

Evolution of anal fistula management: A comprehensive review of novel minimally invasive and regenerative techniques

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Background: Background: Surgical management of complex anal fistulas is a painful and chronic clinical problem, with a delicate balance between full elimination of fistulae and necessity to preserve anal sphincter integrity. The current available treatments for this syndrome for a simple fistula present significantly elevated risks of fecal incontinence. The surgical approach of improving the outcomes of these fistulae has been evolving to sphincter-sparing techniques and minimally invasive, stem cell therapy in the literature. I have performed a systematic review, based on PRISMA guidelines, to assess the current approach for anal fistula removal (VAAFT), FiLaC Laser Closure (FiLaC) with a minimally invasive technique and stem cell therapy using mesenchymal stem cell for the treatment of Crohn's disease-associated fistulas (MSC) treatment. With respect to the diagnosis process, 31.4% of major sphincter-sparing procedures were identified for major sphincter-sparing operations in networks. VAAFT has the lowest failure rate (22.3%) and minimal continence disturbance while FiLaC is able to have a higher failure rate (43.9%) but retain sphincter well. MSC therapy, especially in fistulas associated with Crohn's disease, has achieved a remarkable healing rate exceeding 60%, and a recent (ADMIRE-CD II) Phase 3 trial suggests preconditioning has also achieved good but not necessarily clinical results. Advanced anatomical diagnostic tools like magnetic resonance imaging to detect a RIFIL fistula, which are rapidly surfacing today, are being used for preoperative planning and analysis. No one treatment method is consistently effective at minimally invasive preoperative care. A specialized and multi-modal algorithmic approach that integrates surgical (or biological) interventions and pre-operative outcomes is necessary.

KEYWORDS: Anal fistula, Complex perianal fistula, Minimally invasive surgery, LIFT Procedure, VAAFT, Fistula laser closure (FiLaC)

An anal fistula is a chronic epithelialized communication between the anorectal canal and the perianal skin, affecting 1–2 per 10,000 individuals (1). It is characterized by chronic purulent discharge, recurrent perianal abscesses, and impaired quality of life (1, 19). While fistulotomy remains the gold standard for simple fistulas—boasting over 85% recovery—the management of complex anal fistulas (involving >30% of the external sphincter, anterior female fistulas, multiple tracts, or Crohn's disease) presents a profound anatomical dilemma (3, 5, 18). In these complex cases, traditional muscle-cutting surgeries result in an unacceptable frequency of postoperative fecal incontinence (1, 3). Consequently, proctological surgery is rapidly shifting toward sphincter-sparing, minimally invasive, and regenerative methods (1, 4).

Simultaneously, magnetic resonance imaging (MRI) has revolutionized preoperative diagnostics. MRI-based anatomical mapping has uncovered previously misunderstood sepsis pathways, such as the outersphincteric space and the corresponding Garg

fascia (5, 10). This fascial plane dictates the trajectory of the RIFIL (Roof of Ischiorectal Fossa Inside Levator-ani muscle) fistula. (Figure 4.)

Found in up to 10% of cohorts, RIFIL fistulas are highly complex and carry a surgical failure rate of 30.6%, compared to 7.2% for non-RIFIL fistulas (5, 9, 10). Etiology is equally critical; for example, RT-PCR testing is significantly more effective than histopathology at detecting underlying tuberculosis in fistulas (7.4% vs. 1.5%), which alters the required pharmacological management (11).

To address these challenges without compromising continence, the modern armamentarium includes mechanical ligation (LIFT), advancement flaps (EAF), ablative technologies (FiLaC, VAAFT), mechanical clips (OTSC), and mesenchymal stem cells (MSCs) (1, 4, 6, 7, 15). This review critically synthesizes the latest evidence on these modalities to provide a nuanced, evidence-based algorithmic framework for modern fistula management.

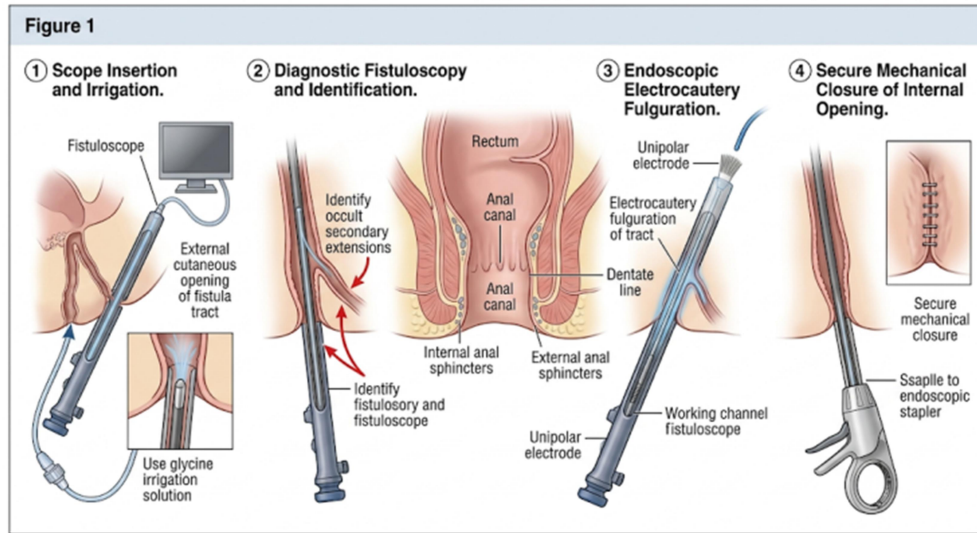


Figure 1. Schematic of Video-Assisted Anal Fistula Treatment (VAAFT). Detailed illustration demonstrating the insertion of the rigid, 8-degree angled fistuloscope through the external cutaneous opening. The image depicts the intraluminal visualization process utilizing glycine irrigation, the electrocautery fulguration of the tract walls using a unipolar electrode, and the critical identification of occult secondary extensions prior to the secure mechanical closure of the primary internal opening.

Methods

Results

This narrative review utilized a systematic approach modeled after the PRISMA guidelines (12). A comprehensive search was executed across PubMed/MEDLINE, EMBASE, Cochrane CENTRAL, Web of Science, and major Chinese databases (CNKI, Wanfang) (3, 5, 13). ClinicalTrials.gov was also reviewed (14). The search focused on literature published between January 2014 and March 2026, targeting keywords like "minimally invasive," "VAAFT," "FiLaC," "OTSC," "LIFT," and "mesenchymal stem cells" (4, 7, 11).

Inclusion criteria prioritized RCTs, prospective/retrospective cohorts, and recent network meta-analyses evaluating adult patients with complex cryptoglandular or Crohn's-associated fistulas (1, 3, 4, 8, 11). Primary outcomes extracted were healing rates, failure/recurrence rates, continence preservation, and complications (1, 4, 11). Methodological quality was appraised using AGREE II, NOS, and RoB 2 instruments (12, 13).

Clinical Guidelines and Diagnostic Consensus

A review of 15 contemporary guidelines establishes MRI as the indispensable diagnostic gold standard, often utilizing the SMART reporting template to standardize anatomical findings (5, 13). Surgical philosophy has shifted: cutting setons have been downgraded in recommendation strength due to incontinence risks, while sphincter-sparing techniques and biological adjuncts have been upgraded (5, 13). Video-Assisted Anal Fistula Treatment (VAAFT)

VAAFT utilizes a rigid fistuloscope for direct endoluminal visualization, allowing the surgeon to map the primary tract and identify occult secondary extensions. The internal opening is closed (via stapler or flap), and the tract is ablated using an electrocautery brush and cleared with an endobrush or cyanoacrylate glue (15). (Figure 1.)

A 2025 network meta-analysis encompassing 3,520 patients revealed VAAFT had the lowest pooled failure rate (22.3%) among evaluated options at 32.4

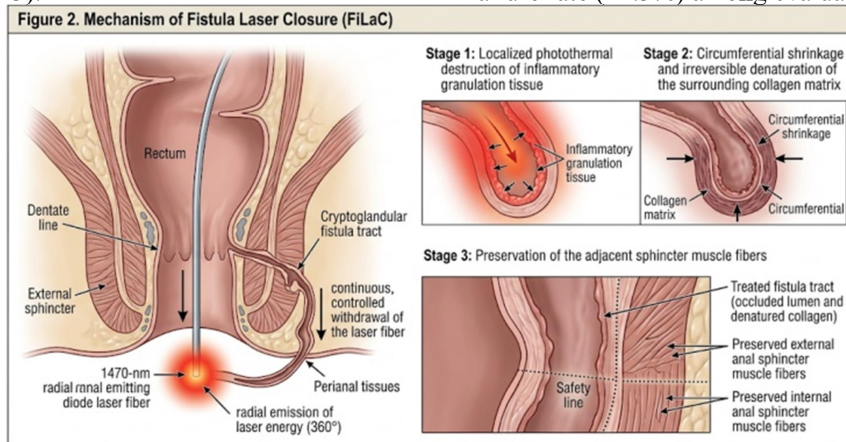


Figure 2. Mechanism of Fistula Laser Closure (FiLaC). Anatomical diagram representing the continuous, controlled withdrawal of a 1470-nm radial emitting diode laser fiber through a complex cryptoglandular fistula tract. The schematic showcases the localized photothermal destruction of the inflammatory granulation tissue and the subsequent circumferential shrinkage and irreversible denaturation of the surrounding collagen matrix, emphasizing the preservation of the adjacent sphincter muscle fibers from thermal collateral damage.

Figure 3. Application of the Over-The-Scope Clip (OTSC) Proctology System

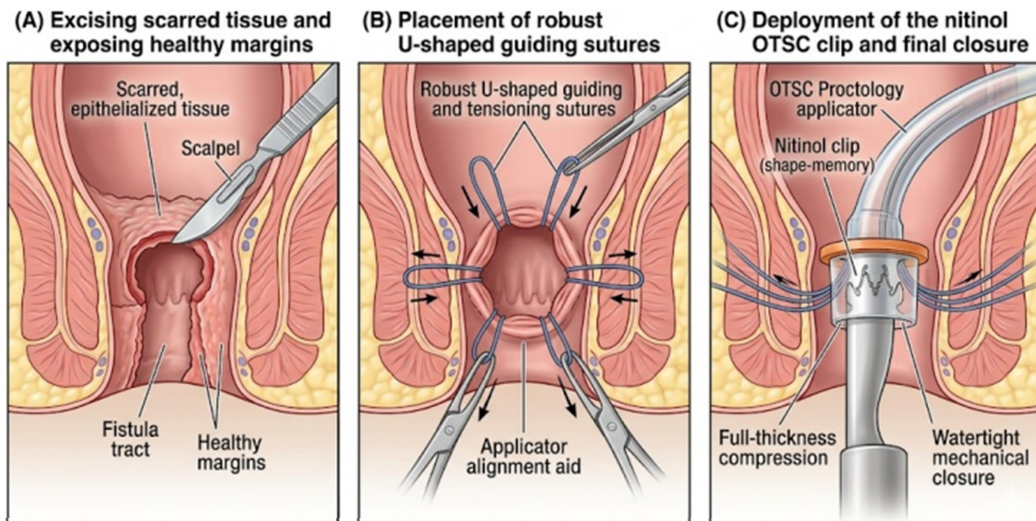


Figure 3. Application of the Over-The-Scope Clip (OTSC) Proctology System. A highly detailed, step-by-step clinical schematic detailing: (A) the 2 cm sharp circumferential excision of scarred, epithelialized tissue surrounding the internal mucosal opening to expose healthy margins; (B) the placement of robust U-shaped guiding and tensioning sutures to facilitate applicator alignment; and (C) the final deployment of the shape-memory nitinol clip in situ, resulting in immense full-thickness compression and instantaneous, watertight mechanical closure of the anatomical defect.

months follow-up (15). It exhibits an exceptional safety profile, with 0% of patients reporting worsening continence and a minor complication rate of 7.2% (15).

Fistula Laser Closure (FiLaC)

FiLaC utilizes a 1470-nm radial emitting diode laser fiber to deliver thermal energy. As the fiber is withdrawn, it denatures the surrounding collagen matrix, shrinking and sealing the tract behind it (9, 15). (Figure 2.)

While popular for its simplicity, a 2025 systematic review of 1,503 patients showed a pooled primary healing rate of 57.46%, with a high overall failure rate of 43.9% (9, 15). Despite suboptimal healing, FiLaC perfectly preserves the sphincter (0% incontinence). However, it carries a 10.2% minor complication rate, largely due to postoperative perianal sepsis (4%–6.54%), likely caused by sealing the tract without adequate external drainage (9, 15).

Ligation of the Intersphincteric Fistula Tract (LIFT) and Endorectal Advancement Flap (EAF)

LIFT involves isolating, ligating, and sharply excising the fistulous tract exactly as it crosses the intersphincteric groove (8, 15). LIFT demonstrates a robust 28.6% overall failure rate over 35.4 months, with an extremely low objective continence disturbance rate of 1.5% and a minor complication rate of 4.3% (8, 15). In contrast, the EAF has a similar failure rate (25.9%) but a highly concerning continence disturbance rate of 7.3%, driven by aggressive mucosal stretching and anal dilation (15).

Over The Scope Clip (OTSC)

The OTSC system uses a highly tensioned, shape-memory nitinol clip to provide mechanical, full-thickness compression to permanently seal the internal mucosal opening without complex suturing (10). (Figure 3.)

Across 622 anal fistula cases, long-term clinical healing was 55.8% (16). While success is intermediate, it offers rapid intraoperative execution and zero risk of direct sphincter transection. Mechanical complications (clip displacement, tissue

Figure 4. Anatomical Pathway of the RIFIL Fistula
Based on advanced preoperative MRI mapping

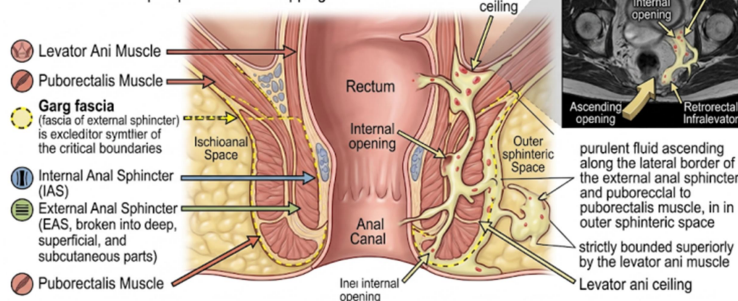


Figure 4. Anatomical Pathway of the RIFIL Fistula. High-resolution anatomical diagram based on advanced preoperative MRI mapping, explicitly demonstrating the outersphincteric space and the critical boundaries of the Garg fascia. The complex pathway illustrates purulent fluid ascending along the lateral border of the external anal sphincter and puborectalis muscle, strictly bounded superiorly by the levator ani muscle. This highlights the severely enclosed, rigid nature of the tract that inherently complicates standard minimally invasive ablative interventions and necessitates specialized reconstructive techniques.

detachment) occur in 4.7% of patients (16).

Regenerative Therapies: MSC Therapy and Plugs

MSCs (adipose or bone-marrow-derived) promote local tissue regeneration and exert profound immunomodulatory effects (11). Recent meta-analyses show MSCs yield robust healing rates in Crohn's disease fistulas (60.4% with ASCs, 63.6% with bone marrow) but drop to 53.8% for cryptoglandular fistulas (11).

However, the global Phase 3 ADMIRE-CD II trial evaluating Darvadstrocel (an ASC suspension) failed its primary endpoint, showing a 48.8% remission rate versus a 46.3% placebo rate (14). Crucially, the protocol mandated rigorous surgical preconditioning (curettage, setons, sutured internal closure) for both arms, proving that meticulous surgical preparation alone achieves near 50% healing in complex Crohn's fistulas (14). Bioprosthetic plugs act as bioresorbable scaffolds but suffer from notoriously heterogeneous outcomes and unacceptably high extrusion rates (13).

Novel Reconstructive Procedures: RIFER and TROPIS

RIFER: Designed for high intersphincteric fistulas, this reconstructive technique intentionally leaves the external perianal wound semi-open to prevent purulent accumulation. A 2025 study reported a 100% surgical cure rate at 6 months with flawless continence maintenance (17).

TROPIS: Transanal deroofing of the intersphincteric space directly into the anal canal. It promotes open healing of the internal opening while completely sparing the external anal sphincter (18).

Discussion

The evolution of fistula management is defined by the "efficacy-continence trade-off." Minimally invasive techniques have virtually eliminated gross continence loss but struggle to match the definitive eradication rates of traditional fistulotomies.

The Efficacy-Continence Trade-off:

FiLaC, while technologically elegant, yields a high 43.9% failure rate because thermal ablation without robust internal closure leaves the tract vulnerable to recanalization (9, 15). VAAFT achieves a much better balance (22.3% failure) because direct endoscopic visualization allows surgeons to locate and destroy occult secondary tracts that blind laser fibers miss (15). LIFT remains a reliable, anatomically sound mechanical approach (28.6% failure) without the 7.3% incontinence risk seen in the EAF (8, 15). Because VAAFT, FiLaC, and LIFT have near-zero incontinence rates, they can be ethically offered as first-line interventions, provided patients accept the higher statistical recurrence as a trade-off for lifelong sphincter preservation.

Pathophysiological Divergence:

MSC therapy highlights the divergent mechanisms between Crohn's and cryptoglandular fistulas. Cryptoglandular fistulas are driven by a localized, mechanical infection requiring physical drainage and closure (11). Crohn's fistulas are driven by a systemic, cytokine-rich autoimmune cascade, which MSCs actively downregulate, explaining their superior efficacy (over 60% healing) in autoimmune cohorts (11).

The Supremacy of Surgical Preconditioning:

The ADMIRE-CD II trial's 46.3% placebo healing rate forcibly reminds the surgical community that expensive biologic agents cannot replace foundational surgical tenets. Aggressive drainage, seton placement, and rigorous curettage remain the true cornerstones of complex fistula healing (14).

Individualized Algorithms:

There is no universal "best" technique. Success relies entirely on MRI-driven anatomical phenotyping (5, 13). For example, a rigid, enclosed RIFIL fistula will mechanically resist collapse and fail under blind FiLaC ablation; it strictly requires reconstructive drainage procedures like TROPIS or RIFER (6, 17, 18). Conversely, a straightforward transsphincteric tract may be elegantly managed with an OTSC or FiLaC, sparing the patient deep dissection (9, 10). Furthermore, fistulas with nonlocatable internal openings (up to 25% of cases) carry a massive recurrence risk and require specialized, MRI-guided approaches like the Garg protocol rather than blind probing (5).

Current literature is limited by heterogeneous follow-up durations (6 to 155 months) and disparate definitions of "healing," often conflating clinical closure with true radiological eradication (11, 15). Furthermore, the high cost of equipment (lasers, fistuloscope towers, stem cells) poses a significant barrier to global standardization.

Conclusion

Sphincter-sparing techniques (VAAFT, FiLaC, LIFT, OTSC) have successfully neutralized the profound dread of iatrogenic incontinence in complex anal fistula management. While offering exceptional safety, they carry intermediate recurrence rates, necessitating transparent patient counseling regarding potential staged interventions. Currently, VAAFT and LIFT offer the most mathematically favorable balance of definitive eradication and sphincter preservation. Regenerative MSC therapies offer profound potential for refractory Crohn's disease, but their efficacy is intrinsically tied to uncompromising surgical preconditioning and sepsis drainage. Ultimately, maximizing surgical success requires abandoning uniform approaches in favor of highly individualized,

multimodal algorithms dictated by high-resolution MRI phenotyping.

Conflicts of interests

The authors declare that there are no financial, personal, or institutional conflicts of interest that could have influenced the work reported in this manuscript.

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