



**TOSHKENT TIBBIYOT AKADEMIYASI URGANCH FILIALI
JANUBIY OROLBO'YI TIBBIYOT JURNALI**

1-TOM, 4-SON. 2025

14.00.00 - TIBBIYOT FANLARI ISSN: 3093-8740

UDC: 616.351-002-089

**REVIEW OF CURRENT MINIMALLY INVASIVE AND REGENERATIVE APPROACHES
FOR THE TREATMENT OF ANAL FISTULA (FISTULOUS PARAPROCTITIS)**

(LITERATURE REVIEW)

Sherbekov Ulugbek Akhrarovich

Doctor of Medical Sciences, Associate Professor,

Head of Department of general surgery,

Samarkand State Medical University.

e-mail: ulasher67@gmail.com

(ORCID: 0000-0001-5082-9966)



Lutfullaev Xafizullo Zaynullaevich

Student of the Pediatric Faculty,

Samarkand State Medical University.

e-mail: lutfullayevhafizullo@gmail.com

(ORCID: 0009-0000-9614-3652)



Alkov Ruslan Alimjonovich

Student of the Pediatric Faculty,

Samarkand State Medical University.

e-mail: alkovruuslan61@gmail.com

(ORCID: 0009-0007-0121-4587)





Abstract

Anal fistula (fistulous paraproctitis) is a chronic anorectal condition characterized by an abnormal tract connecting the anal canal or rectum with the perianal skin. It significantly impairs patients' quality of life due to pain, discharge, and risk of recurrence. This review provides a comprehensive analysis of classification systems, diagnostic approaches, and both conventional and emerging treatment strategies for anal fistulas. Modern imaging techniques, including MRI and endoanal ultrasound, have improved preoperative assessment and surgical planning. Surgical management remains the cornerstone of treatment, with sphincter-preserving approaches such as LIFT, VAAFT, and advancement flaps aiming to balance healing and continence preservation. In this article, we summarized and critically analyzed current literature on the etiology, diagnostic methods, and management options of anal fistula, emphasizing the shift from purely surgical to regenerative and minimally invasive strategies. We also outlined future perspectives integrating imaging precision with biological repair techniques.

Keywords: Anal fistula, fistulous paraproctitis, minimally invasive surgery, sphincter-preserving techniques, regenerative therapy, stem cell therapy, fibrin glue, MRI, endoanal ultrasonography, recurrence

**ANAL FISTULA (FISTULOUS PARAPROCTITIS) NI DAVOLASHDA ZAMONAVIY
MINIMAL INVASIV VA REGENERATIV YONDASHUVLARNING SHARHI
(ADABIYOTLAR TAHLILI)**

Annotatsiya

Anal fistula (fistulous paraproctitis) — bu surunkali anorektal kasallik bo'lib, anal kanal yoki to'g'ri ichakni peri-anal teri bilan bog'laydigan patologik trakti bilan tavsiflanadi. Bu kasallik og'riq, ajralma va qaytalash xavfi tufayli bemorlarning hayot sifatiga sezilarli ta'sir ko'rsatadi. Ushbu sharh anal fistulalarning klassifikatsiya tizimlari, diagnostika yondashuvlari, shuningdek, an'anaviy va yangi davolash usullarini kompleks tahlil qiladi. Zamonaviy tasvirlash usullari, jumladan MRI va endoanal ultratovush, operatsiyaga tayyorgarlik va jarrohlik rejalashtirishni yaxshiladi. Jarrohlik davolash asosiy usul bo'lib qolmoqda, shu bilan birga LIFT, VAAFT va advancement flaps kabi sfinkterni saqlashga qaratilgan yondashuvlar davolanish va kontinensiyani saqlash o'rtasida muvozanatni ta'minlashga qaratilgan.

Ushbu maqolada anal fistulalarning etiologiyasi, diagnostikasi va davolash usullari bo'yicha zamonaviy adabiyotlar umumlashtirilib, tanqidiy tahlil qilingan bo'lib, faqat jarrohlik yondashuvlaridan minimal invaziv va regenerativ strategiyalarga o'tish jarayoni ta'kidlangan. Shuningdek, tasvirlash aniqligi va biologik tiklash texnologiyalarini integratsiyalashning kelajak istiqbollari ko'rsatildi.

Kalit so'zlar: anal fistula, fistulous paraproctitis, minimal invaziv jarrohlik, sfinkterni saqlash usullari, regenerativ terapiya, stem hujayra terapiyasi, fibrin glue, MRI, endoanal ultratovush, qaytalash

**ОБЗОР СОВРЕМЕННЫХ МИНИМАЛЬНО ИНВАЗИВНЫХ И РЕГЕНЕРАТИВНЫХ
МЕТОДОВ ЛЕЧЕНИЯ СВИЩЕВОГО ПАРАПРОКТИТА (ОБЗОР ЛИТЕРАТУРЫ)**

Аннотация

Свищевой парапроктит (анальная фистула) — хроническое аноректальное заболевание, характеризующееся формированием патологического канала, соединяющего анальный канал



или прямую кишку с кожей перианальной области. Заболевание значительно ухудшает качество жизни пациентов из-за боли, выделений и риска рецидива. Настоящий обзор представляет собой комплексный анализ систем классификации, диагностических подходов, а также традиционных и современных методов лечения анальных свищей. Современные методы визуализации, включая МРТ и эндоанальный ультразвук, улучшили предоперационную оценку и планирование хирургического вмешательства. Хирургическое лечение остается основным методом терапии, при этом подходы с сохранением сфинктера, такие как LIFT, VAAFT и advancement flaps, направлены на баланс между заживлением и сохранением контроля над дефекацией.

В статье обобщена и критически проанализирована современная литература по этиологии, диагностике и методам лечения анальных свищей, с акцентом на переход от чисто хирургических подходов к минимально инвазивным и регенеративным стратегиям. Также представлены перспективы интеграции точной визуализации с биологическими методами восстановления.

Ключевые слова: анальная фистула, свищевой парапроктит, минимально инвазивная хирургия, методы с сохранением сфинктера, регенеративная терапия, терапия стволовыми клетками, фибриновый клей, МРТ, эндоанальная ультрасонография, рецидив

Introduction

Anal fistula (fistulous paraproctitis) is a common chronic proctological disorder characterized by the formation of a pathological tract connecting the lumen of the rectum or anal canal with the perianal skin (Owen et al., 2016). The disease is accompanied by local pain, inflammation, purulent discharge, and, in some cases, fecal incontinence, all of which significantly reduce patients' quality of life (Garcia-Olmo et al., 2019; Sarveazad et al., 2022). Overall, patients with anal fistula exhibit lower quality-of-life indicators compared with population norms (Ferrer-Márquez et al., 2017). According to standardized questionnaires, the median quality-of-life scores correspond to a moderate negative impact on daily activities (Ferrer-Márquez et al., 2017).

Epidemiological studies show that the prevalence of anal fistulas in Europe is 1.69 per 10,000 population (Garcia-Olmo et al., 2019), and globally around 18.37 per 100,000 individuals (Sarveazad et al., 2022). Although the disease can be classified as rare (less than 5 cases per 10,000 population), its clinical significance remains high (Garcia-Olmo et al., 2019). In the United Kingdom, approximately 5,000 patients undergo surgical treatment for anal fistulas annually, and considering recurrences, the incidence reaches about 1:10,000 (Owen et al., 2016). The main etiological factors include cryptoglandular infection and Crohn's disease (Garcia-Olmo et al., 2019).

Surgical intervention remains the cornerstone of treatment for fistulous paraproctitis, yet it poses significant challenges. On one hand, fistulotomy is the most effective radical method for eliminating the fistula, but the risk of postoperative incontinence ranges from 4% to 62% (Visscher et al., 2015). On the other hand, for high or complex fistulas, sphincter-preserving techniques such as advancement flap or core fistulectomy are preferred (Visscher et al., 2015). Therefore, a key challenge in modern proctology is to achieve an optimal balance between surgical efficacy and preservation of anal sphincter function (Owen et al., 2016).



In conclusion, fistulous paraproctitis is a disease with a pronounced impact on patients' quality of life, a high recurrence rate, and a risk of complications. These factors underscore the need for further research aimed at improving diagnostic and therapeutic approaches.

Anatomy and Cryptoglandular Origin

Perianal abscesses and fistulas are considered the acute and chronic manifestations of the same pathological process — infection of the anal glands (Whiteford, 2007). These glands, typically numbering up to ten, are situated at the base of the anal crypts around the dentate line, equally distributed circumferentially (Gosselink et al., 2015). While most glands are confined to the submucosa, approximately 20% penetrate the internal sphincter, though rarely extending into the external sphincter (Sugrue et al., 2017).

According to the **cryptoglandular hypothesis**, first proposed by Parks in 1961, obstruction of the proctodeal glands and their ducts initiates the process of abscess formation (Włodarczyk et al., 2021). The obstruction — often secondary to fecal material or local trauma — leads to stasis, bacterial overgrowth, and subsequent abscess formation within the intersphincteric groove (Whiteford, 2007). Depending on the route of extension, these abscesses may track downward to form perianal abscesses, laterally through the external sphincter to the ischiorectal fossa, or superiorly toward the supralelevator space (Whiteford, 2007).

When the abscess drains spontaneously or surgically, persistence of septic foci and epithelialization of the draining tract may occur, giving rise to a chronic fistula-in-ano — the chronic phase of perirectal sepsis (Whiteford, 2007; Gosselink et al., 2015).

Pathogenesis in Crohn's Disease-Related Fistulas

While the cryptoglandular pathway accounts for approximately 90% of cases, about 10% of perirectal abscesses arise from alternative etiologies such as Crohn's disease (CD), trauma, HIV infection, sexually transmitted diseases, radiation therapy, or foreign bodies (Whiteford, 2007). In Crohn's disease, fistulization occurs as a consequence of **mucosal inflammation** leading to epithelial defects. These defects allow microbial antigens to penetrate the lamina propria and trigger cytokine-mediated cascades involving TNF- α , TGF- β , IL-13, and MMPs (Haddow et al., 2019). The resulting **epithelial-to-mesenchymal transition (EMT)** promotes cell migration and invasion, ultimately producing a fistulous tract lined by transitional cells. This mechanism underscores the immunological and molecular differences between cryptoglandular and Crohn's-related fistulas.

Histological and Molecular Features

Histologically, anal fistulas share a common architecture: a central fissure that penetrates through the lamina propria and muscularis mucosae, often lined by granulation tissue rich in histiocytes and neovascularization (Bataille et al., 2004). Epithelialization of the fistulous tract — observed in approximately one-third of cases — contributes to persistence and recurrence (Gosselink et al., 2015).

On a molecular level, **matrix metalloproteinases (MMPs)** facilitate extracellular matrix degradation and promote fistula progression (Włodarczyk et al., 2021). Immune infiltration varies depending on etiology: CD-associated fistulas show T-cell and B-cell predominance, while cryptoglandular fistulas contain mainly CD68-positive macrophages (Bataille et al., 2004). Even in



the absence of live bacteria, bacterial remnants such as peptidoglycan can sustain inflammation via IL-1 β secretion (Włodarczyk et al., 2021).

Role of Microbiota

The proximity of the anorectal region to the intestinal microbiome highlights the microbial contribution to fistula development. The presence of gut-specific bacteria, notably *E. coli*, in anorectal abscesses predicts fistula formation (Sugrue et al., 2017; Dowling Enez & Izarra Henriquez, 2020). Polymicrobial infections involving *Klebsiella pneumoniae*, *E. coli*, and *Enterococcus faecalis* correlate with complex, high-level fistulas (Dowling Enez & Izarra Henriquez, 2020).

Recent metagenomic studies suggest that microbial communities in anal fistulas may originate both from intestinal and skin sources, indicating a mixed microbial etiology (Yang et al., 2024). This dual origin provides new insight into chronicity and recurrence mechanisms. **Classification of Anal Fistulas.**

Traditional Systems

The classification of anal fistulas serves as a guide for determining treatment strategies and predicting outcomes regarding recurrence and continence (Idris, Abdalla, & Hamza, 2015). The most widely used system is the **Parks classification** (1976), which categorizes fistulas based on their relationship to the anal sphincter complex: **intersphincteric**, **transsphincteric**, **suprasphincteric**, and **extrasphincteric** types (Whiteford, 2007). This system remains clinically valuable because it allows prediction of the continence risk associated with fistulotomy (Idris, Abdalla, & Hamza, 2015).

Fistulas with tracts confined below the dentate line are considered **low**, while those traversing more than 30–50% of the external sphincter or located above are **high** fistulas (Włodarczyk et al., 2021). In addition, Goodsall's rule provides a simple correlation between the external and internal openings based on their position relative to the anal verge (Whiteford, 2007).

Simple vs. Complex Fistulas

Fistulas are broadly classified as **simple** or **complex**, depending on anatomical and clinical factors. Simple fistulas have low tracts without abscesses or secondary openings, whereas complex fistulas involve high tracts, multiple openings, associated abscesses, or conditions such as Crohn's disease, previous irradiation, or incontinence (Whiteford, 2007; Kotze et al., 2018).

This distinction is critical since complex fistulas carry a higher risk of recurrence and postoperative incontinence, requiring sphincter-sparing approaches.

Advancements and Comparative Systems

Since the original Parks classification, several refinements have emerged. The **St. James University Hospital (SJHU) classification** (2000) utilized MRI findings to define five grades of fistulas, improving anatomical precision (Garg, 2017). Subsequently, the **Standard Practice Task Force (SPTF)** (2005) introduced a more pragmatic system dividing fistulas simply into “simple” and “complex” types based on continence risk.

However, both systems were limited in predicting surgical feasibility and postoperative outcomes. Addressing these gaps, **Garg (2017)** proposed a **five-grade classification** integrating MRI and operative data from 440 patients. Grades I and II represent simple fistulas amenable to fistulotomy, whereas Grades III–V correspond to highly complex fistulas requiring sphincter-sparing procedures. Unlike previous purely anatomical systems, Garg's model incorporates outcome-based validation, improving predictive accuracy for surgical planning.



Regional variations also exist: while the **Parks classification** predominates in Western countries, the **Sumikoshi classification** is commonly employed in Japan (Yamana, 2018). Recent approaches further incorporate high-resolution imaging modalities such as ultrasound, CT, and MRI to provide enhanced anatomical detail and guide personalized surgical management (Yamana, 2018; Sohrabi et al., 2024).

Traditional Surgical Management

The management of fistula-in-ano has historically relied on traditional surgical approaches aimed at complete eradication of the fistulous tract while preserving sphincter function. Among these, **fistulotomy** and **fistulectomy** remain the cornerstone procedures, with adjunctive methods such as **seton placement** and **endorectal advancement flap** being reserved for more complex or high-lying fistulas (Abcarian, 2011; Ommer et al., 2012; Parks, 1976).

Fistulotomy

Fistulotomy is considered the simplest and most effective surgical option for low and simple fistulas, with reported healing rates of 90–100% (Vasilevsky & Gordon, 1984; Zanotti et al., 2007). The technique involves laying open the tract, allowing it to heal by secondary intention. Its main limitation lies in the potential risk of postoperative fecal incontinence due to sphincter division, particularly in transsphincteric or suprasphincteric fistulas (Garg, 2017). Despite this, numerous studies have shown that when performed in appropriately selected patients—typically those with intersphincteric or low transsphincteric tracts—the functional outcome is excellent, with minimal impairment of continence (Ratto et al., 2015).

Fistulectomy

Fistulectomy entails complete excision of the fistulous tract. While this technique ensures thorough removal of granulation tissue and potential epithelial remnants, it is associated with longer healing times and a higher risk of sphincter injury compared to fistulotomy (Vasilevsky & Gordon, 1984; Ratto et al., 2015). Some comparative studies report that fistulectomy provides no significant advantage over fistulotomy in terms of recurrence but carries a higher morbidity burden (Zanotti et al., 2007). Consequently, its use has gradually declined and is currently recommended only in cases where malignancy or epithelialization within the tract is suspected (Ommer et al., 2012).

Seton Placement

For high or complex fistulas where direct fistulotomy would compromise continence, **seton placement** remains a valuable sphincter-preserving strategy. A seton—usually a surgical thread, rubber band, or vessel loop—is inserted through the fistula tract to maintain drainage and prevent premature closure of the external opening. Two main variations exist: the *cutting seton* and the *draining seton*. The cutting seton gradually divides the sphincter muscle while inducing fibrosis, allowing controlled healing and minimizing the risk of incontinence (Garg, 2017; Ratto et al., 2015). Conversely, the draining seton is often used as a temporizing measure prior to definitive surgery in patients with active infection or multiple tracts. Although effective in preserving continence, seton techniques may require multiple procedures and prolonged healing time, which can impact patient comfort and compliance (Abcarian, 2011).

Advancement Flap Procedures

Endorectal or advancement flap procedures represent another important traditional approach, particularly for high transsphincteric and suprasphincteric fistulas where sphincter preservation is



paramount. The technique involves curettage of the fistulous tract, closure of the internal opening, and advancement of a well-vascularized rectal or anodermal flap to cover the defect (Ommer et al., 2012). Healing rates vary between 60% and 80%, depending on surgeon experience and fistula complexity (Ratto et al., 2015). The main limitations include the potential for flap necrosis, recurrence, or postoperative sepsis. Nevertheless, advancement flap repair remains an important option for patients unsuitable for more invasive sphincter-dividing techniques.

Summary

Traditional surgical methods, while highly effective in achieving fistula closure, remain limited by the balance between recurrence prevention and continence preservation. The challenge of minimizing postoperative incontinence without compromising healing has driven the evolution of newer **minimally invasive** and **regenerative** techniques, which aim to achieve equivalent or superior healing outcomes with reduced morbidity (Garg, 2017; Ratto et al., 2015).

Minimally Invasive & Sphincter-Saving Techniques

The optimal surgical approach for anal fistula aims to eradicate sepsis, achieve durable healing, and maintain anal continence. Conventional operations, such as fistulotomy, are effective for simple and low-lying fistulas but can jeopardize sphincter integrity in high or complex tracts that cross a substantial portion of the external sphincter or occur in patients with pre-existing incontinence. Consequently, the pursuit of definitive yet function-preserving procedures has driven the evolution of multiple sphincter-sparing techniques (Limura & Giordano, 2015; Adegbola et al., 2017). Preoperative anal manometry can further guide management, as patients with low resting or squeeze pressures benefit more from sphincter-preserving rather than sphincter-dividing interventions (Khafagy et al., 2010).

Endorectal Advancement Flap Repair (EAFR)

The endorectal advancement flap repair (EAFR) is one of the earliest sphincter-sparing procedures and remains a well-established standard for high or complex fistulas (Uribe et al., 2007; Sileri et al., 2011). The technique involves excision of the internal opening and advancement of a mucosal–submucosal flap to close the defect securely without dividing the external sphincter (Uribe et al., 2007). Although conceptually sound, clinical outcomes vary widely. Reported recurrence rates range from 7% to 49%, and minor to moderate postoperative incontinence may occur in up to one-third of patients (Jiang et al., 2017; Limura & Giordano, 2015; Song, 2012). Manometric assessments have confirmed significant reductions in both maximum resting and squeeze pressures postoperatively (Uribe et al., 2007; Khafagy et al., 2010). Despite these limitations, EAFR still provides a reasonable balance between healing and functional preservation, with pooled healing rates around 60–65% (An et al., 2023).

Ligation of the Intersphincteric Fistula Tract (LIFT)

Introduced by Rojanasakul in 2007, the ligation of the intersphincteric fistula tract (LIFT) procedure has gained widespread adoption due to its simplicity, reproducibility, and continence-preserving nature (Sileri et al., 2011; Limura & Giordano, 2015). It involves identification of the tract within the intersphincteric plane, secure ligation near the internal sphincter, and removal of infected tissue without sphincter division (Song, 2012). This minimally invasive design limits tissue trauma and shortens recovery time. A systematic review reported a mean success rate of approximately 75%, with minimal risk of continence disturbance (Limura & Giordano, 2015). A biologically reinforced



TOSHKENT TIBBIYOT AKADEMIYASI URGANCH FILIALI JANUBIY OROLBO‘YI TIBBIYOT JURNALI

1-TOM, 4-SON. 2025

14.00.00 - TIBBIYOT FANLARI ISSN: 3093-8740

modification, Bio-LIFT, incorporates a bioprosthetic graft within the intersphincteric space, enhancing mechanical support and potentially improving long-term outcomes. Ellis reported a 94% healing rate after Bio-LIFT at 12 months of follow-up (Ellis, 2010).

Endoscopic and Energy-Based Approaches

The recent decade has witnessed an expansion of endoscopic and energy-based therapies, emphasizing tract obliteration under direct visualization. The Video-Assisted Anal Fistula Treatment (VAAFT), introduced by Meinerio and Mori in 2006, integrates diagnostic and therapeutic phases using a fistuloscope to visualize the internal opening and tract (Meinerio & Mori, 2011; Adegbola et al., 2017). Fistula walls are destroyed via diathermy and the internal opening is closed by sutures, staples, or flaps. VAAFT offers high diagnostic precision and minimal sphincter injury, with reported success rates between 66% and 87% and negligible incontinence (Jiang et al., 2017). However, the need for specialized equipment and cost constraints limit its accessibility (Limura & Giordano, 2015).

Fistula Laser Closure (FiLaC) — also known as Endofistula Laser Ablation (EFLA) — employs a 1470-nm radial laser fiber to ablate the fistula epithelium and promote tract fibrosis (Wilhelm, 2011; Wilhelm et al., 2017). The method may be combined with closure of the internal opening using a flap. FiLaC achieves moderate primary healing rates (60–70%) but demonstrates higher cumulative success (up to 88%) after repeat sessions, with minimal risk of incontinence (Wilhelm et al., 2017). Nevertheless, it remains a “blind” technique, lacking direct visualization of secondary tracts (Limura & Giordano, 2015).

Novel Sphincter-Preserving Devices

Mechanical closure systems, such as the Over-the-Scope Clip (OTSC®), apply a shape-memory alloy clip to the internal opening to achieve continuous compression and closure (Adegbola et al., 2017). The method is entirely sphincter-sparing and may be combined with debridement of the tract. However, outcomes remain inconsistent, with reported success ranging from 20% to 79%, depending on fistula complexity and operator experience (Adegbola et al., 2017).

Regenerative and Emerging Therapies

Recent years have witnessed the growing application of regenerative and biologically based techniques in the treatment of anal fistula, aiming to enhance healing, reduce recurrence, and preserve sphincter function. Conventional surgical methods often fail to achieve complete closure while maintaining continence; thus, regenerative tools such as fibrin glue, biologic and synthetic plugs, and stem cell-based therapies have emerged as promising alternatives (Scoglio, Walker, Fichera, 2014).

Fibrin and Biologic Glues

Fibrin glue, first introduced by Hjortrup et al. in 1991, represents one of the earliest minimally invasive biological approaches. It is injected into the fistulous tract after curettage, where it polymerizes to create a matrix that promotes collagen deposition and fibroblast migration, facilitating tissue healing. Various formulations—such as autologous cryoprecipitate, reconstituted bovine thrombin, and donor plasma—have been tested to improve seal durability. The BioGlue surgical adhesive, composed of purified bovine serum albumin and glutaraldehyde, offers a stronger and more persistent bond, maintaining integrity for up to two years (Scoglio, Walker, Fichera, 2014). Despite variable success rates, fibrin-based therapies remain attractive due to their safety, simplicity, and sphincter-preserving nature.

Fistula Plugs and Bio-LIFT



The concept of fistula closure using biologic plugs was introduced in 2006 by Robb et al. and Johnson et al., who proposed sealing the internal opening without sphincter division. The **Surgisis anal fistula plug**, composed of lyophilized porcine small intestinal submucosa, acts as a scaffold for host cell infiltration and tissue remodeling within three months. Synthetic variants such as the **GORE BIO-A plug**, made from bioabsorbable PGA/TMC copolymers, provide a porous, interconnected matrix that gradually degrades, leaving behind native tissue regeneration (Scoglio, Walker, Fichera, 2014; Köckerling et al., 2015).

Further evolution of the LIFT technique has led to the **Bio-LIFT procedure**, in which a bioprosthetic material reinforces the intersphincteric closure, enhancing mechanical support and reducing recurrence. Han et al. later proposed a hybrid LIFT-plug technique that combines the benefits of both methods (Scoglio, Walker, Fichera, 2014).

Studies comparing biologic plugs made of porcine submucosa, human acellular dermal matrix, and synthetic bioabsorbable polymers demonstrate comparable success rates, typically ranging from 50% to 75% depending on complexity and prior interventions (Köckerling et al., 2015). Autologous cartilage plugs derived from nasal or auricular tissue have also shown encouraging early results in refractory cases.

Stem Cell–Based and Cellular Therapies

Stem cell therapy represents one of the most exciting frontiers in fistula management. Expanded adipose-derived stem cells (eADSCs) can be easily harvested via liposuction and exhibit anti-inflammatory and pro-regenerative effects when injected into fistulous tracts. Multicenter randomized controlled trials have demonstrated that eADSC therapy promotes durable closure in cryptoglandular, Crohn’s-related, and rectovaginal fistulas (Garcia-Olmo et al., 2009).

Similarly, bone marrow–derived mesenchymal stromal cells (MSCs) and fibroblast-based approaches have shown potential in refractory Crohn’s fistulas. Experimental use of collagen paste loaded with cultured autologous fibroblasts resulted in complete histological healing in pilot studies, indicating that combining scaffolds with viable cells can enhance regenerative potential (Scoglio, Walker, Fichera, 2014).

Imaging and Preoperative Evaluation

Anal fistula remains a common and challenging condition with a high recurrence rate, often resulting from undetected secondary tracts or residual infection despite adequate surgery (Halligan, 2006). The cornerstone of successful management lies in precise preoperative evaluation. Surgeons must answer two critical questions before intervention:

1. What is the exact relationship of the fistula tract to the anal sphincter complex, and can it be safely divided without risking postoperative incontinence?
2. Are there secondary extensions that require treatment to prevent recurrence, and where are they located? (Halligan, 2006).

Traditionally, examination under anesthesia (EUA) was considered the diagnostic standard. However, modern evidence highlights the importance of preoperative imaging in identifying occult sepsis that would otherwise remain undetected (Halligan, 2006). Accurate preoperative mapping correlates strongly with improved surgical outcomes, better sphincter preservation, and reduced recurrence rates (Han, 2021).

Evolution of Imaging Modalities



Fistulography and Computed Tomography (CT)

Fistulography was historically the first imaging technique applied to anal fistulas (Halligan, 2006). Yet, it presents major limitations: secondary tracts may not opacify, the sphincter complex cannot be directly visualized, and the internal opening is often difficult to localize. In one study, the internal opening and its branches were correctly demonstrated in only 16% of cases (Halligan, 2006). Consequently, fistulography is now considered obsolete (Han, 2021).

CT imaging, particularly with rectal and intravenous contrast, may visualize associated abscesses but lacks the soft-tissue resolution needed to delineate sphincter anatomy or classify fistula types (Halligan, 2006). Recent advances in CT image processing using deep learning algorithms have shown potential to improve diagnostic precision (Han, 2021).

Endoanal Ultrasonography (EAUS)

Developed by Clive Bartram, EAUS was the first modality to provide detailed visualization of the anal sphincter complex (Halligan, 2006). It remains widely used for preoperative classification and is particularly effective for identifying the internal opening, which typically lies close to the probe surface.

However, traditional EAUS has inherent limitations: restricted penetration beyond the external sphincter limits visualization of ischioanal and supralelevator infections, and infection cannot be reliably distinguished from fibrosis, as both appear hypoechoic (Halligan, 2006).

These drawbacks are partly overcome by contrast enhancement techniques using hydrogen peroxide (H_2O_2) or microbubble ultrasound contrast agents introduced through the external opening during examination (Halligan, 2006; Han, 2021). H_2O_2 -enhanced EAUS produces a bright hyperechoic image of the fistula tract and is a safe, inexpensive, and effective method for delineating its anatomy (Han, 2021).

A newer approach, trans-fistulous contrast-enhanced endoanal ultrasonography (TF-CEEAUS), utilizes acoustic scattering from microbubbles to increase contrast between lesions and surrounding tissue. Studies show that TF-CEEAUS provides superior diagnostic accuracy for internal openings located within 3 cm of the anal verge compared with MRI (Han, 2021). Overall, EAUS achieves approximately 81% accuracy for identifying the main tract and 91% for detecting the internal opening (Halligan, 2006).

Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging has emerged as the gold standard for preoperative classification of anal fistulas (Halligan, 2006). MRI's success stems from its excellent soft-tissue contrast, high sensitivity for sepsis detection, and multiplanar capabilities in anatomically relevant planes.

Key advantages of MRI include:

- **Detection of hidden sepsis and secondary tracts:** MRI surpasses all other techniques, including EUA, in identifying remote infection foci, a critical factor in preventing recurrence (Halligan, 2006).
- **High diagnostic accuracy:** Comparative studies report ~90% accuracy for overall fistula classification, outperforming EAUS (81%) and digital rectal examination (61%), with 97% accuracy in locating the internal opening (Halligan, 2006).
- **Impact on surgical strategy:** MRI findings frequently alter operative planning and significantly reduce recurrence risk—up to 75% in complex cases (Halligan, 2006).



TOSHKENT TIBBIYOT AKADEMIYASI URGANCH FILIALI JANUBIY OROLBO'YI TIBBIYOT JURNALI

1-TOM, 4-SON. 2025

14.00.00 - TIBBIYOT FANLARI ISSN: 3093-8740

For optimal imaging, T2-weighted fat-suppressed sequences should be used to differentiate hyperintense fluid-filled tracts from hypointense fibrotic walls, while ensuring visualization of sphincter anatomy. Proper alignment of axial, coronal, and sagittal planes relative to the anal canal is crucial; coronal images are particularly valuable for distinguishing supralelevator from infralevator disease (Halligan, 2006).

Role of Imaging in Surgical Planning

Given the strong evidence that MRI improves surgical planning and clinical outcomes, it should be routinely performed in recurrent or complex cases and in patients with Crohn's disease (Halligan, 2006). When MRI is unavailable or interpretation expertise is limited, EAUS represents a viable alternative, particularly effective for localizing the internal opening and monitoring medical therapy in Crohn-related fistulas (Halligan, 2006).

Conclusion

The modern approach to the treatment of anal fistula is based on precise preoperative imaging and the implementation of minimally invasive and regenerative technologies aimed at preserving sphincter function and reducing the risk of recurrence. MRI and contrast-enhanced endoanal ultrasonography provide high diagnostic accuracy, allowing surgeons to thoroughly assess the anatomy of the fistulous tract and select the optimal surgical strategy. Minimally invasive methods, including LIFT, VAAFT, FiLaC, and other sphincter-sparing techniques, have proven effective in eliminating fistulas with minimal tissue trauma and a low rate of postoperative incontinence.

In parallel, regenerative approaches are actively developing, including the use of biomaterials, tissue matrices, fibrin glues, cellular technologies, and growth factors that promote natural tissue repair and increase the likelihood of complete healing without compromising anal function. Despite the variability of results and the absence of a unified standard, the accumulated data demonstrate the high potential of combining bioengineering and minimally invasive methods as a new direction in the treatment of anal fistula.

Further research should focus on the standardization of protocols, optimization of cell and biomaterial delivery methods, and long-term evaluation of clinical outcomes to improve the effectiveness of therapy and enhance patients' quality of life.

References

1. Mateescu, Tudor, et al. "Exploring Health-Related Quality of Life in Patients with Anal Fistulas: A Comprehensive Study." *Life* 13.10 (2023): 2008.
2. Van Koperen, Paul J., et al. "Long-term functional outcome and risk factors for recurrence after surgical treatment for low and high perianal fistulas of cryptoglandular origin." *Diseases of the colon & rectum* 51.10 (2008): 1475-1481.
3. Baghel, Praveen Singh, et al. "An Observational Study on Surgical Outcome Predictors In Patients With Anal Fistula." *Gas* 2.2.
4. Lynch, A. Craig, et al. "Clinical outcome and factors predictive of recurrence after enterocutaneous fistula surgery." *Annals of surgery* 240.5 (2004): 825-831.
5. Emile, Sameh Hany. "Recurrent anal fistulas: when, why, and how to manage?." *World Journal of Clinical Cases* 8.9 (2020): 1586.



TOSHKENT TIBBIYOT AKADEMIYASI URGANCH FILIALI JANUBIY OROLBO'YI TIBBIYOT JURNALI

1-TOM, 4-SON. 2025

14.00.00 - TIBBIYOT FANLARI ISSN: 3093-8740

6. Khan, Sidrah, et al. "Predictors of recurrence and long-term patient reported outcomes following surgical repair of anal fistula, a retrospective analysis." *International Journal of Colorectal Disease* 39.1 (2024): 37.
7. van Koperen, Paul J., et al. "Anal fistula plug for closure of difficult anorectal fistula: a prospective study." *Diseases of the colon & rectum* 50.12 (2007): 2168-2172.
8. Köckerling, Ferdinand, et al. "Treatment of fistula-in-ano with fistula plug—a review under special consideration of the technique." *Frontiers in Surgery* 2 (2015): 55.
9. Narang, Sunil K., et al. "Delayed absorbable synthetic plug (GORE® BIO-A®) for the treatment of fistula-in-ano: a systematic review." *Colorectal Disease* 18.1 (2016): 37-44.
10. Eisenstein, Samuel, and Alex Jenny Ky. "Biologic fistula plugs." *Anal fistula: principles and management*. Springer New York, 2013. 83-88.
11. Scoglio, Daniele, Avery S. Walker, and Alessandro Fichera. "Biomaterials in the treatment of anal fistula: hope or hype?." *Clinics in colon and rectal surgery* 27.04 (2014): 172-181.
12. Johnson, Eric K., Janette U. Gaw, and David N. Armstrong. "Efficacy of anal fistula plugs vs. fibrin glue in closure of anorectal fistulas." *Diseases of the colon & rectum* 49.3 (2006): 371-376.
13. Zarin, Mohammad, et al. "VAAFT: video assisted anal fistula treatment; bringing revolution in fistula treatment." *Pakistan journal of medical sciences* 31.5 (2015): 1233.
14. Jiang, Hui-hong, et al. "Video-assisted anal fistula treatment (VAAFT) for complex anal fistula: a preliminary evaluation in China." *Medical science monitor: international medical journal of experimental and clinical research* 23 (2017): 2065.
15. Wilhelm, A., A. Fiebig, and M. Krawczak. "Five years of experience with the FiLaC™ laser for fistula-in-ano management: long-term follow-up from a single institution." *Techniques in coloproctology* 21.4 (2017): 269-276.
16. Jongen, Johannes HPM, and Faramarz Pakravan. "Current State-of-the Art of Anal Fistula Surgery in Germany." *Iranian Journal of Colorectal Research* 11.2 (2023): 55-64.
17. Garg, Pankaj. "Newer procedures need to demonstrate efficacy in high complex anal fistulas." *Annals of Coloproctology* 39.4 (2023): 371.
18. Adegbola, S. O., et al. "Short-term efficacy and safety of three novel sphincter-sparing techniques for anal fistulae: a systematic review." *Techniques in coloproctology* 21.10 (2017): 775-782.
19. Lunniss, Peter J. "LIFT procedure: a simplified technique for fistula-in-ano." *Techniques in coloproctology* 13.3 (2009): 241-242.
20. Song, Kee Ho. "New techniques for treating an anal fistula." *Journal of the Korean Society of Coloproctology* 28.1 (2012): 7.
21. Sileri, P., et al. "Ligation of the intersphincteric fistula tract (LIFT) to treat anal fistula: early results from a prospective observational study." *Techniques in coloproctology* 15.4 (2011): 413-416.
22. Qiu, Jian-ming, et al. "Feasibility of ambulatory surgery for anal fistula with LIFT procedure." *BMC gastroenterology* 19.1 (2019): 81.



TOSHKENT TIBBIYOT AKADEMIYASI URGANCH FILIALI
JANUBIY OROLBO'YI TIBBIYOT JURNALI

1-TOM, 4-SON. 2025

14.00.00 - TIBBIYOT FANLARI ISSN: 3093-8740

23. van Koperen, Paul J., et al. "The anal fistula plug treatment compared with the mucosal advancement flap for cryptoglandular high transsphincteric perianal fistula: a double-blinded multicenter randomized trial." *Diseases of the colon & rectum* 54.4 (2011): 387-393.
24. Khafagy, Wael, et al. "Treatment of anal fistulas by partial rectal wall advancement flap or mucosal advancement flap: a prospective randomized study." *International journal of surgery* 8.4 (2010): 321-325.
25. Uribe, Natalia, et al. "Clinical and manometric results of endorectal advancement flaps for complex anal fistula." *International journal of colorectal disease* 22.3 (2007): 259-264.
26. Leng, Qiang, and Hei-Ying Jin. "Anal fistula plug vs mucosa advancement flap in complex fistula-in-ano: a meta-analysis." *World journal of gastrointestinal surgery* 4.11 (2012): 256.
27. Durgun, Cemalettin, and Abidin Tüzün. "The use of a loose seton as a definitive surgical treatment for anorectal abscesses and complex anal fistulas." *Advances in Clinical and Experimental Medicine* 32.10 (2023): 1149-1157.
28. Almughamsi, Asim M., et al. "Evaluation of the cutting seton technique in treating high anal fistula." *Cureus* 15.10 (2023).
29. Zhi, Congcong, et al. "Long-term follow-up study of loose combined cutting seton surgery for patients with high anal fistula." *Annals of Translational Medicine* 9.14 (2021): 1160.
30. Buchanan, G. N., et al. "Long-term outcome following loose-seton technique for external sphincter preservation in complex anal fistula." *Journal of British Surgery* 91.4 (2004): 476-480.
31. Kelly, M. E., et al. "The role of loose seton in the management of anal fistula: a multicenter study of 200 patients." *Techniques in coloproctology* 18.10 (2014): 915-919.
32. Subhas, Gokulakrishna, et al. "Setons in the treatment of anal fistula: review of variations in materials and techniques." *Digestive surgery* 29.4 (2012): 292-300.
33. Sheikh, Irfan Ali, et al. "Fistulotomy vs fistulectomy in the treatment of simple low anal fistula of male patients." *Pakistan Armed Forces Medical Journal* 6 (2015): 798.
34. Choudhury, Chishti Tanhar Bakth, Mohammad Al Mamun, and Md Shahadat. "Relative comparisons in surgical outcomes of fistulectomy and fistulotomy in low variety perianal fistula." *Public Health* 3 (2023): 30-43.
35. Bhatti, Yasmeen, et al. "Fistulotomy versus fistulectomy in the treatment of low fistula in ano." *Rawal Med J* 36.4 (2011): 284-286.
36. Xu, Yansong, Siyuang Liang, and Weizhong Tang. "Meta-analysis of randomized clinical trials comparing fistulectomy versus fistulotomy for low anal fistula." *Springerplus* 5.1 (2016): 1722.
37. Quinn, Rakesh, Alexandra Peacock, and Rebecca J. Lenzion. "Fistulotomy versus fistulectomy for simple fistula-in-ano: a systematic review and meta-analysis of randomized controlled trials." *ANZ Journal of Surgery* (2025).
38. Lin, Tao, et al. "A comparison of trans-fistula contrast-enhanced endoanal ultrasound and MRI in the diagnosis of anal fistula." *Annals of Palliative Medicine* 10.8 (2021): 9165173-9169173.



39. Toyonaga, T., et al. "Comparison of accuracy of physical examination and endoanal ultrasonography for preoperative assessment in patients with acute and chronic anal fistula." *Techniques in coloproctology* 12.3 (2008): 217-223.
40. Sayed, Alaa, et al. "Role of endoanal ultrasound in the assessment of perianal fistula in correlation with MRI fistulography." *Egyptian Journal of Radiology and Nuclear Medicine* 53.1 (2022): 195.
41. Toyonaga, Takayuki, et al. "Microbiological analysis and endoanal ultrasonography for diagnosis of anal fistula in acute anorectal sepsis." *International journal of colorectal disease* 22.2 (2007): 209-213.
42. Felt-Bersma, R. J. F. "Endoanal ultrasound in perianal fistulas and abscesses." *Digestive and liver disease* 38.8 (2006): 537-543.
43. Visscher, Arjan Paul, and Richelle JF Felt-Bersma. "Endoanal ultrasound in perianal fistulae and abscesses." *Ultrasound quarterly* 31.2 (2015): 130-137.
44. Siddiqui, Muhammed RS, et al. "A diagnostic accuracy meta-analysis of endoanal ultrasound and MRI for perianal fistula assessment." *Diseases of the colon & rectum* 55.5 (2012): 576-585.
45. Beets-Tan, Regina GH, et al. "Preoperative MR imaging of anal fistulas: does it really help the surgeon?." *Radiology* 218.1 (2001): 75-84.
46. Halligan, Steve, and Jaap Stoker. "Imaging of fistula in ano." *Radiology* 239.1 (2006): 18-33.
47. Sharma, Ashish, et al. "Current imaging techniques for evaluation of fistula in ano: a review." *Egyptian Journal of Radiology and Nuclear Medicine* 51.1 (2020): 130.
48. Han, Lingling, et al. "Deep Learning-Based CT Image Characteristics and Postoperative Anal Function Restoration for Patients with Complex Anal Fistula." *Journal of Healthcare Engineering* 2021.1 (2021): 1730158.
49. Sohrabi, Masoudreza, et al. "Perianal fistula; from etiology to treatment-a review." *Middle East journal of digestive diseases* 16.2 (2024): 76.
50. Yamana, Tetsuo. "Japanese practice guidelines for anal disorders II. Anal fistula." *Journal of the Anus, Rectum and Colon* 2.3 (2018): 103-109.
51. Garg, Pankaj. "Comparing existing classifications of fistula-in-ano in 440 operated patients: Is it time for a new classification? A Retrospective Cohort Study." *International Journal of Surgery* 42 (2017): 34-40.
52. Idris, Saadeldin Ahmed, A. Abdalla, and A. Hamza. "Classification of fistula in ano." *Med J* 2 (2015): 99-102.
53. Van Koperen, P. J., et al. "Histological identification of epithelium in perianal fistulae: a prospective study." *Colorectal Disease* 12.9 (2010): 891-895.
54. Mitalas, L. E., et al. "Identification of epithelialization in high transsphincteric fistulas." *Techniques in coloproctology* 16.2 (2012): 113-117.
55. Yang, Jun, et al. "Microbiomic signatures of anal fistula and putative sources of microbes." *Frontiers in cellular and infection microbiology* 14 (2024): 1332490.
56. Jaiswal, Prakhar, et al. "Significant presence of biofilm-producing gut-derived bacteria in anal fistula of chronic duration." *International Wound Journal* 18.4 (2021): 519-524.



**TOSHKENT TIBBIYOT AKADEMIYASI URGANCH FILIALI
JANUBIY OROLBO‘YI TIBBIYOT JURNALI**

1-TOM, 4-SON. 2025

14.00.00 - TIBBIYOT FANLARI ISSN: 3093-8740

57. Enez, Victoria Eugenia Dowling, and Carla Virginia Izarra Henriquez. "Anal abscess microbiology as an anal fistula predictor." *Journal of Coloproctology* 40.02 (2020): 129-134.
58. Kotze, Paulo Gustavo, et al. "Modern management of perianal fistulas in Crohn's disease: future directions." *Gut* 67.6 (2018): 1181-1194.
59. Bataille, F., et al. "Morphological characterisation of Crohn's disease fistulae." *Gut* 53.9 (2004): 1314-1321.
60. Haddow, James B., et al. "Comparison of cytokine and phosphoprotein profiles in idiopathic and Crohn's disease-related perianal fistula." *World journal of gastrointestinal pathophysiology* 10.4 (2019): 42.
61. Whiteford, Mark H. "Perianal abscess/fistula disease." *Clinics in colon and rectal surgery* 20.02 (2007): 102-109.
62. Kawecki, Maciej Przemysław, et al. "Exploring Perianal Fistulas: Insights into Biochemical, Genetic, and Epigenetic Influences—A Comprehensive Review." *Gastroenterology Insights* 16.1 (2025): 10.
63. Ratto, Carlo, et al. "Immunopathological characterization of cryptoglandular anal fistula: a pilot study investigating its pathogenesis." *Colorectal Disease* 18.12 (2016): O436-O444.
64. Sugrue, Jeremy, et al. "Pathogenesis and persistence of cryptoglandular anal fistula: a systematic review." *Techniques in coloproctology* 21.6 (2017): 425-432.
65. Włodarczyk, Marcin, et al. "Current concepts in the pathogenesis of cryptoglandular perianal fistula." *Journal of International Medical Research* 49.2 (2021): 0300060520986669.
66. Gosselink, Martijn Pieter, Robbert Sebastiaan van Onkelen, and Willem Rudolf Schouten. "The cryptoglandular theory revisited." *Colorectal Disease* 17.12 (2015): 1041-1043.
67. An, Yongkang, et al. "Comparison of clinical outcomes of anal fistula plug and endoanal advancement flap repair treating the complex anal fistula: a systematic review and meta-analysis." *Updates in Surgery* 75.8 (2023): 2103-2115.
68. Ji, Lijiang, et al. "Advances in the treatment of anal fistula: a mini-review of recent five-year clinical studies." *Frontiers in surgery* 7 (2021): 586891.
69. Owen, H. A., et al. "Quality of life with anal fistula." *The Annals of The Royal College of Surgeons of England* 98.5 (2016): 334-338.
70. Abramowitz, Laurent, et al. "The outcome of fistulotomy for anal fistula at 1 year: a prospective multicentre French study." *Colorectal Disease* 18.3 (2016): 279-285.
71. Limura, Elsa, and Pasquale Giordano. "Modern management of anal fistula." *World Journal of Gastroenterology: WJG* 21.1 (2015): 12.
72. Abbas, Maher A., Christopher H. Jackson, and Philip I. Haigh. "Predictors of outcome for anal fistula surgery." *Archives of Surgery* 146.9 (2011): 1011-1016.
73. Visscher, A. P., et al. "Long-term follow-up after surgery for simple and complex cryptoglandular fistulas: fecal incontinence and impact on quality of life." *Diseases of the Colon & Rectum* 58.5 (2015): 533-539.
74. Ferrer-Márquez, Manuel, et al. "Analysis and description of disease-specific quality of life in patients with anal fistula." *Cirugía Española (English Edition)* 96.4 (2018): 213-220.



TOSHKENT TIBBIYOT AKADEMIYASI URGANCH FILIALI
JANUBIY OROLBO'YI TIBBIYOT JURNALI

1-TOM, 4-SON. 2025

14.00.00 - TIBBIYOT FANLARI ISSN: 3093-8740

75. Garcia-Olmo, Damian, et al. "Prevalence of anal fistulas in Europe: systematic literature reviews and population-based database analysis." *Advances in therapy* 36.12 (2019): 3503-3518.
76. Sarveazad, Arash, et al. "Prevalence of anal fistulas: a systematic review and meta-analysis." *Gastroenterology and Hepatology From Bed to Bench* 15.1 (2022): 1.

