# Scaffolds for vaginal reconstruction in Mayer-Rokitansky-Küster-Hauser syndrome: An update

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**Abstract**

Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a congenital disorder affecting the female reproductive system in which the vagina and uterus are underdeveloped or absent. The main objective of the surgical treatment for vaginal agenesis in MRKH is to create an anatomically and functionally normal neovagina to allow these women to have a satisfactory sexual life. The ideal reconstructive option should provide adequate dimensions, a physiological mucosal lining, preferably non-invasive or minimally invasive technique and, require minimal use of dilators for maintaining the patency of the vaginal tract. Vaginal dilation therapy is considered the first-line treatment and surgical treatment options are mostly reserved for cases that cannot be treated with merely vaginal dilatation. The most widely used minimally invasive techniques are the laparoscopic Vecchietti's technique and the Abbé-McIndoe procedure which consists of creating a neovagina and lining it with a scaffold material that helps in healing, regeneration and epithelization. Considering the controversy regarding the ideal graft material for lining the neovagina in MRKH reconstruction, the chapter is aimed to evaluate the various graft materials used with their merits and demerits.

**Keywords:** Vaginoplasty, Mayer-Rokitansky-Küster-Hauser syndrome, Scaffolds, Split-thickness skin graft, Full-thickness skin graft, Amnion, Autologous buccal mucosa, Peritoneum, Large and small intestine, Nile Tilapia fish skin, Acellular porcine dermal matrix, Oxidized regenerated cellulose, in vitro autologous vaginal cell cultures

## 1. Introduction

Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a congenital disorder affecting the female reproductive system in which the vagina and uterus are underdeveloped or absent, although external genitalia is normal.[1,2] The prevalence is up to 0.02%.[2]Women with MRKH syndrome usually have primary amenorrhea due to absent uterus. The presenting sign of MRKH syndrome is lack of menstruation till the age 15-16 years in most of the cases. They have a female chromosome pattern- 46, XX with functioning ovaries, normal breast and pubic hair development.[1] Approximately one-third of the cases are associated with renal and skeletal system malformations, rarely are cardiovascular anomalies also seen.[3]

The main objective of the surgical treatment for vaginal agenesis in MRKH is to create an anatomically and functionally normal neovagina to allow these women to have a satisfactory sexual life. The ideal reconstructive option should provide adequate dimensions, a physiological mucosal lining, preferably non-invasive or minimally invasive technique and, require minimal use of dilators for maintaining the patency of the vaginal tract.[3] The best outcomes are achieved with the treatment plan individualized to each case based on the defect size and type. Both non-surgical and surgical treatment options are widely used for MRKH. With a 75-85% overall success rate and low complications rate, vaginal dilation therapy is considered the first-line treatment.[4,5] The surgical treatment options are mostly reserved for cases that cannot be treated with merely vaginal dilatation.[6]

The most widely used minimally invasive techniques are the laparoscopic Vecchietti's technique and the Abbé-McIndoe procedure. [3, 7] The Vecchietti's technique uses an acrylic olive placed in the vaginal dimple with two passed through the abdominal cavity attached to a traction device placed on the supra-pubic region to elongate the vaginal canal.[8] In contrast, the Abbé-McIndoe procedure consists of the creation of a canal in between the bladder and the rectum, which is covered with a skin graft.[3, 7] Several modifications of this original technique have been reported based on the various grafts used for the neovaginal lining.

Considering the controversy regarding the ideal graft material for lining the neovagina in MRKH reconstruction, the chapter is aimed to evaluate the various graft materials used with their merits and demerits.

## 2. Conventional graft materials used for neovagina lining

### *2.1 Autografts*

#### *2.1A Split-thickness skin graft*

Using a split-thickness skin graft (STSG) to line the neovagina was first pioneered by the world-renowned American surgeon Robert Abbe.[9] The procedure was popularized further by the plastic surgeon Sir Archibald McIndoe.[10]

The initial technique described by McIndoe using STSG for lining the neovagina is widely used to date.[7, 11] The STSG is harvested from either the gluteal region or the thigh with the gluteal region. [11] The thickness and the size of graft depends on the vaginal defect.[11] The

advantages of STSG being its ability to provide the neovagina the epithelial lining with own tissue, a simple surgical technique, very low morbidity and near normal capability of neovagina for the sexual intercourse.[11] However, the use of STSG for neovaginal lining in MRKH is shown to be associated with vaginal canal stenosis and shortening, as well as potential hair growth affecting the functional efficacy of the neovagina.[11–13]

*2.1 B Full-thickness skin graft*

Because of the complications of using STSG for neovaginal lining such as vaginal canal stenosis and shortening, a modification was suggested in the classic McIndoe-Abbe procedure by using full-thickness skin grafts (FTSGs) for lining the neovagina in MRKH syndrome. The application of FTSGs for vaginal reconstruction was first described by Sadove and Horton in 1988. [14] STSG classically contract by 40 % of their original size, whereas FTSG contracts only up to 10-20% of their original size. [15] Another advantage of FTSG is the conservation of dermis with intact vascular plexus, resulting into improved graft texture and thickness. Additionally, due to preserved glandular components, FTSG can provide better lubrication and reinnervation due to intact neurilemmal sheath, thus offering improved sensation with the fully healed graft.[16]

FTSG are commonly harvested from the groin and placed on the vaginal stent in order to line the neovagina. It is essential to consider the donor-site morbidity and monitor for donor-site healing complications, including necrosis. Care must be taken to harvest the minimal required tissue allowing the primary closure of the donor site.[13] Granulation tissue is another bothersome complication of FTSG and STSG which usually epithelizes within 12 months[17] If it is persistent, it can be managed with silver nitrate or CO2 laser.[13]

*2.1 C Amnion*

The human amniotic membrane is harvested from the amniotic sac of infants at term and delivered by healthy women. The thickness of the amnion is similar to that of a thin STSG. The amniotic membranes are chemically processed, tested, sterilized and, freeze-dried.[18] It is readily available in unlimited quantities and has a low cost. It is easy to harvest and more physiologic as facilitates the complete epithelialization of the neovagina. There is no hair growth, unlike skin grafts or malodourous vaginal discharge, such as with sigmoid or ileal graft.[18] Amnion doesn't cause any immunologic rejection as it does not have human leukocyte antigen.[19,20] It has antimicrobial properties.[21] Amnion also exhibits anti-fibroblastic activity and thus helps in preventing fibrosis. It promotes cell migration and epithelialization. [22]

Amnion has achieved satisfactory outcomes in trials using it for the neovaginal lining.[18,23] The primary disadvantage of amnion is the potential risk of transmitting viral infections and contamination. Proper screening of donors is needed to avoid such complications.

*2.1 D Autologous buccal mucosa*

Oral mucosa has been reported for various reconstructions such as conjunctiva, tongue, cheek, larynx, trachea, and urethra.[24,25] The histology of the buccal mucosa has shown that the buccal mucosa has a thicker epithelium and thinner lamina propria than the STSG, which is proposed to promote revascularization of the graft.[26] It is easily accessible, non-hair bearing, rich in

vascularity, and provides superior cosmetic results. [24] Additionally, the use of buccal mucosa provides the autologous tissue without any scar, and mucous secretions gives additional lubrication benefits.

Buccal mucosa has been applied as a material for vaginoplasty with promising postoperative results in various trials.[25] Buccal mucosa is harvested from the inner lip or inner cheeks as multiple full-thickness mucosal pieces and then minced before spreading on the sponge, which is placed in close contact with the neovaginal lining.[25] Each micrograft serves as a seed for epithelial regeneration, and the epithelialization is completed over the lining of the entire neovagina over of a few weeks.

The data regarding the use of buccal mucosa in vaginal reconstruction is limited, and all these studies are mostly case reports, including a small number of patients. The major limitation of buccal mucosal grafts is the longer time it takes to complete the neovagina epithelization due to its limited availability. Damage to the buccal neurovascular bundle, bleeding and, infection are the potential donor site complications.[24]

*2.1 E Peritoneum*

The Davydov procedure uses an autologous peritoneal graft for lining and epithelization of the neovagina. The initial concept used laparotomy, which was later modified by the use of laparoscopy for the dissection and mobilization of the peritoneum of the pouch of Douglas. By vaginal approach, neovagina is created until the peritoneum is reached. The mobilized peritoneal sac using laparoscopy is pulled downward and joined in continuity with the vaginal epithelium. The peritoneum is closed abdominally over a vaginal stent. Vaginal dilatation is needed to maintain the patency.[27]

The most common complications of this approach were vaginal canal stenosis, increased morbidity due to an additional procedure and, rectal injury.24 In a study comparing different techniques of vaginoplasty, it was found that even though the intestinal graft and the Davydov procedure both achieve a satisfactory length of neovagina length, the use of the peritoneum is associated with less vaginal secretion and relatively less discomfort than the bowel graft.[28]

*2.1 F Large and small intestine*

An intestinal vaginoplasty uses a segment of the ileum, jejunum, or sigmoid colon. The intestinal tissue has certain advantages. There is a low risk of shrinkage, and it avoids the need for long-term vaginal dilation. The secretions provide lubrication, but the discharge can sometimes be malodourous and excessive. The major drawback is harvesting the bowel segment usually requires an additional surgical approach- laparotomy/ laparoscopy and bowel resection and anastomosis, which can increase morbidity.[29,30]

***2.2 Xenografts***

*2.2 A Tilapia fish skin*

Nile Tilapia Fish Skin (NTFS) has non-infectious microbiota[31] and similar morphological structure to human skin.[32] It has exhibited high in vivo bio-resorption.[33] Most importantly addition, NTFS has showed satisfactory outcomes in pediatric[34] and adult burn treatment.[35]

Preparing the NTFS graft includes harvesting, washing, sterilization, and microbiological testing. It is placed in the neovagina similarly to STSG and FTSG. In the trials of NTFS for vaginal reconstruction, the histological and immunohistochemical analyses have shown the presence of stratified squamous epithelium with the expression of cytokeratin and fibroblast growth factor. NTFS acting as a scaffold promoted cell adhesion, proliferation, and epithelialization of the neovagina.[36]

Though NTFS prevents donor-site morbidity and offers satisfactory outcomes in vaginal reconstruction, the evidence is limited to case reports with short-term follow up. Also, the availability of NTFS could be a limiting factor in its use in vaginal reconstruction. [36]

*2.2 B Tissue-engineered biological tissue matrix (Acellular porcine dermal matrix)*

Acellular porcine dermal matrix (ADM) is a non-cross-linked matrix derived from the porcine dermis. It proves to be a solid and durable acellular biologic implant that can be used as a scaffold for tissue regeneration facilitating soft tissue proliferation and healing. The biologic tissue matrix has been previously used in thoracic surgery and abdominal wall reconstruction. [1]

Acellular dermal matrix comes with certain advantages over autologous grafts, such as avoidance of donor site scars and morbidity, the shorter time required for epithelialization of the neovagina and simplicity of the procedure.[37] In one study, the biologic tissue matrix was used with the hymen micro mucosa graft to promote epithelization.[1] The studies have reported near normal sexual function outcomes using the Acellular porcine dermal matrix.[1,37] The main limitation of the use of ADM is the cost for the biomaterial graft,[37] and the data regarding its efficacy is limited to a small number of patients.

***2.3 Synthetic alternatives***

*2.3 Oxidized regenerated cellulose*

The absorbable adhesion barrier Interceed (Ethicon, Johnson & Johnson, Somerville, NJ) was first used in1994 for lining the neovagina.[38] Interceed is approved by the US Food and Drug Administration for its use in abdominal and pelvic surgeries as an adhesion barrier.[39] It allows epithelization to occur in neovagina and is completely absorbed in the period of 4 weeks.[40]

The trials based on the use of Interceed with estrogen cream have reported relatively early epithelization and greater sexual satisfaction due to adequate mucosal sensitivity. [40,41,42] The neovagina created was physiologically and histologically close to a normal adult vagina.[41]

An important limitation in using Interceed is its cost compared to autografts and the longer time taken for complete epithelization of the neovagina, one to four months. [40,41,42]

### *2.4 Bioengineered Cell culture*

#### *2.4 A In vitro autologous vaginal cell cultures*

The advances in the field of tissue engineering and cell-based therapies have shown promising outcomes for tissue rejuvenation, repair, and reconstruction. [43] The use of in vitro autologous vaginal cell cultures obtained by biopsies from the vaginal vestibule in vaginoplasty is an attractive paragon. The technique with a full-thickness biopsy from the vaginal vestibule undergoes enzymatic dissociation and the keratinocytes are cultured on collagen plates.[3] A fully differentiated mucosal tissue is harvested within 2-3 weeks of culture, washed, and embedded on hyaluronic acid embedded gauze, the epithelial layer facing away from the gauze, and placed in the neovaginal lining with the mold.[3]

The graft being autologous, there is no risk of infection and rejection, the procedure is rapid, and it avoids donor site morbidity.[44] The epithelialization occurs swiftly as there is no need for meshing the material while having sufficient tissue to cover the entire neovagina.[3] Autologous vaginal tissue helps restore the physiological neovaginal epithelium, and mucous cells within the culture help in the normal glandular function of the neovagina.[45] The technique has given physiological and functional promising outcomes in the studies reported.[3,44–46]

The limitations are that the cell-culture treatment approaches must be carried out in dedicated tissue culture laboratories compliant with Good Manufacturing Practice. Moreover, the surgery planning needs coordination between the laboratories and the operating team. The use of *in vitro* cultured vaginal mucosa is in its early stages with scarce data. Further experience is needed to establish its effectiveness in vaginal reconstruction. [3, 44]

## 3. Conclusion

Vaginoplasty in MRKH syndrome aims to reconstruct a physiologically similar and functional vaginal passage using the graft tissue. The graft should have minimal donor-site morbidity, complete acceptance, capability for swift epithelization, and undemanding post-operative maintenance. Various newer regenerative options have emerged as promising techniques to overcome the drawbacks of the existing standard treatments. Yet larger studies are still needed to establish the evidence for their efficiency meanwhile, the established conventional grafts as scaffold form the mainstay of vaginoplasty in MRKH syndrome.

## 4. Conflict of Interest

The authors declare no conflict of interest.

## 5. Acronyms and Abbreviations

| | |
|---|---|
| MRKH | Mayer-Rokitansky-Küster-Hauser |
| STSG | Split-thickness skin graft |
| FTSG | Full- thickness skin grafts |
| NTFS | Nile Tilapia Fish Skin |

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