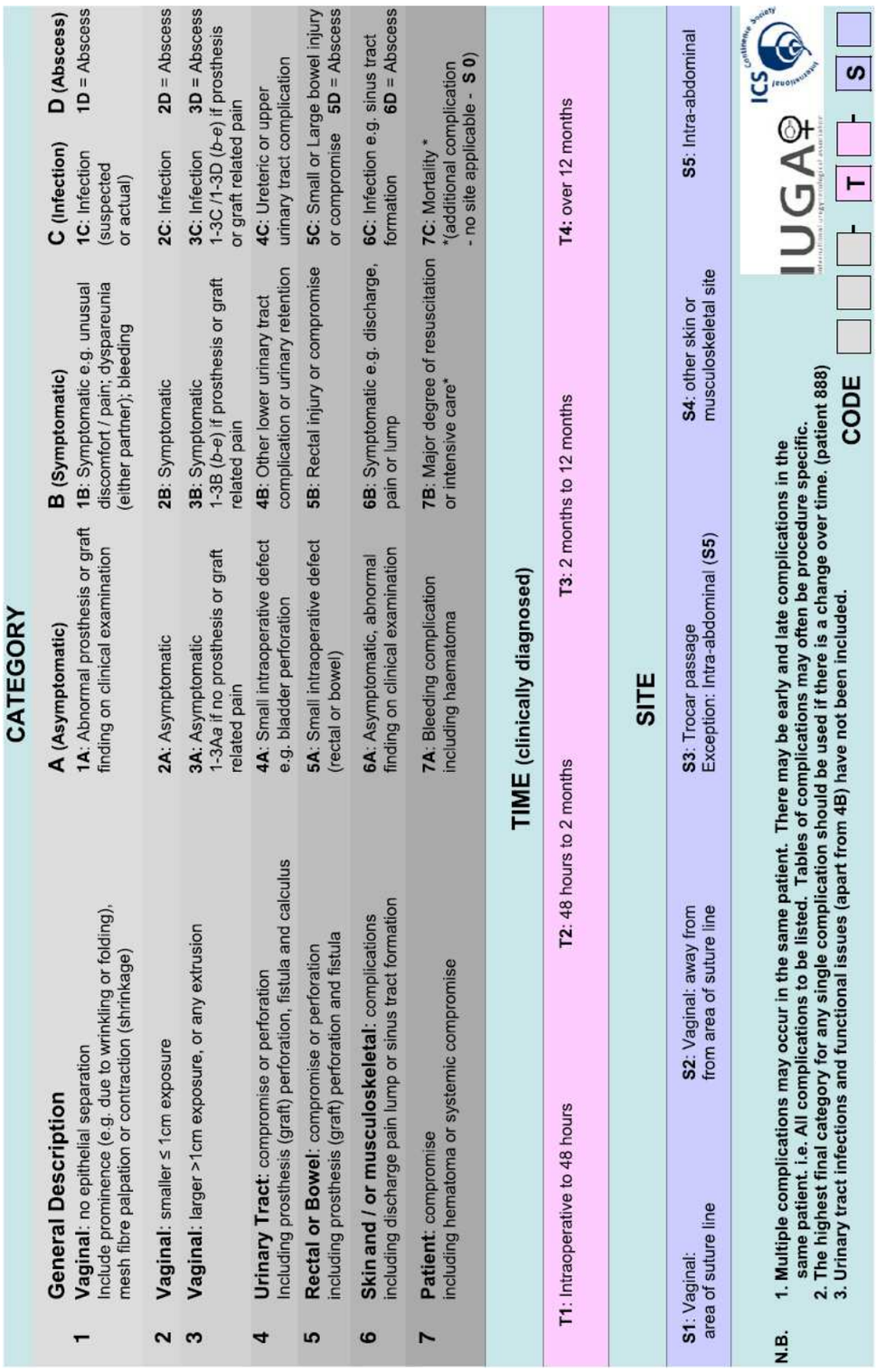

Fig. 4. A classification by category (C), time (T), and site (S) of complications directly related to the insertion of prostheses (meshes, implants, tapes) or grafts in female pelvic floor surgery **(Haylen et al, 2011).**

2.4.1 Intraoperative and early postoperative complications

Bladder perforation: occur during trocar passage in the retropubic space, it is a common intraoperative complication with reported rates of 0.7% to 24%. **(Laurikainen et al, 2007; Andonian et al, 2005)**. Incidence of perforation increases with poor surgeon experience with the procedure or in recurrent cases. Bladder perforation is suspected intraoperatively by observation of hematuria after trocar passage and diagnosed by cystoscopy. Perforation is easily treated by correct reinsertion of the trocar and catheter drainage for 2–4 days. TOT avoids the needle passage in the retropubic space, and hence bladder perforation is much lower than that of TVT.

Bleeding and retro-pubic hematoma: ranges from 0.7% to 8% **(Laurikainen et al, 2007; Rezapour et al, 2001c)** and in majority of cases minor bleeding occur during vaginal dissection and easily controlled. Sometimes excessive bleeding may lead to retropubic hematoma formation usually arises from pelvic floor veins, epigastric, external iliac or obturator vessels injury due to inadvertent trocar passage if laterally directed or externally rotated during the course of insertion. Hematomas size < 100 ml usually asymptomatic, between 100 - 200 ml cause moderate pain, while those >300 ml associated with severe pain and require surgical evacuation of Retzius space **(Flock et al, 2004)**. As perforation, bleeding is not a common complication in TOT procedures, with reported rate 0% to 2% **(Barber et al, 2006; Costa et al, 2004)**.

Bowel perforation: a very rare (< 0.007%) **(Costantini et al, 2007)** but serious complication and may be fatal. A recent review revealed 7 deaths that occurred after TVT placement of which 6 were associated with bowel injury **(Nygaard and Heit, 2004)**. Bowel perforation is not reported with TOT procedures. Risk factors for bowel injury include previous pelvic and abdominal surgery due to presence of adhesions in the retropubic space.

2.4.2 Late postoperative complications

De novo urgency: The rate of de novo urgency after midurethral slings placement as reported in literature ranges from 7.2% to 25% **(Costantini et al, 2007).** The mechanisms of de novo urgency after midurethral slings procedures are poorly understood. Combined outlet obstruction and urethral irritation by the sling has commonly been used as an explanation. TOT procedure is usually associated with a lower rate of de novo urgency than TVT **(Juanos et al, 2011)**. Meanwhile, such complication usually does not improve by time. Holmgren et al reported 14.5% of de novo urgency after long term follow-up of 5.2 years after TVT **(Holmgren et al, 2007)**.

Groin and thigh pain: On the other hand, TOT procedure has a significant risk of post-operative groin and thigh pain. This pain was observed with range of 5% to 26%. **(Meschia et al, 2007; Dobson et al, 2007)**. However, the pain is usually transient and resolves spontaneously within a few months in most of cases. The exact etiology of this pain remains unknown but it may be related to the tape's presence in the adductor muscles or the foreign body reaction to the tape lying in proximity to peripheral obturator nerve branches or secondary to the trauma to the obturator membrane and muscles during the procedure.

Bladder Outlet Obstruction: Postoperative obstruction is another challenging complication after a mid urethral sling procedure which varies from urinary retention (temporary or permanent), difficulty emptying or a weak urinary stream. Obstruction usually arises from excessive tension placed over the midurethra by the tape. The reported rates of postoperative obstruction after TVT range from 1.9% to 19.7% **(Abouassaly et al, 2004; Barber et al, 2006)**, and after TOT the rates actually vary from 0% to 15.6% **(Fischer et al, 2005; Delorme et al, 2004)**. Although urine retention and voiding dysfunction are thought to be less common after TOT approach, a recent multicenter randomized trial did not reveal significant differences in postoperative urinary retention between the TVT and TOT (6% and 3%, respectively) **(Barber et al, 2008).** Early postoperative transient urinary retention could be treated with intermittent sterile self-catheterisation or indwelling catheter and usually resolve spontaneously within 12 wk with restoration of complete bladder emptying in the majority of cases. If no improvement occur, early simple sling lysis should be considered or suburethral tape transaction.

Genitourinary erosion: it is the most frequent and distressing complication after synthetic midurethral sling operations. Costantini and colleagues reported erosion rates after midurethral sling operations based on ranges as reported in the literatures a range from 0.7% - 33%, 2.7% - 33% and 0.5% - 0.6% for vaginal, urethra and urinary bladder erosion respectively **(Costantini et al, 2007)**.

The etiology of the erosion is multifactorial and includes inadequate closure of vaginal wall incision, extensive or incorrect plane of dissection, wound infection, mesh rejection, early sexual activity, tape rolling and abnormal vaginal epithelium i.e. atrophic, scarred or otherwise compromised vaginal mucosa as in post-menopausal women or after previous vaginal surgery and unrecognized vaginal laceration injury during trocar passage. The sling material also plays an important role in this complication.

Patients with genitourinary erosion may be asymptomatic discovered on routine follow-up or presented with a group of symptoms which raise the suspicion of its diagnosis such as pain, dyspareunia, dysuria, discharge and/or bleeding from the urethra or vagina or tape palpable to the patient or partner. Hammad et al, reported that 35% of vaginal erosions were asymptomatic and erosion was discovered on routine follow-up **(Hammad et al, 2005)**. Kobashi et al seemed to confirm these data. In > 90 women who received a polypropylene mesh for the treatment of SUI, 3 developed vaginal erosion, but only 1 had symptoms such as pain, discomfort during sexual activity, and vaginal discharge and erosion was discovered during a routine check-up **(Kobashi et al, 2003)**. Most cases occur in the first few months after surgery but they can also happen much later.

Mesh erosion may be treated with conservative measures or surgically treated depends on the erosion site and size, mesh material, and local tissue condition. Surgical approach ranges from partial simple excision of the exposed mesh to surgical exploration for total graft removal and tissue reconstruction with a Martius flap.

Conservative management with observation might be a viable option if erosion is limited to the vagina and the sling were made of autologous, allograft and new, loosely woven polypropylene material because the latter provides large interstices, which favour tissue ingrowth and healing **(Duckett and Constantine, 2000)**. While some authors stated that

polypropylene tape erosion should be treated with complete mesh removal, without regard to erosion site, size, or local tissue condition **(Sweat et al, 2002)**. Vaginal erosion of synthetic materials, such as polyester and silicone slings, should also be treated with mesh removal because epithelialisation over these materials is unlikely **(Duckett and Constantine, 2000; Stanton, Brindley and Holmes, 1985).**

If the vaginal erosion is small (<1 cm) and local tissue does not appear infected, spontaneous healing by epithelialisation may occur in 6 to 12 weeks with pelvic rest alone **(Kobashi and Govier, 2003)**. If conservative management is unsuccessful or the erosion is (>1 cm), the exposed mesh may be excised with the patient under local anesthesia with vaginal closure after the edges have been freshened. Erosions with copious vaginal discharge or if local tissue appears to be infected may require more extensive resection of the mesh. Surgery is recommended when erosion involves the lower urinary tract (bladder or urethra), independently of sling materials **(Clemens et al, 2000; Duckett and Constantine, 2000)**. A recent meta-analysis of polypropylene midurethral slings revealed a possible trend toward increased erosion rates after TOT approach (OR 1.5, 95% CI 0.51–4.4) **(Latthe et al, 2007)**.

Although rare, erosion of mesh into the urethra can occur. A recent large retrospective series of TVT revealed urethral erosion in 0.3% of cases **(Karram et al, 2003)**.

With the new classification system of IUGA and ICS the description of the complications related to midurethral slings especially genitourinary erosion now become standardized and easy as shown in some the following reported cases of complication related to the use of midurethral tapes (figures 5, 6, 7)

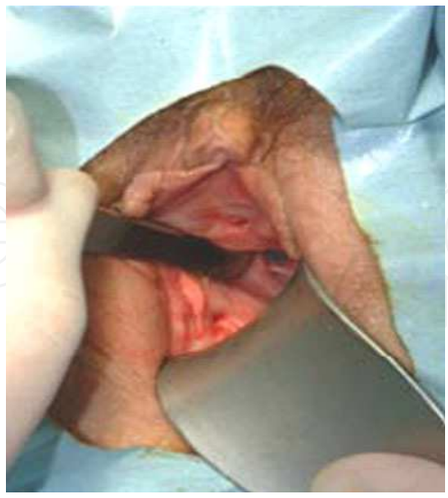

Fig. 5. 52 year old female underwent a transobturator tape. At 6 weeks, she was cured of her USI and reported no vaginal discharge. Vaginal examination revealed a smaller mesh exposure away from vaginal suture line. Classification: 2A T2 S2 **(Haylen et al, 2011)**

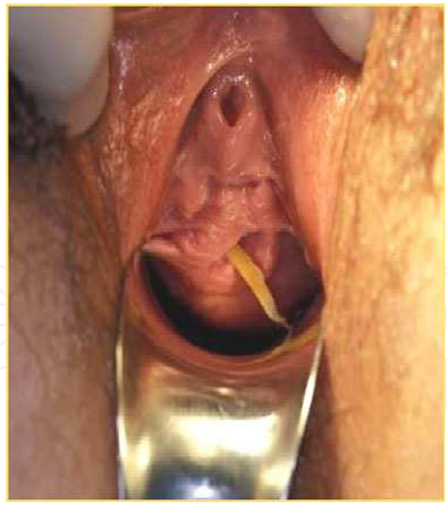

Fig. 6. A 47-year-old woman underwent a transoburator tape for USI. At 5 months follow-up, she reported vaginal discharge. Clinically she was febrile at 38°C with a large sling extrusion as depicted. Classification: 3C T3 S1 **(Haylen et al, 2011)**

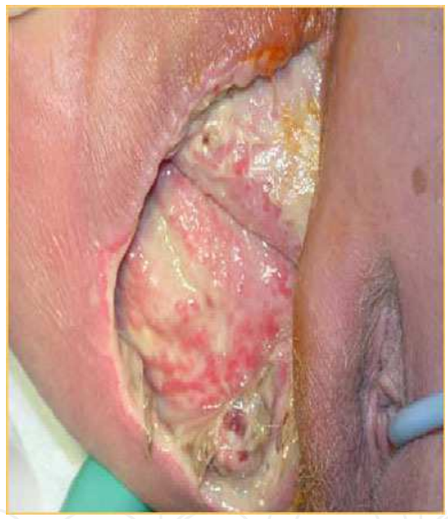

Fig. 7. 65-year-old with urinary incontinence underwent a multifilament transobturator sling. At 14 months follow up, she experienced severe pelvic pain and vaginal discharge. Clinical examination revealed hyperthermia to 40°C, (i) sling exposure at right vaginal sulcus and (ii) severe cellulitis in the genito-crural fold. Classification: 3C T4 S2; (ii) 6C T4 S3 **(Haylen et al, 2011)**

3. Use of biodegradable materials

3.1 Introduction

The perfect implant material currently is not available yet, but in general surgery there is now a consensus, that low weight, large pore (macroporus), monofilament synthetic materials are preferable. However, still serious local complications (e.g. erosion and infection) may occur and related to an increased foreign body reaction. Subsequently,

biologic implants were introduced in an effort to reduce the local complications associated with synthetic materials without compromising the surgical results.

Biological xenograft is a mammalian extracellular matrix (ECM) composed of laminin, fibrinectin, elastin, and collagen. Tissue sources from which xenografts are chosen include: porcine (small intestine, dermis), bovine (pericardium, fetal, dermis) and equine**.** Collagen based implants can either be cross-linked or not. Cross-linking protects the implant against degradation by collagenases, so that they remain intact very long, if not ever. At present, most xenogenic materials are from porcine source and it is the most commonly used, as bovine material became less acceptable. Production is strictly controlled by Food and Drug Administration (FDA) guidelines, which include knowledge of the animal herd, vaccination status, feed source, abattoir approval and bovine spongiform encephalopathy clearance **(Deprest et al, 2006).**

We will discuss below the role of Small intestinal submucosal (SIS) graft as a futuristic biodegradable implant to substitute synthetic slings in the treatment of female SUI.

3.2 Small intestinal submucosal (SIS) graft

SIS xenograft is an acellular, nonimmunogenic, biodegradable, biocompatible, collagen matrix manufactured from porcine small intestinal submucosa, which could induce native tissue regeneration in various organs.

3.2.1 Clinical applications of SIS

SIS graft has gained popularity in the field of urogynecology and reconstructive surgery. Promising results have been reported with the use of SIS as a bladder and urethral substitute material in animals **(Kropp, 1998a; Kropp et al, 1998b; Chen, Yoo and Atala, 1999).** Also, SIS has been used in humans undergoing urogenital procedures such as cystoplasties, ureteral reconstructions, penile chordee, and even urethral reconstruction for hypospadias and strictures **(Dedecker et al, 2005; Atala et al, 1999; Le Roux, 2005; Kassaby et al, 2003; Sharma and Secrest, 2003; Liatsikos et al, 2001).** In the field of urinary incontinence, SIS has been used with encouraging results in treatment of postprostatectomy incontinence **(Jones et al, 2005a),** neuropathic incontinence **(Misseri et al, 2005),** and SUI **(Wiedemann and Otto, 2004; Rutner et al, 2003; Jones et al, 2005b; Farahat et al, 2009).** Practical concerns regarding the use of the SIS implant in clinical practice: The first practical concern is related to the graft biocompatibility and how the tissue would react to the implant. The second practical concern is related to the biomechanical properties of the SIS sling and its suitability for curing SUI **(Farahat et al, 2009).**

3.2.2 Graft biocompatibility

SIS is made by a way that all cells responsible for an eventual immune response are removed, but the ECM and natural growth factors are left intact. It contains collagen, growth factors TGF-beta and FGF-2 **(Wiedemann and Otto, 2004)**. Many clinical trials and histopathological studies support the fact that the SIS graft has excellent biocompatibility as evidenced by lack of significant immunological reaction, foreign body reaction, and chronic inflammatory reaction (figure 8). In addition, the SIS sling is well known for its strength,

durability, and resistance to infection **(Badylak, 2004; Jankowski, et al, 2004; Wiedemann and Otto, 2004; Rutner et al, 2003).**

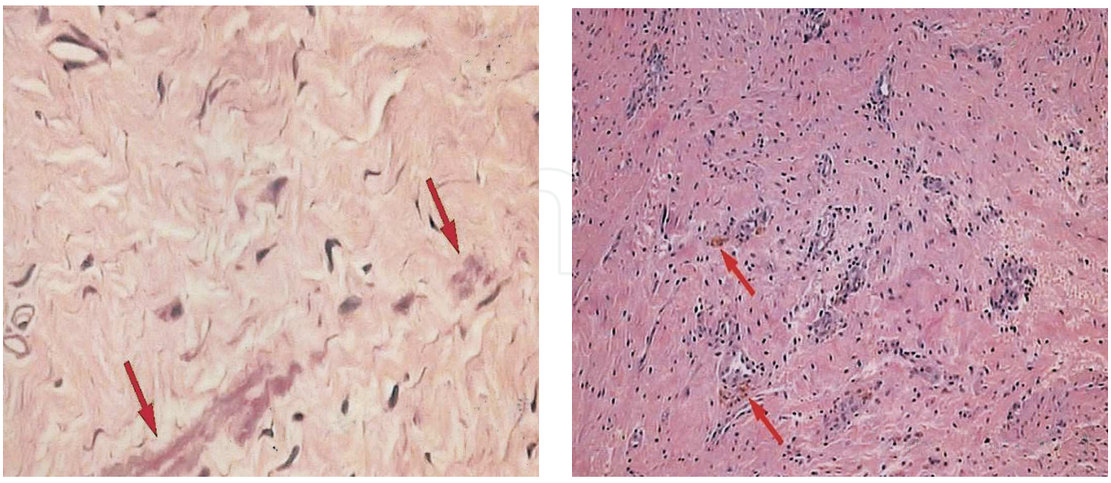

Fig. 8. First histopathological results for SIS pubovaginal slings show: submucosal biopsy with A) minimal SIS residues (red arrows) - B) minimal chronic inflammatory infiltration **(Wiedemann and Otto, 2004)**.

3.2.3 Biomechanical properties

SIS is degraded in 4 to 12 weeks by a "constructive" remodeling process that replaces the graft gradually by host connective tissue **(Clarke et al, 1996; Prevel et al, 1995).** Tensiometric strength initially decreases down to 45% 10 days after implantation, but by 1 month it is identical to that of the native tissue **(Badylak et al, 2001).** The task of the SIS sling is mainly to act as a scaffold that allows in-growth and structural organization of the native host tissue. The implant actively supports connective and epithelial tissue ingrowth and differentiation, as well as deposition, organization, and maturation of ECM components that characterize site-specific tissue remodeling. This phenomenon has been called *smart tissue remodeling* **(Badylak, 1993)** and it is important to note that the balance between implant degradation and host incorporation results in a dynamic implant strength response. The strength of the SIS sling is expected to be the net result between SIS degradation and tissue regeneration. Degradation rates that are too rapid or reconstruction rates that are too slow can result in transient minimum strengths that are below the critical threshold. Supposedly, this carries increased risk of recurrence of incontinence symptoms after an initial successful anti-incontinence surgery **(Jankowski et al, 2004).**

3.2.4 Outcome of the SIS Sling

The suitability of the SIS sling is better reflected by the clinical outcome. In terms of clinical efficacy in correction of SUI, the results of different studies showed that SIS was able to provide a strong suburethral support and durable clinical results (table 7).

Rutner et al, reported in their work utilizing SIS as a pubovaginal slings in the treatment of female SUI that all patients had minimal local reactions and pelvic pain; no cases of erosion

or extrusion were noted. The authors also performed a biopsy for cases which required reoperation for correction of incontinence. They observed absence of the implanted graft on gross examination. Microscopically, only a few remnants of the SIS (< 0.4 mm) could be found **(Rutner et al, 2003)**. Farahat et al, reported also using SIS as TVT (figure 9) in the treatment of female SUI that the SIS sling was accepted nicely by the tissue after 12 months. No erosion, extrusion, or severe inflammatory reactions were noted. Most reactions were mild and usually observed as early as 10 days or as late as 45 days after the procedure. Most reactions were well tolerated and resolved spontaneously **(Farahat et al, 2009).**

Author	Number of patients	Patient group	Technique of SIS graft placement	Treatment outcomes (% cured)
Rutner et al, 2003	152	SUI	Pubovaginal slings + bone anchoring	93.4%
Jones et al, 2005b	34	SUI	TVT	80%
Farahat et al, 2009	17	SUI	TVT	82.3 %

Table 7. Treatment outcome of SIS graft.

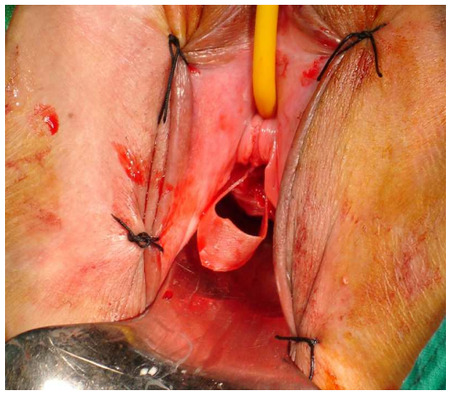

Fig. 9. SIS as TVT sling **(Farahat et al, 2009).**

3.2.5 SIS graft complications

However, unlike most reports confirming the safe use of the SIS graft in the treatment of SUI, Ho et al **(Ho et al, 2004)** reported inflammatory reactions (figure 10) at the abdominal incision (but none at the vaginal incision) in 6 out of 10 patients treated with the 8-ply SIS sling. Most cases resolved with minimal or no intervention. Abscess formation was observed in 2 patients.

John et al **(John et al, 2008)** used both the Cook 4-ply and the 8-ply Stratasis- TF in 16 women with SUI. They reported intense inflammatory complications in 5 patients (nearly one third). Most of the inflammatory reactions were related to the suprapubic region rather than near the vagina or urethra. Four of the 5 patients with complications had the new 8-ply Stratasis-TF. The remaining patient had the 4-ply SIS; however, this patient had a concomitant extensive pelvic floor reconstruction by a gynecologist prior to placement of the SIS sling. Apparently adding more layers to the SIS graft material may have a contributing

role in inflammatory reactions, because these high complication rates were not observed with the older 1-ply and 4-ply formulations **(John et al, 2008; Santucci and Barber, 2005)**. No study till now compared the 1-ply, 4-ply, and 8-ply SIS grafts in humans.

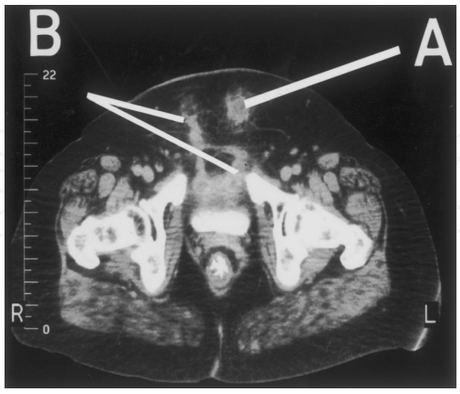

Fig. 10. CT shows inflammation of subcutaneous tissue (*A*) and along arms of the SIS sling **(Ho et al, 2004).**

The SIS graft material is well accepted by the host tissue, and considered safe and effective with lower incidence of erosion and infection than the synthetic midurethral slings. However, Long period of follow up are still required to support the durability of these preliminary results.

4. Stem cell therapy

4.1 Introduction

Stem cells therapy for the regenerative repair of the deficient rhabdosphincter has been the most recent advance in incontinence research. The ultimate goal has been to achieve a permanent cure for SUI by restoration of the intrinsic and extrinsic urethral sphincter and the surrounding connective tissue, including peripheral nerves and blood vessels. Overall, the aim of stem cell therapy is to replace, repair, or enhance the biological function of damaged tissue or organs.

4.2 Cell source

There are two general types of stem cells potentially useful for therapeutic treatment, embryonic stem cells (ESCs) and adult stem cells **(Novara and Artibani, 2007).** The practical use of ESCs has ethical limitations inherent to cell harvesting from fetal tissue and histocompatibility problems. **(Edwards, 2007)**. In contrast, adult stem cells have no significant ethical issues related to their use and have more limited differentiation potential which makes them safer. Tissues engineering therapies are based on autologous multipotent stem cells, of which bone marrow stromal cells are most often used. The bone marrow stromal cells contain mesenchymal stem cells (MSCs) that are capable of differentiating into into adipogenic, osteogenic, chondrogenic and myogenic cells **(Pittenger et al, 1999; Ferrari et al, 1998; Prockop, 1997; Dezawa et al, 2005),** However, bone marrow compartment usage has significant limitations due to its painful nature which usually require general or spinal

anesthesia, and low number of (MSCs) are obtained **(Pittenger et al. 1999**). Muscle derived stem cells (MDCs) and adipose derived stem cells (ADSCs) are advantageous because they can be easily obtained in large quantities under local anesthesia **(Rodríguez et al,. 2006; Strem et al, 2005).**

4.2.1 Bone marrow-derived stem cells (BMSCs)

Bone marrow-derived stem cells (BMSCs) have been most widely studied of all mesenchymal stem cells. BMSCs have been used for the regeneration of cardiac muscle **(Sadek et al, 2009),** bladder detrusor muscle **(Kanematsu et al, 2005),** anal sphincter muscle **(Lorenzi et al, 2008)**, and many other structures **(El Backly and Cancedda, 2010)**. Drost et al. in a pilot study transplanted autologous BMSCs into injured rat urethral sphincter. The cultured BMSCs were injected periurethrally 1 week after the urethral injury. Both histological and immunohistochemistry evaluation showed that transplanted BMSCs survived and differentiated into peripheral nerve cells and striated muscle cells compared to the cell-free group **(Drost et al, 2009).**

4.2.2 Adipose-derived stem cells

Adipose derived stem cells (ADSCs), is a pluripotent cells which have the ability to differentiate into cells of the same and of another germ layer, such as adipogenic, chondrogenic, neurogenic, myogenic and osteogenic cells **(Roche et al, 2010).** In the field of urinary incontinence ADSCs are of special interest for mesodermal and neuronal regeneration and to promote revascularization. Bacou et al, reported that transplantation of ADSCs increases mass and functional capacity of damaged skeletal muscle. They can express specific striated muscle markers (eg, desmin, myod1, myogenin, myosin heavy chain), form multinucleated cells characteristic of myotubules **(Bacou et al, 2004)**. Also, ADSCs can express nerve growth factor at the time of neural differentiation. Zhang et al, reported that neural-differentiated ADSCs present glial characteristics and promote nerve regeneration, after 7 days of transplantation in a rat model in vivo **(Zhang et al, 2010).** Periurethral injection of ADSCs in an immune-competent, incontinent rat model with SUI, exhibited in vivo differentiation into smooth muscle cells and improved urethral resistance **(Lin et al, 2010).** Fu et al. injected predifferentiated ADSCs with 5-azacitidine periurethrally into incontinent rats. A significant difference in bladder capacity and leak point pressure was observed after 3 months of follow-up between the control group and the pretreated group. Also increased number of myoblasts under the mucosa and expression of α-smooth muscle actin was observed 3 months after implantation **(Fu et al, 2010).**

4.2.3 Muscle derived stem cells (MDCs)

Muscle-derived stem cells (MDSCs) can naturally differentiate to multinucleated muscle fibers and display stem cell characteristics **(Seale and Rudnicki, 2000).** MDSCs have also the ability to undergo long-term proliferation, self-renewal, and multipotent differentiation, including differentiation toward endothelial and neuronal lineages **(Lee et al, 2000; Qu-Petersen et al, 2002).** Cannon et al, reported that MDSCs are capable of restoring muscular contraction of the urethral sphincter 2 weeks after injection **(Cannon et al, 2003)**. MDSCs

also may improve neurogenic bladder dysfunction in animal models by reconstitution of damaged peripheral nerve cells (eg, Schwann cells, perineum) and vascular cells (eg, vascular smooth muscle cells, pericytes, endothelial cells) **(Nitta et al, 2010)**. For the treatment of SUI myoblasts have been injected to the striated urinary sphincter of a pig model. The animals have shown an increase in urethral pressure profile and muscular myofibrils **(Mitterberger et al, 2008).**

Advantages of MDSCs injection therapy over conventional treatments for SUI:

1. MDSCs that are derived from the incontinent patient (autologous cell transplantation) will not cause an immunogenic or allergic reaction **(Yokoyama et al, 2001a; Lee et al, 2004).**
2. MDSCs are uniquely different from fibroblasts and smooth muscle cells since MDSCs will fuse to form post-mitotic multinucleated myotubes. This limits persistent expansion and risk of obstruction that may occur with other cell sources such as fibroblasts **(Kwon et al, 2006).**
3. MDSCs form contractile myotubes and myofibers that become innervated into the host muscle by activating the intrinsic nerve regeneration and formation of neuromuscular junctions. Therefore, they can not only serve as a bulking agent, but they are also physiologically capable of improving urethral sphincter function **(Chancellor et al, 2000; Yokoyama et al, 2001b; Huard et al, 2002; Hoshi et al, 2008).**

4.3 Isolation of muscle-derived stem cells in humans

Mitterberger M et al. and Strasser H et al. reported biopsy in the right or left upper limb (biceps muscle) to obtain 0.32 to 2 cm3 of muscle tissue (figure 11). At the same time, 250 mL of blood were drawn for autologous serum **(Mitterberger et al, 2008; Strasser et al, 2007b).**

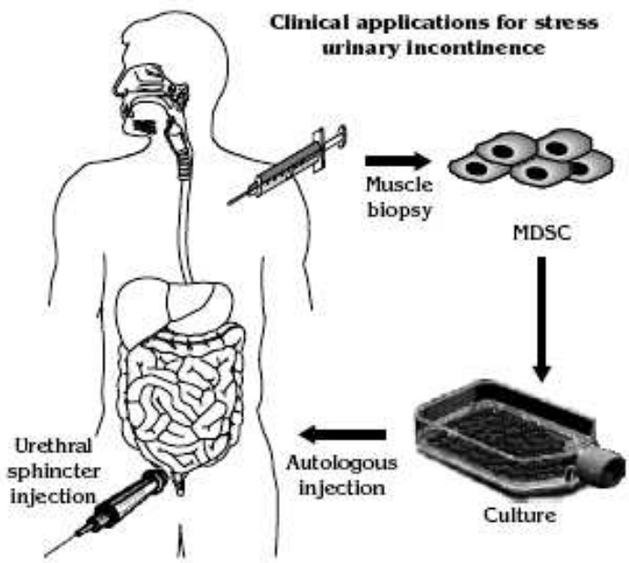

Fig. 11. Diagram showing autologous stem cell injection therapy for SUI. Autologous stem cells are obtained with a biopsy of tissue, the cells are dissociated and expanded in culture, and the expanded cells are implanted into the same host. MDSCs = muscle derived stem cells **(Jankowski et al, 2008)**

Myoblasts and fibroblasts are separated from connective tissue by centrifugation and enzymatic digestion with type I collagenase. Myoblasts are cultured in Ham's F10 medium supplemented with 20% autologous serum, and fibroblasts in DMEM (Dulbecco's modified Eagle medium) and Ham's F12 medium with 10% autologous serum. Cells are accepted when they reach 80% confluence. After 6-8 weeks in culture, fibroblasts and myoblasts are harvested separately by tripsinization and washing with centrifugation. Cell quality is assessed by immunohistochemistry, immunofluorescence, and fluorescence-activated cell sorting. Anti-desmin, vimentin, CD56, CD34 and ASO2 antibodies are used to differentiate myoblasts from fibroblasts. Fusion capacity of myoblasts is measured in differentiation medium without autologous serum to assess their viability, and cells are counted in each culture using the Neubauer chamber (figure 12). Once the cells are "harvested", they are transferred in adequate numbers to sterile syringes, separating myoblasts from fibroblasts. Myoblasts are suspended in 1.4 mL of DMEM/F12 with 20% autologous serum, and fibroblasts in 1 mL of DMEM/F12 with 20% autologous serum mixed with collagen as transport material to prevent cell migration from the injection site, because fibroblasts are mobile following application. Collagen has been shown to stabilize cells so that they remain in place and produce their own extracellular matrix **(Strasser et al, 2007b).**

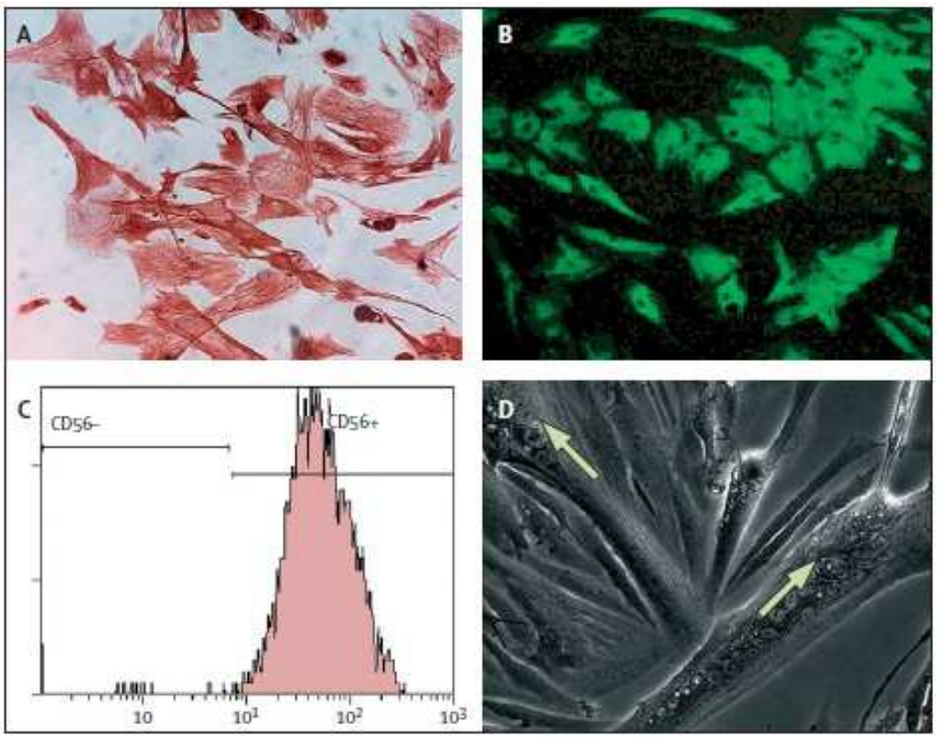

Fig. 12. Characterisation of cells: (A) Immunohistochemical image of human myoblasts stained with antidesmin antibodies. (B) Immunofl uorescence image of human fibroblasts stained with antivimetin antibodies. (C) Fluorescent antibody cell sorter (FACS) analysis of myoblast cell culture showing that 97% of the myoblasts are positive for CD56 antibodies. (D) Phase-contrast microscope image of multinucleated myotubes (marked with arrows) that have formed after fusion of mononucleated myoblasts in diff erentiation medium **(Strasser et al, 2007b).**

4.4 Transurethral ultrasound (TUUS) guided injection of stem cell

At the beginning of the cell injection, the TUUS probe (8 Ch, 15– 20 MHz) was carefully inserted into the urethra. The urethral wall and the rhabdosphincter were visualized. A specially designed patent-pending injection device was used for precisely adjusted injection of several small portions. First, 15–18 portions of the myoblast suspension were injected directly into the omega-shaped rhabdosphincter at two different levels. Then, 25–30 depots of the fibroblast/collagen suspension were injected into the submucosa circumferentially at three levels (Figure 13). After implantation of the cells the patients were instructed to perform PFT and FES for 4 wk postoperatively to support integration of the cells and to improve formation of new muscle tissue **(Strasser et al, 2007).**

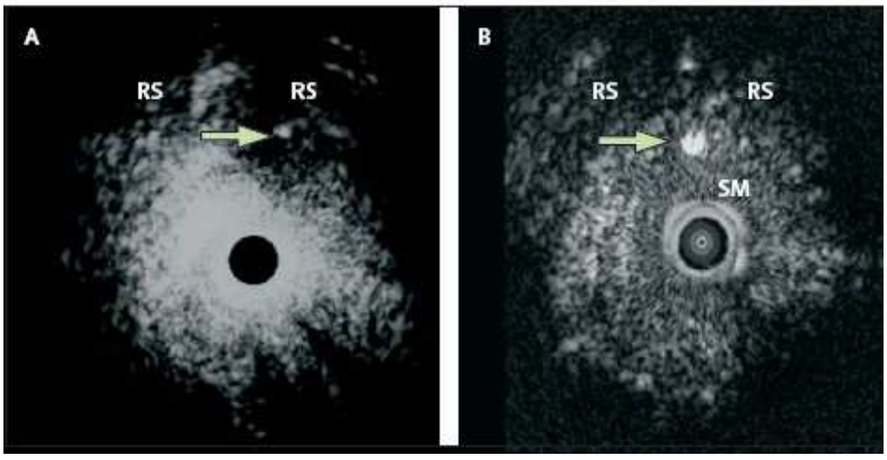

Fig. 13. Cross-sectional ultrasonography images of the urethra and the rhabdosphincter (A) The tip of the needle (marked with an arrow) is positioned at the inner aspect of the rhabdosphincter (RS) for injection of myoblasts. (B) The tip of the needle is placed at the outer aspect of the submucosa (SM) for injection of fibroblasts **(Strasser et al, 2007b).**

4.5 Clinical results of stem cell therapy

Few human trials have been conducted using autologous derived stem cells in the treatment of female SUI, which mainly involved the use of MDSCs. Stem cell therapy, shows an early encouraging results and these results suggest the ability of pure cellular therapy to treat female SUI (Table 8).

Strasser et al. conducted the first clinical experiments in women with SUI. 42 women suffering from SUI were recruited and subsequently treated with transurethral ultrasonography- guided injections of autologous myoblasts and fibroblasts obtained from skeletal muscle biopsies. After a follow-up of 12 months incontinence was cured in 39 women **(Strasser et al, 2007a)**. In another trial 42 women were randomly assigned to receive transurethral ultrasonography guided injections of autologous myoblasts and fibroblasts, at 12-months' follow-up, 38 of the 42 women injected with autologous cells were completely continent **(Strasser et al, 2007b).** Mitterbarger et al. studied 20 female patients suffering from SUI after TUUS guidance injection of autologous myoblasts and fibroblasts. At 1 year follow-up 18 patients were cured and 2 patients improved. At 2 years after therapy 16 of the

18 patients presented as cured, 2 others were improved, and 2 were lost to follow-up **(Mitterbarger et al, 2008a)**. Other studies have been reported early good results for stem cell injection in female with SUI **(Carr et al, 2008; Herschorn et al, 2010).**

Not only stem cell injection therapy is limited to the field of female SUI, however its usage has been extended to treat males with post-prostatectomy incontinence **(Mitterbarger et al, 2008b; Yamamoto et al, 2010).**

Clinical study	Patients (n)	Patient group	Stem cell source	Symptomatic improvement
Strasser et al, 2007a	63 (42) women (21) men	SUI	MDSC, fibroblasts	85%
Strasser et al, 2007b	42 women	SUI	MDSC, fibroblasts	91%
Mitterbarger et al, 2008a	20 women	SUI	MDSC, fibroblasts	90% at 1 yr 89% at 2 yr
Carr et al, 2008	8 women	SUI	MDSCs	63%
Herschorn et al, 2010	29 women	SUI	MDSC	50% cured

Table 8. Results of the first clinical studies have recently become available**.**

In general, stem cell injection therapy into the middle urethra may restore the contractile response of the striated muscle and rhabdosphincter. Early results were encouraging with no reported serious side effects. Autologous MDSCs and ADSC pure injection therapy may be a promising treatment to restore urethral sphincter function. These promising early clinical results warrant further evaluation to validate results, determine durability and focus on safety and possible adverse reactions.

5. References

Abrams P, Cardozo L, Magnus F, et al. (2002). The standardization of terminology of lower urinary tract function: report from the standardization sub-committee of the International Continence Society. *Neurourol Urodynam*, Vol. 21, pp. 167–178

Abouassaly R, Steinberg JR, Lemieux M, et al. (2004). Complications of tension-free vaginal tape surgery: a multi-institutional review. *BJU Int*, Vol. 94, pp. 110

Aigmueller T, Trutnovsky G, Tamussino K, et al. (2011). Ten-year follow-up after the tension-free vaginal tape procedure. *American Journal of Obstetrics and Gynecology*. Article in Press. doi:10.1016/j.ajog.2011.07.010

Amid P. (1997). Classification of biomaterials and their relative complications in an abdominal wall hernia surgery. *Hernia*, Vol. 1, pp. 15–21

Andonian S, Chen T, St-Denis B, et al. (2005). Randomized clinical trial comparing suprapubic arch sling (SPARC) and tension-free vaginal tape (TVT): one-year results. *Eur Urol*, Vol. 47, pp. 537

Angioli R, Plotti F, Muzii L, et al. (2010). Tension-Free Vaginal Tape Versus Transobturator Suburethral Tape: Five-Year Follow-up Results of a Prospective Randomised Trial. *European Urology*, Vol. 58, pp. 671–677

Atala A, Guzman L, Retik AB. (1999). A novel inert collagen matrix for hypospadias repair. *J Urol*, Vol. 162, pp. 1148–51

Bacou F, el Andalousi RB, Daussin PA, et al. (2004). Transplantation of adipose tissue-derived stromal cells increases mass and functional capacity of damaged skeletal muscle. *Cell Transplant*, Vol. 13, pp. 103–111

Badylak SF. (1993). Small intestinal submucosa (SIS): a biomaterial conducive to smart tissue remodeling. In: Bell E, ed. *Tissue Engineering: Current Perspectives,* 179-189, Cambridge, MA: Burkhauser Pub

Badylak SF, Kokini K, Tullius B, et al. (2001). Strength over time of a resorbable bioscaffold for body wall repair in a dog model. J Surg Res, Vol. 99, pp. 282–287

Badylak SF. (2004). Xenogeneic extracellular matrix as a scaffold for tissue reconstruction. *Transplant Immunology, Vol.* 12, pp. 367-377

Barber MD, Gustilo-Ashby AM, Chen CC, et al. (2006). Perioperative complications and adverse events of the MONARC transobturator tape, compared with the tension-free vaginal tape. *Am J Obstet Gynecol*, Vol. 195, pp. 1820

Barber MD, Kleeman S, Karram MM, et al. (2008). Transobturator tape compared with tension-free vaginal tape for the treatment of stress urinary incontinence: a randomized controlled trial. Obstet Gynecol, Vol. 111, pp. 611

Botlero R, Urquhart DM, Davis SR, et al. (2008). Prevalence and incidence of urinary incontinence in women: review of the literature and investigation of methodological issues. *Int J Urol*, Vol. 15, pp. 230–4

Cannon TW, Lee JY, Somogyi G, et al. (2003). Improved sphincter contractility after allogenic muscle-derived progenitor cell injection into the denervated rat urethra. *Urology*, Vol. 62, pp. 958–963

Carr LK, Steele D, Steele S, et al. (2008). 1-year follow up of autologous muscle-derived stem cell injection pilot study to treat stress urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct, Vol.* 19; pp. 881–883.

Chen F, Yoo JJ, Atala A. (1999). Acellular collagen matrix as a possible ''off the shelf'' biomaterial for urethral repair. *Urology*, Vol. 54, pp. 407–9

Cindolo L, Salzano L, Rota G, et al. (2004). Tension-free transobturator approach for female stress urinary incontinence. *Minerva Urol Nefrol*, Vol. 56, pp. 89–98

Clarke KM, Lantz GC, Salisbury SK, et al. (1996). Intestine submucosa and polypropylene mesh for abdominal wall repair in dogs. *J Surg Res*, Vol. 60, pp. 107–114

Clemens JQ, DeLancey JO, Faerber GJ, et al. (2000). Urinary tract erosions after synthetic pubovaginal slings: diagnosis and management strategy. *Urology*, Vol. 56, pp. 589–94

Chancellor MB, Yokoyama T, Tirney S, et al. (2000). Preliminary results of myoblast injection into the urethra and bladder wall: a possible method for the treatment of stress

urinary incontinence and impaired detrusor contractility. *Neurourol Urodyn,* Vol. 19, pp. 279–87

Costa P, Grise P, Droupy S, et al. (2004). Surgical treatment of female stress urinary incontinence with a trans-obturator-tape (T.O.T.) Uratape: short term results of a prospective multicentric study. *Eur Urol*, Vol. 46, pp. 102

Costantini E, Lazzeri M & Porena M. (2007). Managing Complications after Midurethral Sling for Stress Urinary Incontinence. *EAU - EBU update series*, Vol. 5, pp. 232-40

Daneshgari F, Kong W and Swartz M. (2008). Complications of Mid Urethral Slings: Important Outcomes for Future Clinical Trials. *The Journal of Urology*, Vol. 180, pp. 1890-1897

Dedecker F, Grynberg M, Staerman F. (2005). Small intestinal submucosa (SIS): prospects in urogenital surgery. *Prog Urol*, Vol. 15, pp. 405–7

Deffieux X, Donnadieu AC, Porcher R, et al. (2007). Long-term results of tension-free vaginal tape for female urinary incontinence: follow-up over 6 years. *Int J Urol*, Vol. 14, pp. 521–526

DeLancey JO. (1994). Structural support of the urethra as it relates urinary incontinence: the hammock hypothesis. *Am J Obstet Gynaecol*, Vol. 170, No. 20, pp. 1713

De Leval J. (2003). Novel Surgical Technique for the Treatment of Female Stress Urinary Incontinence: Transobturator Vaginal Tape Inside-Out. *European Urology*, Vol. 44, pp. 724–730

DeLorme E. (2001). Transobturator tape urethral suspension: mini-invasive procedure in the treatment of stress urinary incontinence in women. *Prog Urol,* Vol. 11, pp. 1306–1313

Delorme E, Droupy S, de Tayrac R, et al. (2004). Transobturator tape (Uratape): a new minimally-invasive procedure to treat female urinary incontinence. *Eur Urol*, Vol. 45, pp. 203

Deng DY, Rutman M, Raz S, Rodriguez LV. (2007). Presentation and management of major complications of midurethral slings: are complications under-reported? *Neurourol Urodyn*, Vol. 26, pp. 46–52

Deprest J., Zheng F. and Konstantinovic M, et al. (2006). The biology behind fascial defects and the use of implants in pelvic organ prolapse repair. Int Urogynecol J, Vol. 17, pp. S16–S25

Dobson A, Robert M, Swaby C, et al. (2007). Trans-obturator surgery for stress urinary incontinence: 1 year follow-up of a cohort of 52 women. *Int Urogynecol J Pelvic Floor Dysfunct,* Vol. 18, pp. 27–32

Drost AC, Weng S, Feil G, et al. (2009). In vitro myogenic differentiation of human bone marrow-derived mesenchymal stem cells as a potential treatment for urethral sphincter muscle repair. *Ann N Y Acad Sci,* Vol. 1176, pp. 135–143.

Duckett JRA, Constantine G. (2000). Complications of silicone sling insertion for stress urinary incontinence. *J Urol*, Vol. 163, pp. 1835–7

Dwyer PL. (2006). Evolution of biological and synthetic grafts in reconstructive pelvic surgery. *Int Urogynecol J*, Vol. 17, pp. S10–S15

Dezawa M, Ishikawa H, Itokazu Y, et al. (2005). Bone marrow stromal cells generate muscle cells and repair muscle degeneration. *Science, Vol.* 309, pp. 314–7

Edwards RG. (2007). A burgeoning science of embryological genetics demands a modern ethics. *Reprod Biomed Online*, Vol. 15, pp. 34–40

El Backly RM, Cancedda R: (2010). Bone marrow stem cells in clinical application: harnessing paracrine roles and niche mechanisms. *Adv Biochem Eng Biotechnol,* Aug 27 (Epub ahead of print).

Farahat Y, Eltatawy H, Haroun H et al: (2009). The Small Intestinal Submucosa (SIS) as a Suburethral Sling for Correction of Stress Urinary Incontinence: *UroToday International Journal,* Vol. 2/Iss 3/June doi:10.3834/uij.1944-5784.2009.06.02

Fischer A, Fink T, Zachmann S, et al. (2005). Comparison of retropubic and outside-in transoburator sling systems for the cure of female genuine stress urinary incontinence. *Eur Urol*, Vol. 48, pp. 799

Ferrari G, Cusella-De Angelis G, Coletta M, et al. (1998). Muscle regeneration by bone marrow-derived myogenic progenitors. *Science,* 279, pp. 1528–30

Flock F, Reich A, Muche R, et al. (2004). Hemorrhagic complications associated with tension-free vaginal tape procedure. *Obstet Gynecol*, Vol. 104, pp. 989

Fu Q, Song XF, Liao GL, et al. (2010). Myoblasts differentiated from adipose-derived stem cells to treat stress urinary incontinence. *Urology,* Vol. 75, pp. 718–723

Giberti C, Gallo F, Cortese P, et al. (2007). Transobturator tape for treatment of female stress urinary incontinence: objective and subjective results after a mean follow-up of two years. *Urology*, Vol. 69, pp. 703–707

Grise P, Droupy S, Saussine C, et al. (2006). Transobturator tape for stress urinary incontinence with polypropylene tape and outside-in procedure: Prospective study with 1 year of minimal follow-up and review of transobturator tape sling. *Urology*, Vol. 68, 759–763

Hammad FT, Kennedy-Smith A, Robinson RG. (2005). Erosions and urinary retention following polypropylene synthetic sling: Australasian survey. *Eur Urol*, vol. 47, pp. 641–7

Hannestad YS, Rortveit G, Sandvik H, et al. (2000). A community based survey of female urinary incontinnce: the Norwegian EPINCONT study. *J Clin Epidemiol*, Vol. 53, pp. 1150–7

Huard J, Yokoyama T, Pruchnic R, et al. (2002). Muscle-derived cell-mediated *ex vivo* gene therapy for urological dysfunction. *Gene Ther,* Vol. 9, pp. 1617–26

Haylen BT, Freeman RM, Swift SE, et al. (2011). An International Urogynecological Association (IUGA) / International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) & grafts in female pelvic floor surgery. *Int Urogynecol J*, Vol. 22, pp. 3–15

Herschorn S, Carr L, Birch C, et al. (2010). Autologous muscle-derived cells as therapy for stress urinary incontinence: A randomized blinded trial. *Neurourol Urodyn,* Vol. 29, pp. 243–326 [abstract]

Ho KL, Witte MN, Bird ET. (2004). 8-ply small intestinal submucosa tension-free sling: spectrum of postoperative inflammation. *J Urol, Vol.* 171, pp. 268-271

Holmgren C, Nilsson S, Lanner L, et al. (2007). Frequency of de novo urgency in 463 women who had undergone the tension-free vaginal tape (TVT) procedure for genuine

stress urinary incontinence – a long-term follow-up. *Eur J Obstet Gynecol*, Vol. 132, pp. 5 – 121

Hoshi A, Tamaki T, Tono K, et al. (2004). Reconstruction of radical prostatectomy-induced urethral damage using skeletal musclederived multipotent stem cells. Transplantation, Vol. 85, pp. 1617–1624

Jankowski R, Pruchnic R, Hiles M, et al. (2004). Advances toward tissue engineering for the treatment of stress urinary incontinence. *Rev Urol*, Vol. 6, pp. 51-57

Jankowski R, Pruchnic R, Wagner D et al. (2008). Regenerative Therapy for Stress Urinary Incontinence. *Tzu Chi Med J*, Vol. 20, pp. 169-176

John TT, Aggarwal N, Single AK, et al. (2008). Intense inflammatory reaction with porcine small intestine submucosa pubovaginal sling or tape for stress urinary incontinence. *Urology*, Vol. 72, pp. 1036-1039

Jones JS, Vasavada SP, Abdelmalak JB, et al. (2005a). Sling may hasten return of continence after radical prostatectomy. *Urology, Vol.* 65, pp. 1163-1167

Jones JS, Rackley RR, Berglund R, et al. (2005b). Porcine small intestinal submucosa as a percutaneous mid-urethral sling: 2-year results. *BJU Int,* 96, pp. 103-106

Juanos JL, Sanchez EB, Soler JP, et al. (2011). De novo urgency after tension-free vaginal tape versus transobturator tape procedure for stress urinary incontinence. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, Vol. 155, pp. 229-32

Kanematsu A, Yamamoto S, Iwai-Kanai E, et al. (2005). Induction of smooth muscle cell-like phenotype in marrow-derived cells among regenerating urinary bladder smooth muscle cells. *Am J Pathol,* Vol. 166, pp. 565–573.

Karram MM, Segal JL, Vassallo BJ, et al. (2003). Complications and untoward effects of the tension-free vaginal tape procedure. *Obstet Gynecol*, Vol. 101, pp. 929

Kassaby EA, Retik AB, Yoo JJ, et al. (2003). Urethral stricture repair with an off-the-shelf collagen matrix. J Urol, Vol. 169, pp. 170–3 Kobashi KC, Govier FE. (2003). Management of vaginal erosion of polypropylene mesh slings. *J Urol*, Vol. 169, pp.2242–3

Kropp BP. (1998a). Small-intestinal submucosa for bladder augmentation: a review of preclinical studies. *World J Urol*, Vol. 16, pp. 262–5

Kropp BP, Ludlow JK, Spicer D, et al. (1998b). Rabbit urethral regeneration using small intestinal submucosa onlay graft. Urology, Vol. 52, pp. 138–42

Kwon D, Kim Y, Pruchnic R, et al: (2006). Periurethral cellular injection: comparison of muscle-derived progenitor cells and fibroblasts with regard to efficacy and tissue contractility in an animal model of stress urinary incontinence. *Urology*, Vol. 68, pp. 449–454

Latthe P, Foon R and Toozs-Hobson P. (2007). Transobturator and retropubic tape procedures in stress urinary incontinence: a systematic review and meta-analysis of effectiveness and complications. *BJOG*, Vol. 114, pp. 522

Laurikainen E, Valpas A, Kivela A, et al. (2007). Retropubic compared with transobturator tape placement in treatment of urinary incontinence: a randomized controlled trial. *Obstet Gynecol*, Vol. 109, pp. 4

Le Roux PJ. (2005). Endoscopic urethroplasty with unseeded small intestinal submucosa collagen matrix grafts: a pilot study. *J Urol*, Vol. 173, pp. 140–3

Liapis A, Bakas P and Creatsas G. (2010). Efficacy of inside-out transobturator vaginal tape (TVTO) at 4 years follow up. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, Vol. 148, pp. 199–201

Liatsikos EN, Dinlec CZ, Kapoor R, et al. (2001). Ureteral reconstruction: small intestine submucosa for the management of strictures and defects of the upper third of the ureter. J Urol, Vol. 165, pp. 1719–23

Lin G, Wang G, Banie L, et al. (2010). Treatment of stress urinary incontinence with adipose tissue-derived stem cells. *Cytotherapy,* Vol. 12, pp. 88–95

Lee JY, Qu-Petersen Z, Cao B, et al. (2000) Clonal isolation of muscle-derived cells capable of enhancing muscle regeneration and bone healing. *J Cell Biol, Vol.* 150, pp. 1085–100

Lee JY, Paik SY, Yuk SH, et al. (2004) Long term effects of muscle-derived stem cells on leak point pressure and closing pressure in rats with transected pudendal nerves. *Mol Cells, Vol.* 18, pp. 309–313

Lorenzi B, Pessina F, Lorenzoni P, et al. (2008). Treatment of experimental injury of anal sphincters with primary surgical repair and injection of bone marrow-derived mesenchymal stem cells. *Dis Colon Rectum*, Vol. 51, pp. 411–420.

Mariappan P, Alhasso A, Ballantyne Z, et al.b(2007). Duloxetine, a Serotonin and Noradrenaline Reuptake Inhibitor (SNRI) for the Treatment of Stress Urinary Incontinence: A Systematic Review. *European urology*, Vol. 51, pp. 67–74

Meschia M, Bertozzi R, Pifarotti P, et al. (2007). Peri-operative morbidity and early results of a randomised trial comparing TVT and TVT-O. *Int Urogynecol J Pelvic Floor Dysfunct, Vol.* 18, pp. 1257–1261

Misseri R, Cain MP, Casale AJ, et al. (2005). Small intestinal submucosa bladder neck slings for incontinence associated with neuropathic bladder. *J Urol, Vol.* 174, pp. 1680-1682

Mitterberger M, Pinggera GM, Marksteiner R, et al. (2007). Functional and histological changes after myoblast injections in the porcine rhabdosphincter. *Eur Urol*, Vol. 52, pp. 1736–1743. (Published erratum appears in Eur Urol 2008, 54:1208

Mitterberger M, Pinggera GM, Marksteiner R, et al. (2008a). Adult Stem Cell Therapy of Female Stress Urinary Incontinence. *European urology*, Vol. 53, pp. 169-175

Mitterberger M, Marksteiner R, Margreiter E, et al. (2008b). Myoblast and fibroblast therapy for post-prostatectomy urinary incontinence: 1-year follow-up of 63 patients. *J Urol*, Vol. 179, pp. 226–231.

Morley R & Nethercliffe J. (2005). Minimally invasive surgical techniques for stress incontinence surgery. *Best Practice & Research Clinical Obstetrics and Gynaecology*, Vol. 19, pp. 925-940

Neuman M & Shaare-Zedek MC. (2007). Training TVT SECUR: the first 150 teaching operations. *Int Urogynecol J,* Vol. 18, S27

Nilsson CG, Falconer C & Rezapour M. (2004). Seven-year follow-up of the tension-free vaginal tape procedure for treatment of urinary incontinence. *Obstet Gynecol*, Vol. 104, pp. 1259–1262

Nilsson CG, Palva K, Rezapour M, et al. (2008). Eleven years prospective follow-up of the tension-free vaginal tape procedure for treatment of stress urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct*, Vol. 19, pp. 1043–7

Nitta M, Tamaki T, Tono K, et al. (2010). Reconstitution of experimental neurogenic bladder dysfunction using skeletal muscle-derived multipotent stem cells. *Transplantation*, Vol. 89, pp. 1043–1049

Novara G, Artibani W. (2007). Myoblasts and fibroblasts in stress urinary incontinence. Lancet, Vol. 369, pp. 2139-40

Novara G, Artibani W, Barber MD, et al. (2010). Updated Systematic Review and Meta-Analysis of the Comparative Data on Colposuspensions, Pubovaginal Slings, and Midurethral Tapes in the Surgical Treatment of Female Stress Urinary Incontinence. *European Urology*, Vol. 58, pp. 218 – 238

Nygaard IE and Heit M. (2004). Stress urinary incontinence. *Obstet Gynecol*, Vol. 104, pp. 607

Petros P, Ulmsten U. (1993). An integral theory and its method for the diagnosis and management of female urinary incontinence. *Scand J Urol Nephrol Suppl*, Vol. 153, pp. 1-93

Pittenger MF, Mackay AM, Beck SC, et al. (1999). Multilineage potential of adult human mesenchymal stem cells. *Science,* Vol. 284, pp. 143–7

Prevel CD, Eppley BL, Summerlin DJ, et al. (1995). Small intestinal submucosa: use in repair of rodent abdominal wall defects. *Ann Plast Surg*, Vol. 35, pp. 374–380

Price N, Dawood R and Jackson SR. (2010). Pelvic floor exercise for urinary incontinence: A systematic literature review. *Maturitas,* Vol. 67, pp. 309–315

Prockop DJ. (1997). Marrow stromal cells as stem cells for nonhematopoietic tissues. *Science, Vol.* 276, pp. 71–4

Qu-Petersen Z, Deasy B, Jankowski R, et al. (2002). Identification of a novel population of muscle stem cells in mice: potential for muscle regeneration. *J Cell Biol*, Vol. 157, pp. 851–864

Rezapour M & Ulmsten U. (2001a): Tension-free vaginal tape (TVT) in women with recurrent stress urinary incontinence–a long-term follow-up. *Int Urogynecol J Pelvic Floor Dysfunct*, Vol. 12, pp. S9–S11

Rezapour M & Ulmsten U. (2001b): Tension free vaginal tape (TVT) in women with mixed urinary incontinence–a long-term follow-up. *Int Urogynecol J Pelvic Floor Dysfunct*, Vol. 12, pp. S15–18

Rezapour M, Falconer C & Ulmsten U. (2001c). Tension-free vaginal tape (TVT) in stress incontinent women with intrinsic sphincter deficiency (ISD)–a long-term follow-up. *Int Urogynecol J Pelvic Floor Dysfunct*, Vol. 12, pp. S12–14

Roche R, Festy F, Fritel X. (2010). Stem cells for stress urinary incontinence: The adipose promise. *J Cell Mol Med*, Vol. 14, pp. 135–142

Rodríguez L, Alfonso Z, Zhang R, et al. (2006). Clonogenic multipotent stem cells in human adipose tissue differentiate into functional smooth muscle cells. Proc Natl Acad Sci USA, Vol. 103, pp. 12167-72

Rosch R, Junge K, Hölzl F et al. (2004). How to construct a mesh. In: Schumpelick V, Nyhus LM (eds) Meshes: benefits and risks, 179–184, Springer, Berlin Heidelberg New York.

Roumeguere T, Quackels T, Bollens R, et al. (2005). Trans-obturator vaginal tape (TOT) for female stress incontinence: one year follow-up in 120 patients. *Eur Urol*, Vol. 5, pp. 805–809

Rutner AB, Levine SR, Schmaelzle JF. (2003). Processed porcine small intestine submucosa as a graft material for pubovaginal slings: durability and results. *Urology,* 62, pp. 805-809

Sadek HA, Martin CM, Latif SS, et al. (2009). Bone-marrow-derived side population cells for myocardial regeneration. *J Cardiovasc Transl Res*, Vol. 2, pp. 173–181.

Santucci RA, Barber TD. (2005). Resorbable extracellular matrix grafts in urologic reconstruction. *Int Braz J Urol*, Vol. 31, pp. 192-203

Sharma AK, Secrest CL. (2003). Small intestinal submucosa (SIS) graft reconstruction of urethra. *J Urol*, Vol. 169, pp. 101 (Abstract no. 393)

Stanton SL, Brindley GS, Holmes DM. (1985). Silastic sling for urethral sphincter incompetence in women. *Br J Obstet Gynaecol*, Vol. 92, pp. 747–50

Seale P, Rudnicki MA. (2000). A new look at the origin, function, and "stem-cell" status of muscle satellite cells. *Dev Biol*, Vol. 218, pp. 115–124

Strasser H, Marksteiner R, Margreiter E, et al (2007a). Transurethral ultrasonography-guided injection of adult autologous stem cells versus transurethral endoscopic injection of collagen in treatment of urinary incontinence. *World J Urol, Vol.* 25, pp. 385–92

Strasser H, Marksteiner R, Margreiter E, et al. (2007b). Autologous myoblasts and fibroblasts versus collagen for treatment of stress urinary incontinence in women: a randomized controlled trial. *Lancet*, Vol. 369, pp. 2179-86

Strem B, Hicok K, Zhu M, et al. (2005). Multipotential differentiation of adipose tissue-derived stem cells. *Keio J Med,* Vol. 54, pp. 132-41

Sweat SD, Itano NB, Clemens JQ, et al. (2002). Polypropylene mesh tape for stress urinary incontinence: complications of urethral erosion and outlet obstruction. *J Urol*, Vol. 168, pp. 144–7

Ulmsten U, Henriksson L, Johnson P, et al. (1996). An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence. *Int Urogynecol J*, Vol. 7, pp. 81–86

Villet R, Atallah D, Cotelle-Bernede O, et al. (2002). Treatment of stress urinary incontinence with tension-free vaginal tape (TVT). Mid-term results of a prospective study of 124 cases [in French]. *Prog Urol*, Vol. 12, pp. 70–76

Waltregny D, Gaspar Y, Reul O, et al. (2008). for the treatment of female stress urinary incontinence: results of a prospective study after a 3-year minimum follow-up. *Eur Urol,* Vol. 53, pp. 401–408

Ward KL & Hilton P. (2004). The United Kingdom and Ireland Tension- Free Vaginal Tape Trial Group: A prospective multicenter randomized trial of tension-free vaginal tape and colposuspension for primary urodynamic stress incontinence: 2-year follow-up. *Am J Obstet Gynecol*, Vol. 190, pp. 324–331

Ward KL & Hilton P. (2008). The United Kingdom and Ireland Tension- Free Vaginal Tape Trial Group: Tension-free vaginal tape versus colposuspension for primary urodynamic stress incontinence: 5-year follow-up. *BJOG*, Vol. 15, pp. 226-233

Wiedemann A, Otto M. (2004). Small intestinal submucosa for pubourethral sling suspension for the treatment of stress incontinence: first histopathological results in humans. *J Urol,* Vol. 172, pp. 215-218

Winters JC, Fitzgrerald MP and Barber MD. (2006). The use of synthetic mesh in female reconstructive surgery. *BJU International*, Vol. 98 (suppl 1), pp. 70–76

Yamamoto T, Gotoh M, Hattori R, et al. (2010). Periurethral injection of autologous adipose-derived stem cells for the treatment of stress urinary incontinence in patients undergoing radical prostatectomy: report of initial two cases. *Int J Urol*, Vol. 17, pp. 75–82 (Retraction in *Int J Urol*, 2010, Vol. 17, pp. 896)

Yokoyama T, Yoshimura N, Dhir R, et al. (2001a). Persistence and survival of autologous muscle derived cells versus bovine collagen as potential treatment of stress urinary incontinence. *J Urol, Vol.* 165, pp. 271–6

Yokoyama T, Pruchnic R, Lee JY, et al. (2001b). Autologous primary muscle-derived cells transfer into the lower urinary tract. *Tissue Eng*, Vol. 7, pp. 395–404

Zhang Y, Luo H, Zhang Z, et al. (2010). A nerve graft constructed with xenogeneic acellular nerve matrix and autologous adipose-derived mesenchymal stem cells. *Biomaterials*, Vol. 31, pp. 5312–532416.

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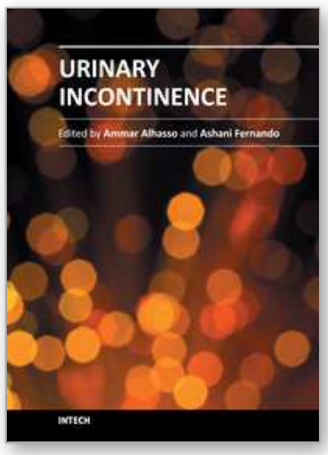

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