



Dogma versus Evidence in Benign Proctology Anal Fistula, From Radical Fistulotomy to Sphincter-Sparing Repair

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Abstract

For more than a century, laying open the fistula tract was held to be the only reliable cure for anal fistula, with division of the traversed sphincter accepted as a necessary consequence; the functional cost of this approach was chronically underestimated. This critical narrative review, conducted in accordance with the SANRA criteria, confronts the historical dogma of radical fistulotomy with contemporary evidence and defines the current place of sphincter-sparing techniques in cryptoglandular and Crohn's-related anal fistula. PubMed/MEDLINE, Scopus, Web of Science, the Cochrane Library and EMBASE were searched from 1 January 1990 to 30 April 2026, supplemented by the guidelines of international learned societies (ESCP, ASCRS, ECCO); randomised controlled trials, meta-analyses, systematic reviews, large prospective cohorts and official guidelines were eligible. Because no single anatomical threshold defines a complex fistula, explicit criteria combining tract anatomy, the proportion of external sphincter traversed, prior surgery and patient-level continence risk are set out at the outset and applied throughout; cryptoglandular and Crohn's-related disease are considered separately in every technique section, since healing mechanisms, therapeutic objectives and eligibility for medical therapy differ substantially. High-resolution pelvic MRI and three-dimensional endoanal ultrasound have not replaced the Parks classification but have transformed the accuracy of anatomical mapping and operative planning, and show that 30% - 40% of fistulas are complex; in these, and particularly where additional risk factors coexist (anterior fistula in a woman, previous anal or obstetric sphincter

injury, pre-existing continence impairment, chronic diarrhoea, Crohn's disease), the functional cost of dividing the sphincter is generally judged unacceptable; the 2024 European Society of Coloproctology guidelines now enshrine sphincter preservation as the priority objective in complex disease. Ligation of the intersphincteric fistula tract achieves healing in approximately 80% with no reported incontinence in prospective series, and 96.2% when combined with a bioprosthetic plug in a selected cohort. Fistula laser closure, in a meta-analysis of 24 studies and 1503 patients, yields a primary healing rate of 57.5% (95% CI 49.4 - 65.3) with de novo incontinence of only 0.57% (0.00 - 2.15). Figures reported for other procedures derive from separate series that differ in case mix, in the definition of healing and in the instruments and timing used to assess continence, and are therefore reported here as descriptive safety profiles rather than head-to-head comparisons. Video-assisted anal fistula treatment achieves pooled healing of 76.0% but is now regarded principally as a diagnostic and preparatory tool. Mesenchymal stem cell therapy achieves pooled healing of 58.1% across heterogeneous cell products, doses and fistula phenotypes; the only licensed product, allogeneic expanded adipose-derived darvadstrocel, is indicated in complex perianal fistula of Crohn's disease refractory to conventional or biological therapy, although the confirmatory ADMIRE CD II phase 3 trial did not meet its primary endpoint (48.8% versus 46.3% with placebo), and its use in cryptoglandular disease remains investigational. Radiofrequency thermocoagulation, by contrast, has shown healing rates of only 28% - 35% in the two published studies and cannot currently be recommended. The dogma of universal laying open belongs to the past: sphincter preservation is the default objective rather than one option among several in complex fistula, and therapeutic individualisation is the governing rule; the principal limitation of the sphincter-sparing techniques is not morbidity but primary failure and recurrence.

Subject Areas

Gastroenterology & Hepatology

Keywords

Rectal Fistula, Anal Canal, Faecal Incontinence, Crohn Disease, Lasers, Mesenchymal Stem Cells, Sphincter-Sparing Procedures

1. Introduction

For decades, the therapeutic armamentarium in proctology was governed by deeply entrenched empirical practices, transmitted from one generation of surgeons to the next as unquestioned doctrine. The management of benign anorectal disease rested on a radical principle: complete anatomical eradication of the lesion, frequently at the expense of functional integrity [1]. The advent of evidence-based medicine and the expansion of minimally invasive technology have pro-

foundly altered this landscape; success is no longer defined by the absence of recurrence alone, and preservation of continence now ranks among the primary endpoints.

Cryptoglandular anal fistula is among the most frequent and the most anciently described proctological conditions. Its incidence is estimated at 12.3 per 100,000 in men and 5.6 per 100,000 in women, with a peak between 20 and 40 years of age [2] [3]. Beyond the classical cryptoglandular forms, anal fistula may arise in specific contexts, notably Crohn's disease, where it complicates the course in 22% to 80% of cases [4].

This condition, long treated according to an immutable dogma, radical laying open, is today the subject of a complete redesign of its management in the light of evidence-based medicine. The aim of this article is to deconstruct that dogma and to define the current place of sphincter-sparing repair.

The dogma-versus-evidence framework applied here was first set out by the present authors in a French-language narrative review that treated haemorrhoidal disease, chronic anal fissure, anal fistula and pilonidal disease together within a single argument [5]. The present article is not a translation of that work. It is confined to anal fistula, rests on an extended and independently re-run literature search, and develops material that the earlier review could not accommodate: an explicit operational definition of complexity, the systematic separation of cryptoglandular and Crohn's-related disease across every technique, and evidence published after the earlier article was written. The earlier review is cited below wherever the two overlap.

2. Search Strategy and Methods

This is a critical narrative review comparing historical surgical paradigms with contemporary evidence in the management of anal fistula. Its conduct and reporting were informed by the SANRA (Scale for the Assessment of Narrative Review Articles) criteria in order to ensure methodological quality and transparency [6].

A comprehensive literature search was performed covering 1 January 1990 to 30 April 2026, with selective inclusion of earlier foundational papers, notably Parks (1976), in order to contextualise the evolution of the paradigm. The databases interrogated were PubMed/MEDLINE, Scopus, Web of Science, the Cochrane Library and EMBASE. A complementary search covered the guidelines of international learned societies (ESCP, ASCRS, ECCO, SNFCP) and the reference lists of the included articles.

Inclusion criteria: randomised controlled trials, meta-analyses and systematic reviews published between January 1990 and April 2026; large prospective multi-centre cohort studies; official guidelines of international learned societies; foundational historical articles for contextual purposes; publications in English, French, Italian, German or Turkish; and studies reporting clinically relevant endpoints, in particular primary healing, recurrence, postoperative pain, anal continence assessed by validated scoring, quality of life and time to healing.

Exclusion criteria: preclinical studies, isolated case reports, letters to the editor and editorials without original data; small single-centre retrospective series (fewer than 50 patients); duplicate publications across databases; articles without accessible full text; and studies addressing anorectal malignancy or post-radiation complications.

Given the clinical and methodological heterogeneity of the available literature, no quantitative meta-analysis was undertaken. A structured narrative synthesis was performed and supplemented by comparative tables and a decision algorithm. Two conventions govern the synthesis that follows. First, the terms simple and complex are used throughout in the operational sense defined in the next section rather than as loose descriptors. Second, cryptoglandular and Crohn's-related fistulas are reported separately wherever the source data allow it, and studies pooling both phenotypes are identified as such, because the two conditions differ in the mechanism of persistence of the tract, in the realistic objective of treatment and in eligibility for medical therapy.

3. Review

3.1. Defining Simple and Complex Anal Fistula

No universally accepted definition separates a simple from a complex anal fistula, and the 2024 European Society of Coloproctology guidelines explicitly acknowledge that the distinction rests on a combination of anatomical and patient-level factors rather than on any single threshold [7]. Because every therapeutic recommendation that follows depends on this distinction, the criteria applied throughout this review are stated here explicitly.

A fistula is regarded as simple when all of the following apply: the tract is subcutaneous, intersphincteric or low trans-sphincteric, traversing less than approximately one third of the external anal sphincter; there is a single tract with a single, identifiable internal opening; there is no secondary extension, horseshoe component or undrained collection; the disease is primary rather than recurrent; the aetiology is cryptoglandular; and baseline continence is normal, with no anatomical or functional risk factor for impairment [7] [8].

A fistula is regarded as complex when any one of the following is present. Anatomically: a high trans-sphincteric tract involving more than approximately one third of the external sphincter, or a suprasphincteric, extrasphincteric or supralelevator tract; multiple or branching tracts; a horseshoe configuration; an associated abscess or undrained collection; or a rectovaginal or anovaginal component. In relation to previous treatment: recurrence after previous fistula surgery, and in particular after previous division of sphincter muscle, since the functional reserve of the sphincter complex is already reduced. In relation to the patient: an anterior fistula in a woman, where the external sphincter is short and the perineal body may already be attenuated by obstetric injury; documented or suspected pre-existing sphincter injury, whether obstetric or iatrogenic; any pre-existing disturbance of continence, including urgency and soiling; chronic diarrhoea or a func-

tional bowel disorder; and advanced age. In relation to aetiology: Crohn's disease, previous pelvic irradiation, malignancy, tuberculosis, hidradenitis suppurativa and immunosuppression, including HIV infection [7]-[9]. These criteria are summarised in **Table 1**.

Two consequences follow: First, complexity is not a purely anatomical property: an identical low trans-sphincteric tract may reasonably be laid open in a young man with normal continence and be judged unsuitable for division in a multiparous woman with an anterior tract and a Wexner score of 3. Second, because the individual criteria are weighted differently between guidelines and between series, the proportion of fistulas classified as complex varies across the literature, and this variability is one source of the heterogeneity discussed in the Limitations section.

Table 1. Criteria applied in this review to distinguish simple from complex anal fistula.

Domain	Simple fistula	Complex fistula
Tract height and sphincter involvement	Subcutaneous, intersphincteric or low trans-sphincteric; less than approximately one third of the external sphincter traversed	High trans-sphincteric (more than approximately one third of the external sphincter), suprasphincteric, extrasphincteric or supralelevator
Tract anatomy	Single tract, single identifiable internal opening	Multiple or branching tracts; horseshoe configuration; secondary extension; associated undrained collection or abscess; rectovaginal or anovaginal component
Previous treatment	Primary, previously untreated disease	Recurrent after previous fistula surgery, especially after previous division of sphincter muscle
Patient-level continence risk	Normal baseline continence; no anatomical or functional risk factor	Anterior fistula in a woman; documented or suspected obstetric or iatrogenic sphincter injury; any pre-existing continence disturbance, including urgency or soiling; chronic diarrhoea; advanced age
Aetiology	Cryptoglandular	Crohn's disease; previous pelvic irradiation; malignancy; tuberculosis; hidradenitis suppurativa; immunosuppression, including HIV infection

Adapted from the European Society of Coloproctology 2024 guidelines [7], the American Society of Colon and Rectal Surgeons 2022 guidelines [8] and Garg *et al.* [9]. A fistula is regarded as complex when any single criterion in the right-hand column is present.

3.2. The Dogma: "Lay Open at Any Cost"

For more than a century, fistulotomy imposed itself as the gold standard, justified by healing rates reaching 98% in simple fistula. The principle was simple and radical: open the fistula tract and sacrifice the traversed portion of sphincter in order to eradicate the disease definitively.

This philosophy rested on three pillars: complete mechanical eradication of the septic tract; the absence of any technically reproducible alternative; and a chronic underestimation of the functional consequences for the sphincter complex.

3.3. The Evidence: How the Dogma Was Dismantled

The pathophysiological mechanisms of anal fistula, long reduced to the cryptoglandular theory alone (obstruction of the anal glands with stasis and infection),

now appear considerably more complex [2]. Two principal mechanisms have been identified: epithelial-mesenchymal transition, a cellular process implicated in chronic tissue remodelling; and activation of matrix metalloproteinases, enzymes responsible for degradation of the extracellular matrix and for perpetuation of the fistula tract [2].

High-resolution pelvic MRI and three-dimensional endoanal ultrasound have not displaced the Parks classification, which remains the anatomical reference framework and continues to define the categories used in practice and in the literature. What cross-sectional and endoanal imaging have transformed is the reliability with which a given fistula can be assigned to a Parks category, and above all the quality of the preoperative map on which operative planning depends: the proportion of external sphincter traversed, the presence of secondary tracts and horseshoe extensions, occult collections requiring drainage before any closure procedure, and the integrity of the sphincter complex itself [10] [11]. Applied systematically, this improved mapping shows that 30% to 40% of fistulas meet the criteria for complexity set out in **Table 1**, high trans-sphincteric, suprasphincteric, extrasphincteric or multi-branched, and it is in this group that division of the sphincter carries a functional cost that is difficult to justify [7] [10] [11].

This renewed understanding justifies the development of targeted therapies, anti-inflammatory and cell-based, beyond the purely mechanical approach.

Anal incontinence has emerged as the principal functional liability of fistulotomy. The risk is not uniform: it rises with the proportion of external sphincter divided and is further increased by the patient-level factors listed in **Table 1**, so that the same operation may be entirely acceptable in one patient and unacceptable in another. In a young patient with normal baseline continence and a low tract, division of a small amount of muscle carries a low functional cost and remains defensible. In a patient with a high trans-sphincteric tract, or with an anterior tract in a woman, previous sphincter injury, pre-existing urgency or soiling, or chronic diarrhoea, the probability of clinically significant impairment is sufficient that the procedure is generally judged unacceptable [7] [8] [12]. It is this recognition, rather than any global condemnation of fistulotomy, that has driven the development of sphincter-sparing techniques over the past two decades [13].

The 2024 European Society of Coloproctology guidelines now enshrine sphincter preservation as the priority objective in the management of complex fistula [7].

3.4. Cryptoglandular and Crohn's-Related Fistula: Two Distinct Therapeutic Problems

Before the individual techniques are considered, the distinction between cryptoglandular and Crohn's-related disease must be made explicit, because it governs both the objective of treatment and the interpretation of every outcome figure that follows.

In cryptoglandular disease the tract is an epithelialised or chronically granulat-

ing channel within otherwise healthy tissue. The mechanism of persistence is essentially local and mechanical: an internal opening that continues to admit faecal content, an epithelial lining that will not close, and any undrained secondary extension. The objective is therefore definitive anatomical closure, healing is a binary and durable endpoint, and medical therapy has no established role.

In Crohn's disease the tract lies within immunologically active, inflamed tissue, and its persistence reflects ongoing transmural inflammation as much as local anatomy. Healing depends primarily on control of luminal and perineal disease; a tract may close under medical therapy alone and may reopen when that therapy is withdrawn or lost to immunogenicity. Proctitis, anal stenosis and multiple or complex tracts are common, and in a substantial proportion of patients definitive closure is not a realistic objective at all: the aims become control of suppuration, preservation of continence and avoidance of proctectomy. The ECCO guidelines accordingly recommend fistulotomy in Crohn's disease only in carefully selected patients with a simple tract, no proctitis and stable intestinal disease, and advise against chronic seton drainage as sole treatment other than as palliation [14].

This difference has a direct methodological consequence, outcome figures obtained in cryptoglandular series cannot be transferred to Crohn's disease, and the two are separated below wherever the source data permit. Where a study pooled both phenotypes, this is stated explicitly, and the resulting estimate is treated as uninterpretable for either group taken alone.

4. The Modern Sphincter-Sparing Armamentarium

4.1. Ligation of the Intersphincteric Fistula Tract (LIFT)

Described by Rojanasakul *et al.* in 2007 [13], the LIFT technique, ligation of the intersphincteric fistula tract, consists of selective ligation of the fistula tract within the intersphincteric plane, without muscle division.

In cryptoglandular disease, the prospective study by Hegab *et al.* (2022), with two years of follow-up, confirmed a success rate of 80%, a mean operative time of 36.2 minutes, healing at a mean of four weeks, and no reported case of incontinence [15]. The predictors of failure identified were the length of the fistula tract, elevated body mass index and diabetes [15]. In the pooled analysis by Stellingwerf *et al.*, restricted to high cryptoglandular fistula, LIFT achieved healing in 69.1% (95% CI 53.9 - 84.3) with postoperative incontinence in 1.6% (95% CI 0.4 - 2.8) [16].

Zhao *et al.* (2019) reported the long-term results (median follow-up 30 months) of the LIFT-plug technique, combining LIFT with an acellular dermal matrix bioprosthetic plug, in 78 patients [3] (Table 2).

According to the review by Sohrabi *et al.* (2024), combined techniques based on draining seton and LIFT-plug appear relatively effective, although prospective long-term multicentre trials remain necessary to establish their superiority definitively [2]. This caution is reinforced by the network meta-analysis of complex cryptoglandular fistula by Sierra Fernandez *et al.*, in which LIFT performed com-

parably to transanal advancement flap, whereas the plug used alone was associated with a significantly higher risk of failure (OR 3.6, 95% CI 1.1 - 11.5) [17]. The 96.2% healing rate reported for LIFT-plug in **Table 2** must therefore be read as the result of a single selected series and not as a general expectation for plug-based repair.

Table 2. Outcomes of the LIFT-plug technique combining LIFT with an acellular dermal matrix bioprosthetic plug in 78 patients.

Parameter	Result
Healing rate	96.2%
Median operative time	25 minutes
Mean time to healing	16 days
Perfect continence preserved	97.1%
Incontinence to flatus (Wexner 1)	2 patients only

Data from Zhao *et al.* [3]. Single-centre series of selected trans-sphincteric cryptoglandular fistulas; median follow-up 30 months.

It should nevertheless be emphasised that LIFT and the bioprosthetic plug are, in routine use, two distinct and alternative procedures: the plug is placed alone within the fistula tract, without associated intersphincteric ligation. The combination described as LIFT-plug therefore represents a specific technical variant rather than the rule. In practice, LIFT may by contrast be combined with fistula laser closure, the two approaches being complementary. Use of the plug also remains limited by material and economic constraints, high unit cost and unavailability of diameters above 2 mm, which restricts its applicability to narrow tracts [2].

In Crohn's-related fistula the evidence base for LIFT is markedly thinner. The Stellingwerf meta-analysis identified only a single small study (n = 17) reporting healing of 53%, and the ECCO guidelines list LIFT as an option in selected patients with complex perianal Crohn's disease while noting the limited certainty of the underlying evidence [14] [16]. LIFT in Crohn's disease should therefore be undertaken only after control of luminal and perineal inflammation and in the absence of proctitis.

4.2. Fistula Laser Closure (FiLaC)

Introduced by Wilhelm in 2011 [18], fistula laser closure (FiLaC) is a sphincter-sparing technique based on controlled photothermal destruction of the epithelium of the fistula tract. It uses a radially emitting diode laser probe that delivers energy circumferentially, denaturing the proteins of the tract; this process produces retraction and closure of the tract while minimising injury to the surrounding sphincter complex.

The procedure begins with identification of the internal opening and exploration of the tract, ideally after a period of seton drainage. A radial laser fibre is introduced into the tract through the external opening as far as the internal open-

ing, then withdrawn progressively at a controlled rate (approximately 1 to 3 mm/s), delivering energy around the whole circumference of the tract. The standard wavelength is 1470 nm, with power most often between 10 and 15 W. Delivered energy varies from 30 to 120 J per centimetre across studies, the data suggesting better healing rates at higher levels (100 - 120 J/cm). The laser is frequently combined with treatment of the internal opening (suture closure or advancement flap), although subgroup analysis has not demonstrated a significant difference in healing according to whether the internal opening is closed.

FiLaC is principally indicated in complex anal fistula (high trans-sphincteric, suprasphincteric) in which fistulotomy would carry an unacceptable risk of incontinence, and in patients for whom preservation of continence is a priority: women, elderly patients, those with pre-existing continence disturbance, and anterior fistula in women. High trans-sphincteric fistula has been described as its optimal indication. Contraindications include an undrained collection or abscess (prior seton drainage is required to control sepsis before the laser is applied), tracts too short to allow effective fibre withdrawal, and active unstabilised Crohn's disease. Long or wide tracts constitute a relative limitation: tract length has been described as the Achilles heel of the technique, and tracts exceeding 4 to 8 mm in diameter are reported to have reduced healing rates.

The meta-analysis by Elfeki *et al.* (2020) had already established the safety and efficacy of FiLaC [19]. The more recent meta-analysis by Duda *et al.* (2025), covering 24 studies and 1503 patients, provides the most up-to-date data [20] (Table 3). These pooled estimates derive from series that were predominantly, although not exclusively, cryptoglandular, and they are not stratified by aetiology.

Table 3. Outcomes of fistula laser closure: meta-analysis of 24 studies and 1503 patients (Duda *et al.*, 2025).

Parameter	Result (95% CI)
Primary healing rate	57.5% (49.4 - 65.3)
Recurrence rate	18.5% (10.1 - 28.5)
De novo incontinence	0.57% (0.00 - 2.15)
Reintervention rate (any technique)	36.5% (29.0 - 44.4)
Postoperative abscess/infection	6.5% (1.9 - 13.1)
Major complications	≈0%
Mean operative time	≈25 min

Data from Duda *et al.* [20], Series predominantly cryptoglandular; estimates not stratified by aetiology.

These data confirm that FiLaC is a safe option with an intermediate healing rate, although associated with a considerable recurrence rate; its advantage in sphincter preservation is manifest, but randomised trials standardising the technique remain necessary.

The safety profile is the principal asset of the technique. In the pooled analysis by Duda *et al.*, de novo incontinence after FiLaC occurred in 0.57% of patients (95% CI 0.00 - 2.15) and major complications such as severe haemorrhage were almost absent [20]. For orientation, incontinence has been reported in 1.6% (95% CI 0.4 - 2.8) after LIFT and in 7.8% (95% CI 3.3 - 12.4) after endorectal advancement flap in high cryptoglandular fistula [16], and higher figures, of the order of 10% or more, are described after fistulotomy involving a substantial proportion of the external sphincter [7] [8]. These values must not be read as a head-to-head comparison. They originate in separate series that differ in case mix and in the proportion of external sphincter at risk, in the definition and timing of continence assessment, in the instrument used (Wexner, Vaizey or FISI) and, critically, in whether continence was measured with a validated instrument at all; no randomised trial has compared these procedures using a common continence endpoint, and the only network meta-analysis in complex cryptoglandular fistula found no significant difference in postoperative incontinence between the sphincter-sparing techniques, the cutting seton excepted [17]. The figures are therefore best understood as descriptive safety profiles. The principal limitations of FiLaC are accordingly not morbidity but primary failure (approximately 42.5%) and recurrence (approximately 18.5%), which mandate informing the patient of the possibility of reintervention, potentially by a further laser procedure, since FiLaC is repeatable [20].

In Crohn's-related fistula the evidence is separate and much more limited. A systematic review and meta-analysis restricted to perianal fistulising Crohn's disease pooled six studies and only 50 patients, reporting a primary healing rate of 68% (95% CI 53.0 - 84.0) with no major faecal incontinence, while emphasising that the certainty of this evidence is poor [21]. FiLaC may therefore be considered in Crohn's disease only after adequate seton drainage, with luminal and perineal inflammation controlled and in the absence of proctitis; it is not indicated in active, unstabilised disease. Its repeatability constitutes an additional asset in both settings.

4.3. Video-Assisted Anal Fistula Treatment (VAAFT)

Video-assisted anal fistula treatment (VAAFT) is a minimally invasive endoscopic sphincter-sparing technique used in complex fistula, with both diagnostic and therapeutic intent. The principle rests on introduction of a rigid fistuloscope through the external opening, allowing direct visualisation of the tract and identification of the internal opening by fistuloscopy, together with fulguration of the tract under direct vision. The procedure comprises a diagnostic phase (endoscopic exploration of the tract, identification of the internal opening and of any secondary tracts) and a therapeutic phase (destruction of the tract epithelium by electrocoagulation, followed by closure of the internal opening). Closure of the internal opening may be achieved by suture, stapling or advancement flap.

A conceptual evolution of the technique should be noted: VAAFT is now re-

garded more as a diagnostic and preparatory tool than as a therapeutic modality in its own right, since a specific closure method must always be added to the procedure. It is moreover not always clear whether the reported benefits derive from application of the fistuloscope itself or from the associated closure methods.

VAAFT is directed at complex fistula. One important technical limitation concerns horseshoe fistula: the straight configuration of the fistuloscope is a disadvantage in this anatomical setting.

In cryptoglandular disease, the systematic review and proportional meta-analysis by Garg and Singh, covering eight observational studies and 786 patients, found a pooled success rate of 76.0% (95% CI 68.1 - 83.9), with individual values ranging from 52.5% to 92.5% [22]. For recurrence, the systematic review and meta-analysis by Emile *et al.*, covering 11 studies and 788 patients, reported a weighted mean recurrence rate of 17.7% at a median follow-up of nine months, varying with the method used to close the internal opening (15.3% with staplers, 17.7% with suture and 25% with advancement flap), with a repeat VAAFT performed in a majority of recurrences [23]. A more recent meta-analysis of 15 observational studies and 999 patients has confirmed the general direction of these findings [24].

In Crohn's-related fistula the objective and the reported endpoint differ. The principal dedicated study, by Adegbola *et al.*, reported symptom amelioration rather than tract closure, which is consistent with the therapeutic objectives set out above for perianal Crohn's disease and means that its results cannot be compared directly with the cryptoglandular healing rates above [25].

Functionally, the profile is favourable: no study has to date reported significant deterioration of continence, which is consistent with the sphincter-sparing nature of the technique. This reassuring result must nevertheless be qualified: continence was assessed with a validated score in only one of the studies (FISI), another having used manometry, while the remainder did not measure it with a validated instrument.

There is no randomised trial: recommendations rest solely on observational studies, and no study has directly compared VAAFT with other sphincter-sparing procedures. The ESCP consequently formulates a cautious recommendation: VAAFT may be considered in the management of complex perianal fistula (very low certainty of evidence) [7].

5. Mesenchymal Stem Cell Therapy

Local injection of mesenchymal stem cells (MSC) represents the most substantial biological innovation in this field, but the term covers products that differ in tissue source (adipose or bone marrow), in origin (autologous or allogeneic), in expansion protocol and in dose, and the evidence must be read accordingly.

The systematic review and meta-analysis by Emile *et al.* (2025), including 43 studies and 1160 patients, reported an overall healing rate of 58.1% (95% CI 51.5 - 64.7); healing of 60.4% with adipose-derived and 63.6% with bone-marrow-de-

rived cells in Crohn's fistula, 53.8% in cryptoglandular fistula, and an odds ratio for healing versus control of 1.81 ($p = 0.003$) [26]; these figures are consistent with the earlier meta-analysis of clinical trials by Wang *et al.* [27]. Both pooled estimates aggregate heterogeneous products, doses and fistula phenotypes and should not be read as the expected result of any single treatment.

The only product with regulatory approval is darvadstrocel (Cx601), an allogeneic expanded adipose-derived MSC suspension. Its licensed indication is narrow and should be stated precisely: complex perianal fistula in adults with non-active or mildly active luminal Crohn's disease, when the fistula has responded inadequately to at least one conventional or biological therapy. It is administered in a specialist setting, after examination under anaesthesia with curettage of the tracts and closure of the internal openings, and it presupposes prior control of sepsis by seton drainage. In the pivotal ADMIRE-CD trial, extended follow-up confirmed a benefit over control at 52 weeks [28]. The confirmatory phase 3 ADMIRE CD II trial, however, did not meet its primary endpoint: combined remission at week 24 was achieved in 48.8% of patients treated with darvadstrocel and 46.3% of those receiving placebo, a non-significant difference in a study of 568 randomised patients [29]. This result substantially qualifies the earlier enthusiasm and must be presented alongside the pooled healing rates above.

For cryptoglandular fistula the position is different again: no MSC product holds a licensed indication, the available data come from small and heterogeneous series, and no guideline recommends cell therapy in this setting. MSC therapy in cryptoglandular disease should therefore be regarded as investigational and confined to trials [17] [26].

Current specialty guidance reflects this asymmetry. The ECCO guidelines on the surgical management of Crohn's disease address local cell therapy within the treatment of complex perianal Crohn's fistula and, like the primary literature, place it after control of sepsis and of luminal inflammation [14]; the ESCP guidelines on cryptoglandular fistula make no comparable recommendation [7].

5.1. The Particular Case of Crohn's Disease

Crohn's-related anal fistula represents a distinct therapeutic challenge and exemplifies the break with purely surgical dogma.

The central place of biological therapy: Anti-TNF α agents, and infliximab in particular, constitute the reference first-line medical treatment, with an efficacy estimated at 60% for closure of fistula tracts [30]. The combination of surgical seton drainage with infliximab has established itself as the paradigm of modern management, definitively abandoning the notion of isolated radical surgery [4] [14].

Optimisation of infliximab therapy rests on combination with antibiotic therapy to control suppuration [31]; combination immunosuppression to limit immunogenicity [32]; and high target trough concentrations, at least 20 $\mu\text{g/mL}$ at week 2, at least 15 $\mu\text{g/mL}$ at week 6 and at least 7 $\mu\text{g/mL}$ at week 14 [33].

Strategies after infliximab failure. In the event of primary or secondary failure

of infliximab, several alternatives are now validated [4] (Table 4).

Table 4. Validated alternatives after primary or secondary infliximab failure in Crohn's-related anal fistula.

Alternative	Mechanism	Level of evidence
Adalimumab	Anti-TNF α	CHOICE trial: 40% complete healing [34]
Ustekinumab	Anti-IL-12/23	Ongoing studies, promising results
Mesenchymal stem cells (darvadstrocel)	Local immunomodulation	Licensed in complex perianal Crohn's fistula refractory to conventional or biological therapy; benefit at 52 weeks in ADMIRE-CD [28], but primary endpoint not met in ADMIRE CD II [29]
Rectal advancement flap	Sphincter-sparing surgery	Pooled healing 61% (95% CI 45-76) in Crohn's fistula; incontinence 7.8% (95% CI 3.3 - 12.4) in cryptoglandular series [16]
LIFT	Sphincter-sparing surgery	Single small study in Crohn's disease (n = 17), healing 53%; option in selected patients per ECCO [14] [16]

Adapted from Ben Azouz *et al.* [4] and the ECCO 2024 guidelines [14]. All options presuppose control of sepsis by drainage and control of luminal inflammation.

5.2. Emerging Innovations: Radiofrequency and Platelet-Rich Plasma

According to Fathallah (2025), laser and radiofrequency form part of a broader minimally invasive strategy aimed at improving postoperative quality of life and reducing the painful impact of surgery [35]. Platelet-rich plasma constitutes a further avenue under evaluation, but the available evidence is not encouraging: a systematic review of 14 studies and 514 patients reported an overall cure rate of 72.1% (95% CI 64 - 79), falling to 62.4% when platelet-rich plasma was used alone [36], and in the network meta-analysis of complex cryptoglandular fistula it carried the highest risk of failure of any modality assessed (OR 11.5, 95% CI 1.3 - 99), leading the authors to advise against its use [17].

Radiofrequency treatment of anal fistula falls, like FiLaC, within the category of sphincter-sparing techniques. The principle rests on tissue destruction by thermocoagulation: a high-frequency sinusoidal radiofrequency current (of the order of 4 MHz for the device most widely studied, the frequency varying with the generator used) is delivered through an electrode and produces ionic agitation in the tissue in contact with the probe; the resulting heating causes irreversible cellular injury above 60 °C. The electrode is not itself hot: it is heated by back-diffusion of the heat generated in the adjacent tissue [35].

The procedure is performed under anaesthesia as a day case. It is usually preceded by drainage, the fistula having already been managed with a seton. A flexible probe, distinct from that used for haemorrhoids, is introduced into the fistula tract through the external opening; energy is then delivered progressively, starting at the internal opening and along the whole tract. A specific program is available

directly on the generator, without the preliminary adjustment required for laser. Closure of the internal opening with an X-suture may be added.

Radiofrequency treatment is directed at cryptoglandular fistula in which fistulotomy would carry an excess risk of anal incontinence, in the same at-risk situations as FiLaC: high fistula involving more than one third of the external sphincter, multi-branched fistula, previously operated fistula, advanced age, pre-existing continence disturbance, post-surgical or obstetric sphincter injury, chronic diarrhoea and radiation proctitis.

The literature is to date very limited, comprising only two studies (**Table 5**). The first, by Merlini l'Héritier *et al.* (2019), was a comparative study in a small cohort ($n = 31$) that compared radiofrequency with closure of the internal opening by mucosal flap and found a significant difference to the disadvantage of radiofrequency (28% versus 71%; $p < 0.04$) [37]. The second, by Sautereau *et al.* (2023), evaluated the efficacy of radiofrequency at six months in 50 patients and reported a clinical healing rate of only 35% [38]. This second study enrolled a mixed population of cryptoglandular and Crohn's-related fistulas and did not report results separately by aetiology; its healing rate cannot therefore be attributed to either group and is of limited value for either. Current results are therefore not in favour of this technique.

Table 5. Published studies of radiofrequency thermocoagulation in anal fistula.

Study	Population/comparison	Healing (radiofrequency)
Merlini l'Héritier <i>et al.</i> (2019) [37]	$n = 31$; cryptoglandular; radiofrequency versus mucosal advancement flap of the internal opening.	28% versus 71% ($p < 0.04$)
Sautereau <i>et al.</i> (2023) [38]	$n = 50$; mixed cryptoglandular and Crohn's fistula, not analysed separately; six months of follow-up.	35% (whole cohort)

The treatment aims to spare the sphincter and has no impact on anal continence. It is simple to perform, can be undertaken as a day case, and the postoperative course is undemanding for the patient: painless, without wound care and without the need for sick leave. The complication rate was 8.2% and 16% in the two studies, the principal complication being abscess formation.

In the current state of knowledge, radiofrequency in the treatment of anal fistula remains an option that is attractive functionally but whose efficacy is insufficiently demonstrated. Studies of better quality, with larger numbers and longer follow-up, are necessary before its true place in the therapeutic armamentarium can be defined [35] [37] [38].

5.3. Comparative Synthesis and Decision Algorithm

Table 6 sets out the conceptual opposition between the historical paradigm and current practice. The healing figures in the right-hand column are drawn from

separate single-arm series and meta-analyses that differ in case mix, in the definition of healing and in duration of follow-up; they describe the range observed across the modern armamentarium and are not a ranking of the techniques against one another.

Table 6. Comparative synthesis: fistulotomy versus sphincter-sparing techniques in anal fistula.

Criterion	The dogma (conventional fistulotomy)	The evidence (sphincter sparing)
Principal objective	Eradication at any cost	Healing with functional preservation
Healing rate	95% - 98% (simple fistula)	58% - 96% depending on technique and on case mix; figures not directly comparable
Risk of incontinence	Rises with the proportion of external sphincter divided and with patient-level risk factors (Table 1); substantial in complex fistula	Low across techniques; 0.57% after FiLaC, 1.6% after LIFT, 7.8% after advancement flap in separate cryptoglandular series
Current indication	Simple low fistula in a patient without continence risk factors	Complex, high or recurrent fistula, or any fistula in a patient with continence risk factors
Place of medical therapy	Marginal	Central (Crohn's disease: biological therapy)
ESCP 2024 recommendation	Limited to simple fistula	First line for complex fistula [7]

Incontinence figures from Duda *et al.* [20] and Stellingwerf *et al.* [16]; they derive from separate series with different case mix, continence instruments and follow-up, and are presented as descriptive safety profiles rather than as a head-to-head comparison.

According to the 2024 ESCP guidelines [7] and contemporary practice, the decision pathway may be summarised as follows.

Simple low cryptoglandular fistula. Fistulotomy remains acceptable, provided that the criteria in **Table 1** are met and that no patient-level continence risk factor is present.

Complex fistula, or any fistula in a patient with continence risk factors. Sphincter preservation should be the default objective. This applies when the tract traverses more than approximately one third of the external sphincter, and also when the anatomy alone might permit division but the patient carries additional risk: an anterior tract in a woman, previous obstetric or iatrogenic sphincter injury, pre-existing urgency, soiling or a raised baseline Wexner score, chronic diarrhoea, or advanced age. Where these factors coexist, the expected functional cost of division exceeds what most patients and clinicians would accept, and a sphincter-sparing procedure, or seton drainage while a decision is made, should be preferred [7] [8].

Crohn's-related fistula. Any active anal fistula (suppuration, collection, uncon-

trolled sepsis) mandates drainage as the first step, most often by seton, in order to dry and mature the tract before any definitive procedure. Where Crohn's disease is not stabilised, surgical drainage must be combined with initiation or optimisation of maintenance therapy (anti-TNF α biological therapy, infliximab first line). Closure of the fistula tract can be considered only once luminal and perineal disease is controlled; in patients in whom closure is not achievable, symptom control and preservation of continence become the objectives, and chronic seton drainage is used as palliation rather than as definitive treatment [14].

Fistula of specific infective origin. In the presence of an ongoing specific infection, notably anoperineal tuberculosis, specific aetiological treatment (antituberculous therapy) is indispensable; local surgery alone is doomed to fail while the causative infection remains untreated.

The therapeutic paradigm in anal fistula has undergone a major conceptual revolution: the transition from aggressive eradication surgery to a personalised, multimodal and functional approach. Sphincter preservation is the default objective in complex fistula and in any patient carrying the continence risk factors set out in **Table 1**, most notably women with a short anterior sphincter and patients with pre-existing impairment. The modern techniques, LIFT, LIFT-plug, FiLaC, VAAFT, advancement flaps, radiofrequency and cell therapy, offer a varied armamentarium permitting a tailored approach [9] [17] [39] [40]. In the particular context of Crohn's disease, the integration of biological therapy (anti-TNF α , anti-IL-12/23) and of mesenchymal stem cells has profoundly reshaped management, illustrating the need for a combined medical and surgical approach. The dogma of universal laying open now belongs to the past: evidence-based medicine imposes respect for the sphincter as a cardinal principle and therapeutic individualisation as the governing rule [2]-[4] [7] [15] [19].

6. Strengths and Limitations

This review draws on a broad, multi-database search structured according to the SANRA criteria, integrates the recent guidelines of the principal international learned societies, and offers an original comparative analysis opposing historical paradigms to contemporary evidence. It also states explicit operational criteria for complexity and separates cryptoglandular from Crohn's-related disease throughout, so that outcome figures are not transferred between two conditions whose mechanisms and therapeutic objectives differ.

Several limitations must be acknowledged. First, the narrative rather than systematic design exposes the work intrinsically to a risk of selection bias in the choice of references; the search did not follow PRISMA standards, and no formal assessment of risk of bias (RoB 2, ROBINS-I) or of certainty of evidence (GRADE) was systematically applied. Second, the literature analysed shows considerable methodological heterogeneity: variability in the definition of healing, in duration of follow-up and in the continence instruments used (Wexner, Vaizey, FISI scores), which limits direct comparability between techniques, and which is the reason

why the numerical values reported in this review are presented as descriptive profiles rather than as comparisons. The problem is particularly acute for VAAFT, where continence was assessed with a validated instrument in only a minority of studies, and for radiofrequency, where the larger of the two available studies pooled cryptoglandular and Crohn's fistulas without separate analysis. Third, several sphincter-sparing techniques remain evaluated on series with limited follow-up, often under five years, with a scarcity of randomised trials and a marked lack of long-term data on recurrence and sphincter function. Fourth, the absence of a comparative health-economic evaluation is a limitation, given that the cost of new technologies, notably bioprosthetic plugs, laser platforms and cell therapy, is a major determinant of their diffusion, particularly in resource-limited health systems. Fifth, the criteria used here to define complexity, although drawn from current guidelines, are not universally agreed, and applying different thresholds would alter the proportion of fistulas classified as complex and therefore the apparent performance of every technique. Finally, this work does not replace individualised clinical judgement and should be read as a critical and educational synthesis intended to inform therapeutic decision-making, not as a formal practice guideline.

7. Future Perspectives

Priority research directions in anal fistula include validation of cell therapies outside Crohn's disease, where no product is currently licensed and the evidence remains investigational; systematic evaluation of technique combinations (LIFT, plug, FiLaC, advancement flap); clarification of the place of radiofrequency, which current data do not support; development of MRI-based prediction of healing [10] [11]; and exploration of the role of the anorectal microbiome, whose contribution to the pathophysiology of cryptoglandular fistula is beginning to be investigated, recent microbiomic profiling suggests that the organisms recovered from fistula tracts may derive from the perianal skin as well as from the intestinal lumen, and which could constitute an innovative therapeutic target through local modulation [41].

Standardisation of the emerging minimally invasive techniques remains the principal methodological gap. This requires large multicentre randomised trials with prolonged follow-up (five years or more), international consensus on optimal technical parameters using Delphi methodology, prospective international registries capturing real-world practice, and composite success criteria integrating not only healing and freedom from recurrence but also continence assessed by validated scoring, quality of life, return to activity and patient satisfaction. Trials should also report cryptoglandular and Crohn's-related fistulas separately, and should adopt a common definition of complexity, since the pooling of both phenotypes and the absence of an agreed threshold are the two factors that most limit the interpretation of the current literature.

In parallel, innovative biomaterials, acellular matrices, bioactive hydrogels,

new-generation resorbable plugs, fibrin glues enriched with growth factors, open the prospect of a genuinely regenerative proctology, aimed not merely at closing a defect mechanically but at inducing optimal biological healing [9] [17].

Finally, the transition from the excisional paradigm to sphincter sparing imposes a profound redesign of training curricula in colorectal surgery and medical-surgical proctology. Trainees must now master an extended technical range, from conventional procedures to minimally invasive, laser, endoscopic and radiofrequency approaches. The creation of reference and expertise centres, of fellowships dedicated to minimally invasive proctology, and of accredited continuing education programmes constitute strategic priorities to ensure the uniform and safe diffusion of these innovations.

8. Conclusions

The critical appraisal of anal fistula illustrates a profound and irreversible paradigm shift. Radical fistulotomy, at the price of sphincter sacrifice, shaped practice for more than a century. Driven by evidence-based medicine and technological innovation, the contemporary era imposes a fundamentally different view: a functional, graded, minimally invasive and individualised proctology, in which sphincter preservation counts as much as the control of recurrence.

This transition must not, however, give rise to a new dogmatism. Conventional fistulotomy retains a precise indication in simple low fistula in patients without continence risk factors, and several modern techniques still require validation by long-term randomised trials; radiofrequency in particular cannot presently be recommended on the strength of the available data, and the failure of the confirmatory ADMIRE CD II trial to meet its primary endpoint is a reminder that even the most biologically appealing innovation requires confirmation before it enters routine practice [29]. The future of the field lies in a reasoned balance between tradition and innovation, guided by scientific rigour, sound clinical judgement and the primacy of the patient's quality of life.

Author Contributions

Mohamed Amine El Amghari (MAEA) conceived the review, performed the literature search and drafted the manuscript. Nourdin Aqodad (NA) supervised the work and critically revised the manuscript for important intellectual content. Sofia Idrissi (SI) and Moulay El Hassan Tahiri (MEHT) contributed to the surgical interpretation of the data and critically revised the manuscript. All authors read and approved the final version of the manuscript.

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Ethics

Not applicable. This review is based exclusively on previously published data and did not involve human participants or animals; no institutional review board approval was required.

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This article is the third of a four-part English-language series applying the same dogma-versus-evidence framework to benign anorectal disease. The companion papers address haemorrhoidal disease (Part I), chronic anal fissure (Part II) and pilonidal disease (Part IV). The framework was first presented by the same authors in a combined French-language review of all four conditions [5].

Conflicts of Interest

The authors declare no conflicts of interest.

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Abbreviations

ASCRS	American Society of Colon and Rectal Surgeons
CI	Confidence Interval
ECCO	European Crohn's and Colitis Organisation
ESCP	European Society of Coloproctology
FiLaC	Fistula Laser Closure
FISI	Faecal Incontinence Severity Index
GRADE	Grading of Recommendations Assessment Development and Evaluation
IFX	Infliximab
LIFT	Ligation of the Intersphincteric Fistula Tract
MRI	Magnetic Resonance Imaging
MSC	Mesenchymal Stem Cells
OR	Odds Ratio
PRP	Platelet-Rich Plasma
RCT	Randomised Controlled Trial
RF	Radiofrequency
SANRA	Scale for the Assessment of Narrative Review Articles
TNF	Tumour Necrosis Factor
VAAFT	Video-Assisted Anal Fistula Treatment