Fistules anales associées au Crohn: Quand et qui opérer?

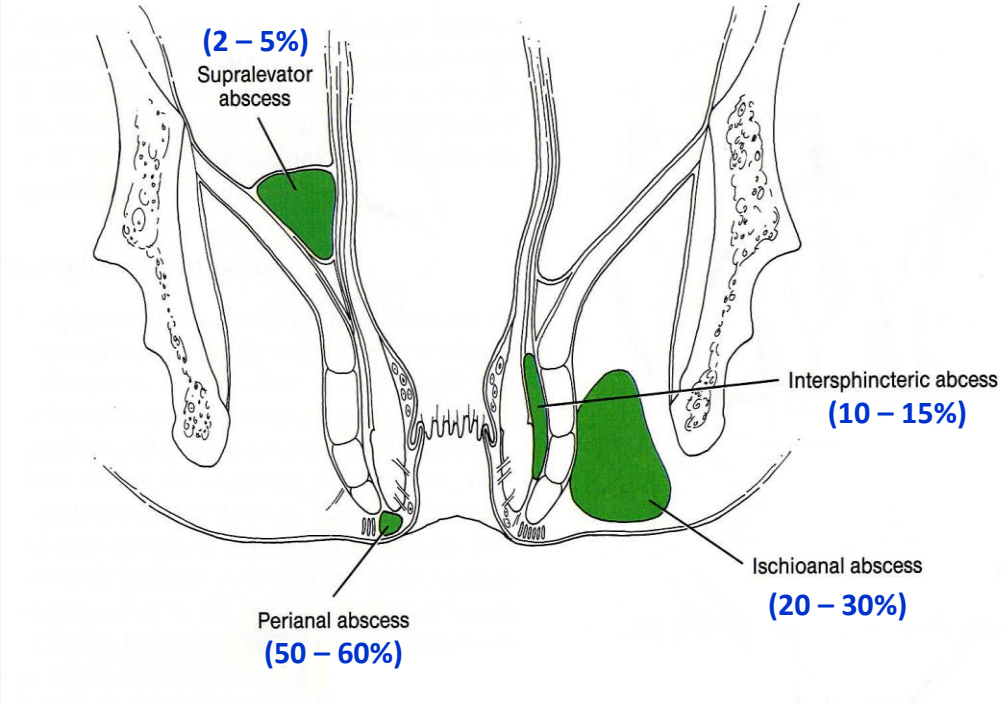
Prof. Dimitri Christoforidis
Ospedale Regionale di Lugano

38. Schweizerische Koloproktologie-Tagung, 14 Januar 2017

content

- Basics on anal fistulas
- How different is CD anal fistula compared to cryptoglandular anal fistula?
- Assessment of anal fistula
- Medical and surgical treatment

Anal abcess

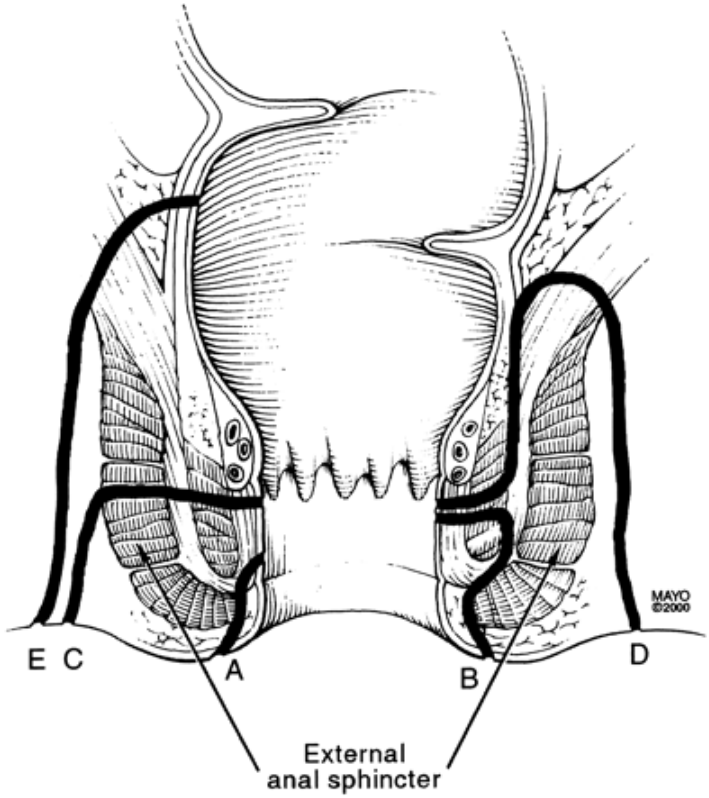

(2 – 5%)
Supralevator abscess
Intersphincteric abcess
(10 – 15%)
Ischioanal abscess
(20 – 30%)
Perianal abscess
(50 – 60%)

Fistula

- infection
- persistent bacterial input
- undrained space
- tracks that may close and reopen
- epithelialisation
- granulation tissue
- cytokine milieu
- other factors?

Parks classification

A. submucosal
B. Inters-phincteric
C. Trans-sphincteric
D. Supra-sphincteric
E. Extra-sphincteric



Practical fistula classification

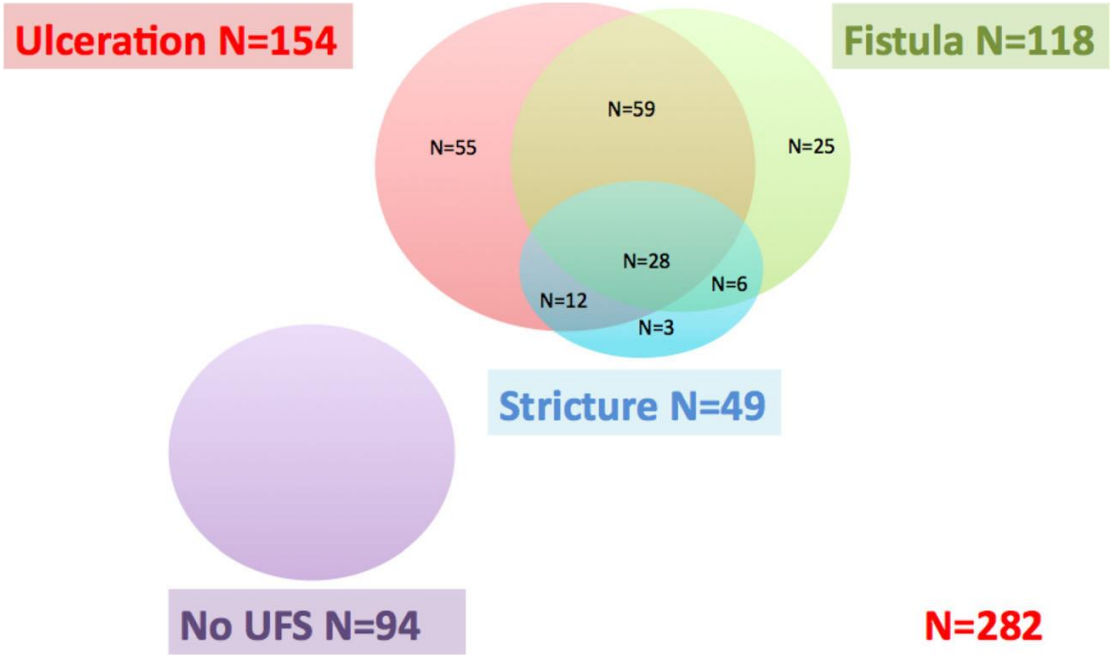
- simple:
  - rectilinear, single track
  - does not involve (or minimally) sphincter muscle
  - fistulotomy would not affect continence
- complex:
  - multitrack
  - involves sphincter muscle
  - deep abcesses
  - fistulotomy would lead to continence disturbance

Incidence of anal fistula in Crohn's disease

- depends of disease location:
  - 12% with ileal disease
  - 15% with ileocolic disease
  - 41% with colonic disease
  - 92% with rectal disease
- Any Crohn's, cumulative incidence of anal fistula with disease evolution:
  - @ 5 years : 15%
  - @ 10 years : 21%
  - @ 20 years : 26%

Schwartz et al, Gastroenterology 2002

Types of perianal Crohn's Disease



- NO correlation between luminal phenotype of disease (penetrating or stricturing) and presence of anal fistula

Wallenhorst T et al, Int J Colorectal Dis 2016

Cryptoglandular vs. Crohn's anal fistula

	cryptoglandular	Crohn's
PATHOGENESIS	infection of anal gland	mucosal inflammation
PRIMARY ORIFICE	dentate line	anorectum
SECONDARY ORIFICE	single or double	often multiple
DISEASE - TIMING	acute/persistent disease	chronic disease
DISEASE - LOCATION	local	systemic
INCONTINENCE RISKS		+ loose stool + future anal disease
INFECTION RISKS	no	immunosuppression/ modulation necessary
HEALING WITH MEDICAL THERAPY POSSIBLE ?	no	yes

Crrohn's vs. cryptoglandular anal fistula: anatomy

- 126 patients with MR (fistula specific protocol)
- MRI features:
  - same % of transsphincteric, intersphincteric, abscess
  - more rectal inflammation (30%)

Oliveira IS et al, Abdominal Radiol 2016

Treatment of anal fistula: aims

1. close the fistula
   - Stop purulent discharge
   - Stop recurrent abcessess

   } perianal discomfort

2. maintain continence

Cryptoglandular vs. Crohn's anal fistula

	cryptoglandular	Crohn's
TREATMENT END-POINT	persistent healing (>6-12 months): closed external and internal orifice	decrease of symptoms
		closure of at least 50% of open and draining fistulas for at least 4 weeks at any time during the 14-week study (Present et al, NEJM 1999)
		« remission »: absence of draining fistulas in two consecutive visits

Aguillera-Castro L et al, Ann Gastroenterol 2017

Treatment endpoints for perianal CD: PDAI

Table 2 Perianal disease activity index [19]

Item	Points
Discharge	
No discharge	0
Minimal mucous discharge	1
Moderate mucous or purulent discharge	2
Substantial discharge	3
Gross fecal soiling	4
Pain/restriction of activities	
No activity restriction	0
Mild discomfort, no restriction	1
Moderate discomfort, some limitation	2
Marked discomfort, marked limitation	3
Severe pain, severe limitation	4
Restriction of sexual activity	
No restriction of sexual activity	0
Slight restriction of sexual activity	1
Moderate limitation of sexual activity	2
Marked limitation of sexual activity	3
Unable to engage in sexual activity	4
Type of perianal disease	
No perianal disease	0
Anal fissure or mucosal tear	1
<3 perianal fistulas	2
>3 perianal fistulas	3
Anal sphincter ulceration or fistulas with significant undermining skin	4
Degree of induration	
No induration	0
Minimal induration	1
Moderate induration	2
Substantial induration	3
Gross fluctuance/abscess	4

What you want to know before treating an anal fistula

1. Where is the internal opening
2. Are there hidden tracks/undrained cavities?
3. How much sphincter is involved?

- Am I allowed to cut open (fistul***oto***my)?

sphincter involvement

non significant

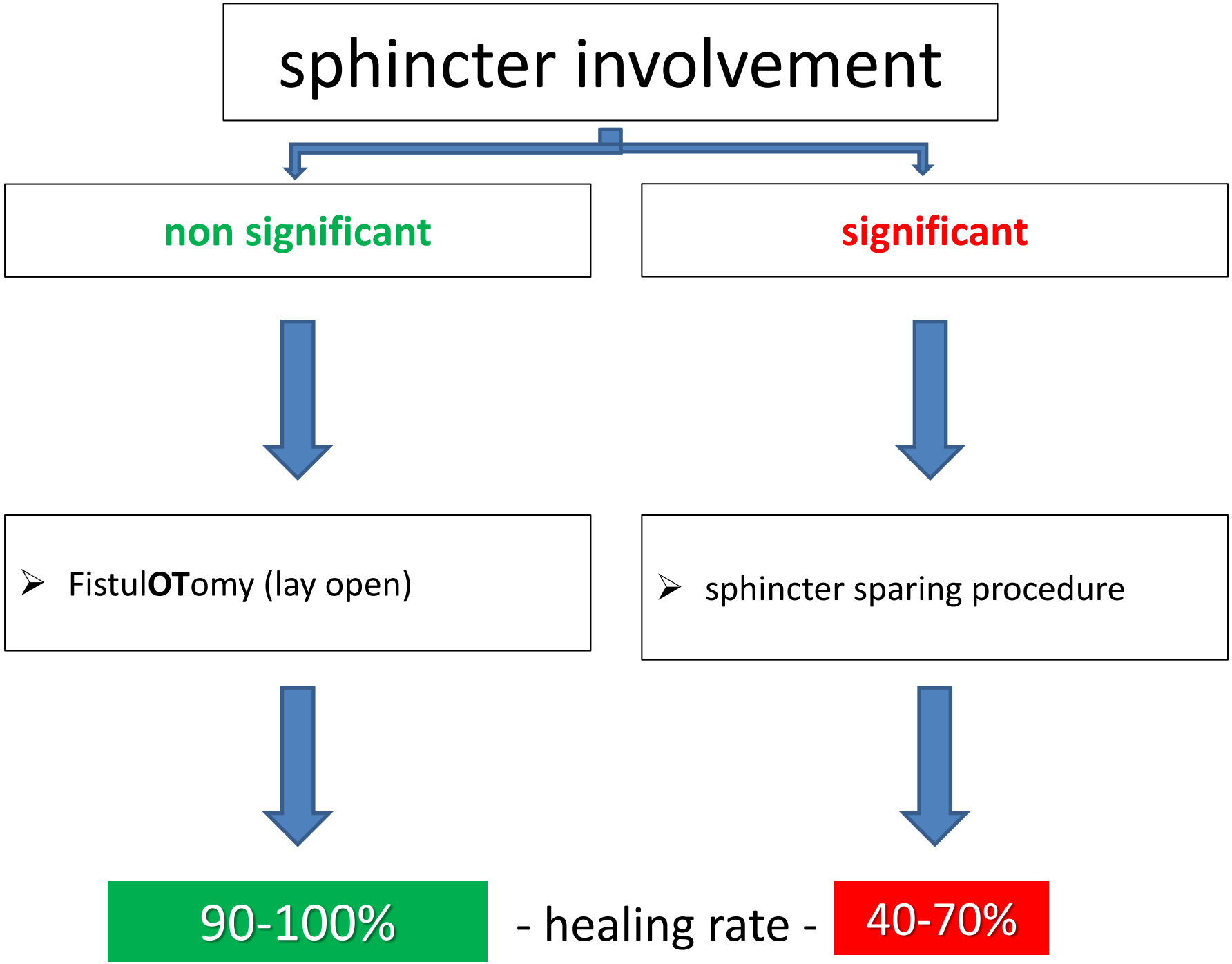
- Fistul**OT**omy (lay open)

significant

- sphincter sparing procedure

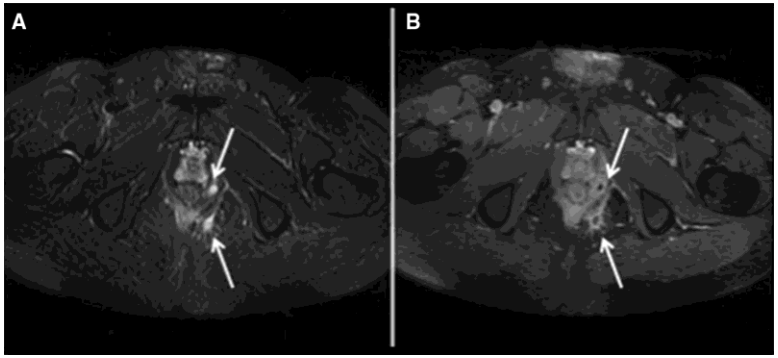
Sphincter sparing techniques

- cutting seton
- fistulectomy + endorectal flap
- FIPS (Fistulotomy and Primary Sphincter reconstruction)
- fibrin glue
- plug
- stem cells
- LIFT (Ligation of Intersphincteric Fistula Tract)
- VAAFT (Video Assisted Anal Fistula Treatment)
- PRP (Platelet Rich Plasma) + ERAF
- OVESCO clip
- FiLac (Fistula Laser closure)
- PERFACT (repeated cleaning of fistula & primary orifice)
- ….


sphincter involvement
non significant
significant
➢ FistulOTomy (lay open)
➢ sphincter sparing procedure
90-100%
- healing rate -
40-70%

Fistula assessment

- clinical exam
  - in office
  - under anesthesia
- Endoanal ultrasound (EAUS)
  - 360°, 3D imaging probe
  - readily available, cheap, repeatable, surgeon operated
- MRI



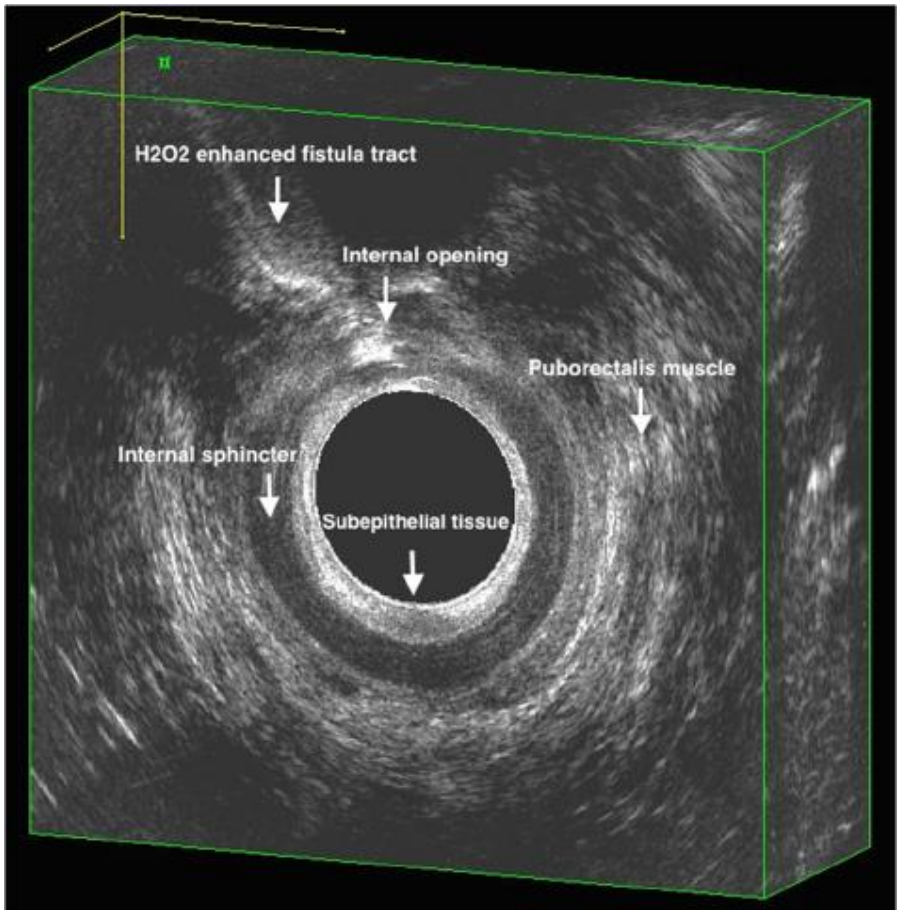
Endoanal ultrasound (EAUS)

- 151 patients with anal fistula
- Correlation EAUS with clinical exmination under anesthesia
- EAUS accuracy:
  - 93% to localize the internal orifice
  - 82% for fistula classification
  - 83% for “depth” of fistula (sphincter involvement)

Lengyel, et al DCR 2002

H_2O_2 contrast enhancement of the tract

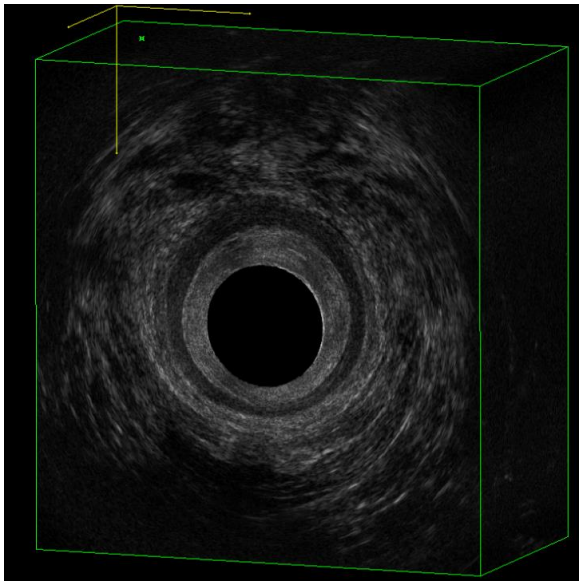
- 102 patients
- Diagnostic accuracy improved by:
  - injection of H2O2 through external openning
  - 3D-immaging
- useful in continence preservation



Ratto et al, Endoscopy 2005

EAUS 3D

- 299 patients: surgery for anal fistulae + preop 3D-EAUS
- Independent review of the 3D-volumes by 2 readers
- intra-operative data: reference standard
  - type of fistula (TS, IS, SS, ES)
  - height of fistula (high vs. low)
- Agreement with surgery:
  - fistula type:
    - proportion of agreement = 0.88, κ = 0.89
  - height:
    - proportion of agreement = 0.90, κ = 0.91



Kolodziejczak M et al, Colorectal Dis 2016

Accuracy of clinical, EAUS and MRI evaluation in patients with anal fistulas

- 104 patients with anal fistula
- Confrontation clinical exam (in office), EAUS and MRI
- correct classification of the fistula:
  - clinical exam: 61%
  - EAUS: 81%
  - MRI: 90%
- correct identification of the internal openning:
  - EAUS: 91%
  - MRI: 97%

Buchanan et al (St. Mark's), Radiology 2004

Accuracy of clinical, EAUS and MRI evaluation in patients with *Crohn's* anal fistulas

- 33 patients with fistula
- pre-op evaluation with EAUS, MRI
- clinical examination under anesthesia by colorectal surgeon

Accuracy to identify all fistulas:

- Exam under anesthesia: 29 / 32
- MRI: 26 / 30
- EAUS: 29 / 32

➢ 100% when any 2 modalities combined

Schwartz et al, Gastroenterology 2001

MRI or EAUS?

ECCO guidelines:

- MRI initial procedure for CD anal fistula
- EAUS is a good alternative
- any modality combined with examination under anesthesia improves accuracy

Treatment of anal fistula in CD

Principles of therapy

- Assess & treat perianal sepsis first:
  - abcesses: drain
  - supeficial fistula: cut open
  - complex fistula: put seton
  - antibiotics

sepsis control surgery

- Assess and treat inflammatory disease activity
- Discuss surgery for definitive fistula closure

fistula closure surgery

Setons

- draining, not cutting
- no consensus when to put them in
  - avoid if fistula uncertain
- no consensus when to pull them out
  - if initial response (↓of drainage) to anti-TNF therapy, after 6 weeks
- may be left in place for ever
  - well tolerated, but abcesses may still occur
- different types: vessel loop, nylon suture (Prolene), etc

Medical therapy of anal fistula in Crohn’s disease

Antibiotics

- Systematic review of 3 trials (123 patients)
- ciprofloxacin and/or metronidazole
- stat significant reduction of fistula drainage
  - RR=0.8; 95% CI=0.66-0.98
  - NNT: 5 (95% CI=3-20).

Khan KJ et al, Am J Gastroenterol 2011

Antibiotics for perianal Crohn's disease

Table 3 Antibiotic trials for fistulizing Crohn's disease

Authors and study design	Group 1	Group 2	Results
Thia *et al* [31] Multicenter, prospective, double-blind, placebo-controlled study (n=25)	Ciprofloxacin (500 mg b.i.d.) or metronidazole (500 mg b.i.d.) for 10 weeks	Placebo for 10 weeks	Ciprofloxacin 40% response vs. metronidazole 14.3% vs. placebo 12.5% (P=0.43)
Dejaco *et al* [32] Prospective, open-label study (n=52)	Ciprofloxacin (500-1000 mg/day) and/or metronidazole (1000-1500 mg/day) for 8 weeks	Ciprofloxacin (500-1000 mg/day) and/or metronidazole (1000-1500 mg/day) for 8 weeks, plus azathioprine (2-2.5 mg/kg) from 0 or 8 week	Azathioprine group 48% response vs. no azathioprine group 15% (P=0.03)
West *et al* [33] Prospective, doubled-blind, placebo-controlled study (n=24)	Ciprofloxacin (1000 mg/day) for 12 weeks plus infliximab 5 mg/kg at weeks 6, 8 and 12	Placebo for 12 weeks plus infliximab 5 mg/kg at weeks 6, 8 and 12	Ciprofloxacin group 73% response vs. placebo group 39% (P=0.12)
Dewint *et al*[34] Prospective, doubled-blind, placebo-controlled study (n=76)	Ciprofloxacin (500 mg b.i.d.) for 12 weeks plus adalimumab (160/80 mg week 0, 2 and 40 mg every other week) for 24 weeks	Placebo for 12 weeks plus adalimumab (160/80 mg week 0, 2 and 40 mg every other week) for 24 weeks	Ciprofloxacin group 71% response vs. placebo group 47% (P=0.047)
Maeda *et al* [35] Prospective, doubled-blind, placebo-controlled study (n=74)	Metronidazole 10% ointment t.i.d. for 4 weeks	Placebo ointment for 4 weeks	Reduction in PCDAI score of at least 5 points in metronidazole group 10 of 27 vs. placebo group 4 of 34 (P=0.031)

PDAI, perianal Crohn's disease activity index

Aguillera-Castro L et al, Ann Gastroenterol 2017

antibiotics- conclusions

- improve symptoms by reduction of drainage
- ciproxine antibiotic of choice
- synergic effect with immunomodulators
- do not heal fistulas, recurrence when stopped

Immunomodulatory agents

Table 4 Immunomodulatory agents trials, metanalysis or systematic reviews for fistulizing Crohn's disease

Authors and study design	Group 1	Group 2	Results
Pearson *et al* [36] Meta-analysis: nine randomized, placebo-controlled trials of azathioprine or 6-mercaptopurine therapy	Azathioprine or 6-mercaptopurine	Placebo	Fistulas improved with azathioprine or 6-mercaptopurine therapy (odds ratio 4.44; 95% CI 1.50 to 13.20)
Sandborn *et al* [37] Multicenter, prospective, double-blind, placebo-controlled study (n=48)	Oral tacrolimus (0.20 mg/kg/day) for 10 weeks	Placebo for 10 weeks	Tacrolimus 43% response vs. placebo 8% (P=0.004)
Cat *et al* [39] Retrospective (n=20)	Intravenous cyclosporine (4 mg/kg/day) for the first week, followed by oral cyclosporine at 8 mg/kg/day	No comparison arm	80% patients had symptomatic improvements on days 15 and 30 At 3, 6, 7, and 20 months 45% of fistulas were closed
Yang *et al* [41] Systematic review: 4 case series (n=40)	Thalidomide (50-300 mg/day)	No comparison arm	25% achieved remission, 27.5% partial response and 35% withdrew from the study due to adverse events

95% CI, 95% confidence interval

Aguillera-Castro L et al, Ann Gastroenterol 2017

RCTs anti-TNF for any fistula in CD

Study	Therapy	Patients study (N)	Patients fistula (N)	FU weeks	Partial (>50%) fistula closure N (%)	Complete closure N (%)	*p*-value complete closure
Present *et al.* 1999	Infliximab	31	63	18	39 (62%)	46%	0.003
(ACCENT)[4]	Placebo	31	31		8 (26%)	4 (13%)	
Hanauer *et al.* 2006	Adalimumab	225	26	4	6 (23%)	3 (12%)	NS (0.73)
(CLASSIC)[22]	Placebo	74	6		2 (33%)	1 (17%)	
Colombel *et al.* 2007	Adalimumab	172	70	26	NR	30%	0.043
(CHARM)[23]	Placebo	170	47		NR	6 (13%)	
Sandborn *et al.* 2007	Adalimumab	159	20	4	3 (15%)	1 (5%)	NS (0.69)
(GAIN)[24]	Placebo	166	25		5 (20%)	2 (10%)	

Table 5 Characteristics of included randomized controlled trials in meta-analysis on anti-TNF treatment. (N = number, FU = follow-up,

- no mention of Setons
- short f-up

de Groof EJ et al, Colorectal Dis 2016

Meta-analysis of RCTs anti-TNF vs. placebo for complete closure

Study or Subgroup	Risk Difference	SE	Weight	Risk Difference IV, Random, 95% CI	Year
Present 1999	0.3313	0.087	26.5%	0.33 [0.16, 0.50]	1999
Hanauer 2006	–0.0513	0.1645	16.2%	–0.05 [–0.37, 0.27]	2002
Colombel 2007	0.1723	0.0733	28.6%	0.17 [0.03, 0.32]	2007
Sandborn 2007	–0.03	0.0729	28.7%	–0.03 [–0.17, 0.11]	2007
Total (95% CI)			100.0%	0.12 [–0.06, 0.30]	

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 11.71$, df = 3 ($P = 0.008$); $I^2 = 74\%$

Test for overall effect: Z = 1.34 ($P = 0.18$)

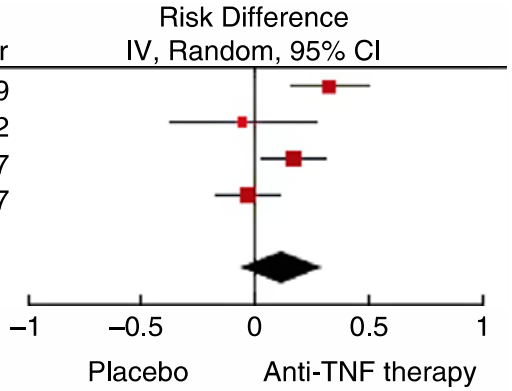


Figure 3 Meta-analysis of four randomized controlled trials comparing anti-TNF therapy with placebo for complete fistula closure.

de Groof EJ et al, Colorectal Dis 2016

Anti-TNF with or without setons: cohort studies

Author	Year	Country	Study design	Comparison group	Pts perianal fistulas (N)	M/F	Age	Anti-TNF	Concomitant therapy	In/Ma	FU	Complete closure N (%)	Partial closure N(%)	*p* value response	Recurrence N (%)	*p* value recurrence
Uchino M. *et al.* *[26]*	2011	Japan	Retrospective cohort		62	43/19	27.0 (12-58)	IFX	No	Ma	15 weeks			0.25		
,,	,,	,,	,,	anti-TNF + seton	26	16/10	27.5 (16-55)	,,	,,	,,	,,	0	22 (88.5%)		NR	
,,	,,	,,	,,	seton	36	27/9	27.5 (16-41)	x	,,	x	,,	0	26 (72.2%)		,,	
Sciaudone G. *et al.* *[27]*	2010	Italy	Prospective cohort		35	13/22	36.3 (19-63)	IFX	Yes, medical	Ma	18.8 (8-38) months			0.74		0.2
,,	,,	,,	,,	anti-TNF	11	4/7	36.3 (19-63)	,,	,,	,,	,,	7 (63.6%)	3 (27.3%)		3 (42.9%)	
,,	,,	,,	,,	seton	10	3/7	33.1 (16-58)	x	,,	x	,,	7 (70%)	2 (20%)		3 (42.9%)	
,,	,,	,,	,,	anti-TNF + seton	14	6/8	35.3 (18-65)	IFX	,,	,,	,,	11 (79%)	2 (14.3%)		2 (18.2%)	
Gaertner WB. *et al.* *[28]*	2007	USA	Retrospective cohort		226	105/121	39* (16-83)	IFX	Yes, medical	Ma	30* (6-216) months			0.001		
,,	,,	,,	,,	anti-TNF + seton	49	NR	NR	,,	,,	,,	,,	22 (45%)	NR		NR	
,,	,,	,,	,,	seton	63	NR	NR	x	,,	x	,,	11 (17%)	,,		,,	
Regueiro M. *et al.* *[25]*	2003	USA	Retrospective cohort		32	16/16	34.7* (12-58)	IFX	Yes, medical	In	18 weeks		NR	0.014		0.001
,,	,,	,,	,,	anti-TNF + seton	9	4/5	NR	,,	,,	,,	,,	9 (100%)	,,		4 (44.4%)	
,,	,,	,,	,,	anti-TNF	23	12/11	NR	,,	,,	,,	,,	19 (82.6%)	,,		15 (78.9%)	

Table 4 Characteristics of included cohort studies directly comparing (combined) anti-TNF and seton drainage on closure and recurrence rates of perianal fistulas. (Pts = patients, N = number of patients, M/F = male/female, FU = follow-up, * = mean, IFX/ADA = infliximab/adalimumab, In/Ma = induction/maintenance,).

de Groof EJ et al, Colorectal Dis 2016

Improving anti-TNF efficacy

- Infliximab + EUA/Setons > Infliximab alone[1]
- Adalimumab + Ciprofloxacine > Adalimumab alone[2]
- higher residual levels?[3]

[1]*Riguiero et al, Inflamm Bowel Dis 2003*
[2]*Dewint P et al, Gut 2014*
[3]*Yarur A et al, DDW, May 216*

Medical therapy - summary

Table 1. Summary of the available Crohn's disease (CD) therapeutics and their role in the treatment of perianal fistulas

CD therapeutics	Positive influence on fistula activity?	Short-term efficacy?	Feasible for long-term use?	Fistula recurrence after discontinuation?
5-ASA	no	no	–	–
Corticosteroids	no	no	no	–
Antibiotics (ciprofloxacin/metronidazole)	yes	yes	no	yes
Calcineurin inhibitors	yes	yes	no?	yes
Thiopurines	yes	after 3 months	yes	–?
Anti-TNF-alpha antibodies	IFX/ADA yes; CERT?	IFX/ADA yes; CERT?	yes	yes, in a proportion of patients
Vedolizumab	yes	?	yes	?

IFX = Infliximab; ADA = adalimumab; CERT = certolizumab.

Klag T et al, Viszeralmedizin 2015

Guidelines for complex perianal Crohn's disease

ECCO statement 9G

- **Seton** placement after surgical treatment of sepsis is recommended for complex fistulae [EL2]. The timing of removal depends on subsequent therapy

ECCO statement 9H

- Active **luminal Crohn's disease** should be treated if present, in conjunction with appropriate surgical management of fistulae [EL5]

ECCO statement 9I

- In complex perianal fistulising disease **infliximab** [EL1] **or adalimumab** [EL2] can be used as first line therapy following adequate surgical drainage if indicated. A combination of **ciprofloxacin** and anti-TNF improves short term outcomes [EL1]. To enhance the effect of anti-TNF in complex fistulising disease, combination of anti-TNF treatment with **thiopurines** may be considered (EL5]

ECCO statement 9J

- **Imaging** before surgical drainage is recommended. EUA for **surgical drainage** of sepsis is mandatory for complex fistulas [EL4]. In complex fistulas, abscess drainage and loose seton placement should be performed [EL4]

Are CD anal fistulas dangerous? Malignant transformation?

- Dutch pathology registry based research over 17 years (1990-2007)
- Adenocarcinoma arising in anal fistula:
  - CD: 4/6058 (0.0007%); 0 in non CD
  - Time to malignancy:
    - 25 years (IQR 10-38) after CD diagnosis
    - 10 years (IQR 6-22) after fistula diagnosis
    - Median age @ diagnosis: 48.3 years (IQR 43-58)
    - ¾ asymptomatic

Baars JE et al, Scand J Gastroenterol 2011

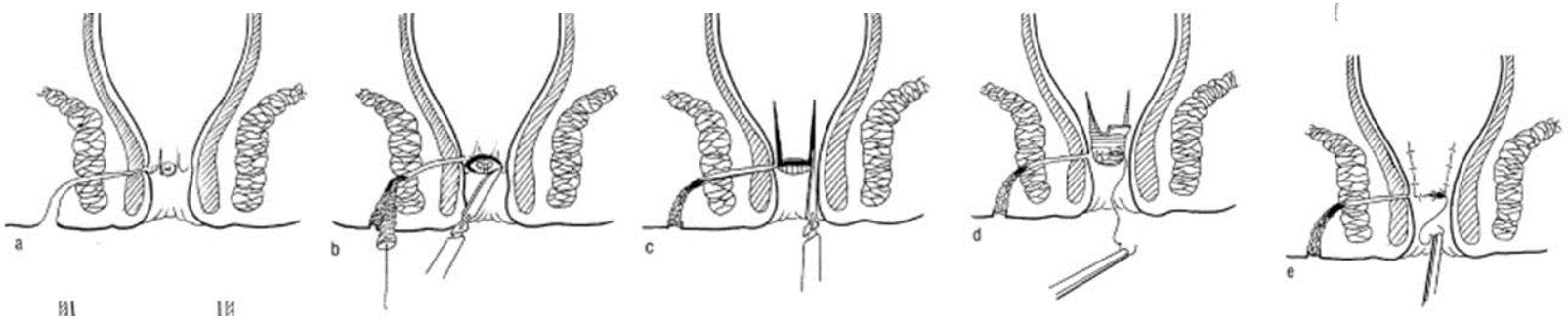
Sphincter sparing techniques

- cutting seton
- fistulectomy + endorectal flap
- FIPS (Fistulotomy and Primary Sphincter reconstruction)
- fibrin glue
- plug
- stem cells
- LIFT (Ligation of Intersphincteric Fistula Tract)
- VAAFT (Video Assisted Anal Fistula Treatment)
- PRP (Platelet Rich Plasma) + ERAF
- OVESCO clip
- FiLac (Fistula Laser closure)
- PERFACT (repeated cleaning of fistula & primary orifice)
- ….

Sphincter sparing techniques

- cutting seton
- fistulectomy + endorectal flap
- FIPS (Fistulotomy and Primary Sphincter reconstruction)
- fibrin glue
- plug
- stem cells
- LIFT (Ligation of Intersphincteric Fistula Tract)
- VAAFT (Video Assisted Anal Fistula Treatment)
- PRP (Platelet Rich Plasma) + ERAF
- OVESCO clip
- FiLac (Fistula Laser closure)
- PERFACT (repeated cleaning of fistula & primary orifice)
- ….

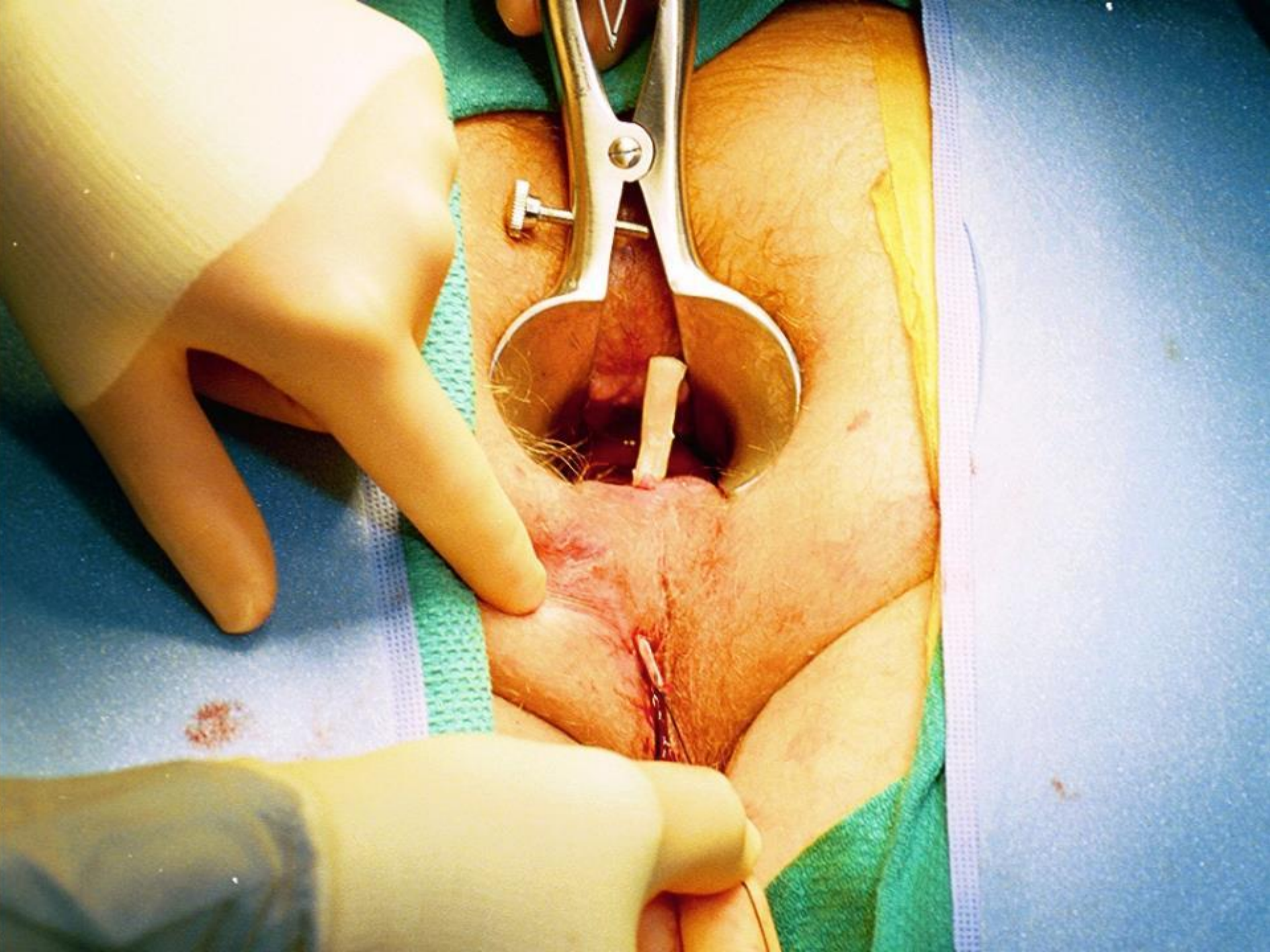
Fistulectomy + endorectal advancement flap



- Systematic review
- cohort studies/RCT 1978-2008
- patients with cryptoglandular / CD anal fistula
- Success rate / Incontinence rate:
  - cryptoglandular: 81% / 13%
  - Crohn's disease: 64% / 9%

Soltani A et al, Dis Colon Rectum 2010

PLUGS



plug for Crohn's?

- Systematic review
- Anal fistulas (no rectovaginal)
- 20 studies (8 retro, 10 pro, 2 RCTs)
- F-up 3-48 months
- % success:
  - Crohn: 23/42 (54.8%)
  - No Crohn : 265/488 (54.3%)

O'Riordan JM et al, DCR 2012

plug for Crohn's?

- Systematic review
- 12 studies (case-series)
- 84 patients (n = 1-20 per study)
- median follow-up time of 9 (3-24) months
- success rate: 49/84 (58.3%, 95% CI 47-69)
- Lower success rate with Gore- BIO A plug, in patients with recurrence or receiving immunomodulators

Nasseri Y et al, Colorectal Dis 2016

plug for Crohn's? - RCT

- open label multicenter RCT
- Plug (Surgisis®) vs. seton removal
- 106 patients with mild or non-active Crohn's disease
- stratified according to simple or complex fistula
- 1° endpoint: Fistula closure@ week 12
- Plug: 31.5%
- no plug: 23.1%

} p=ns

- no difference if simple or complex

Senejoux A et al (GETAID), J Crohns Colitis. 2016

Results according to year of publication

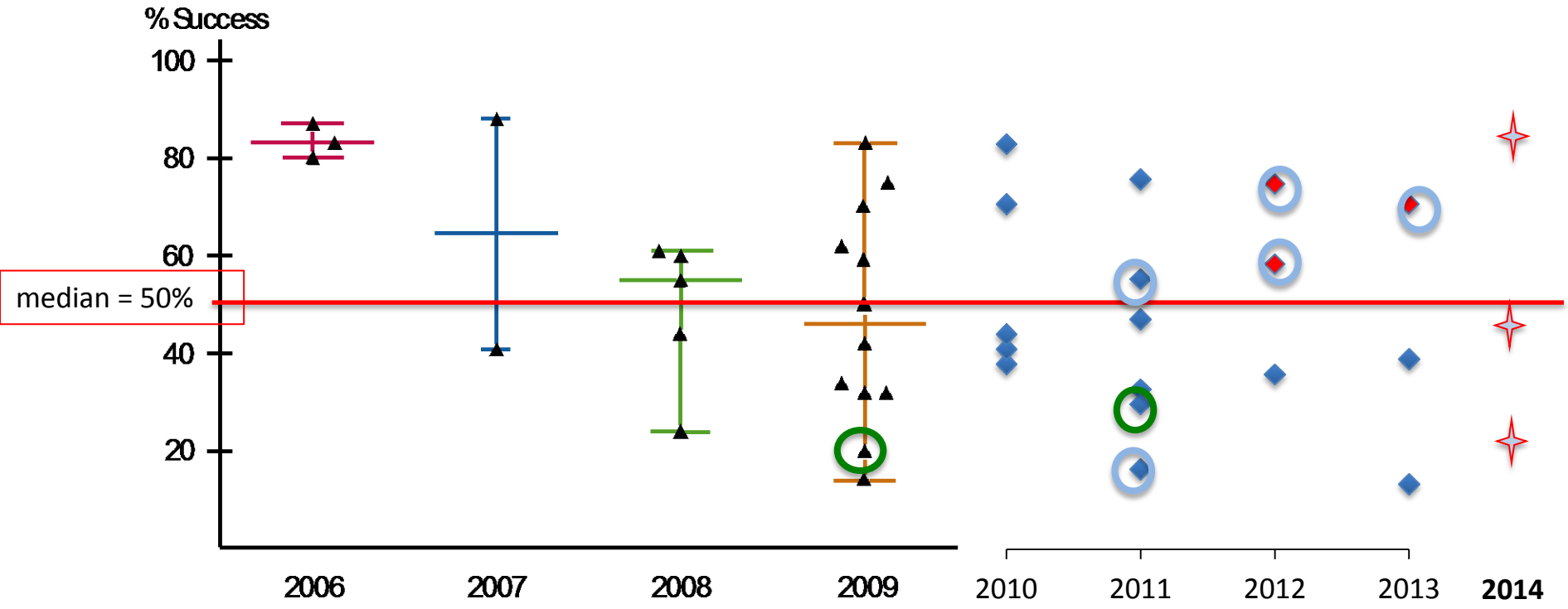


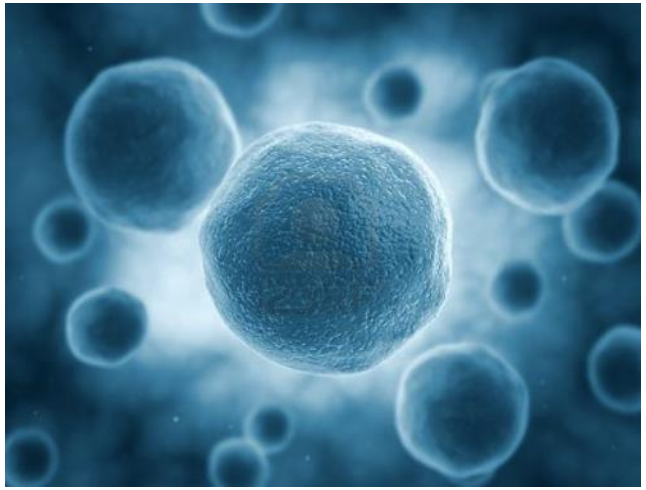
FIGURE 1. Fistula healing rates with the anal fistula plug as reported in articles found in PubMed over the past 4 years. Each triangle represents a publication. The horizontal bars represent median and range of values.

Christoforidis D. Dis Colon Rectum 2010

=RCT

= non-Cook plug

Stem cells



Expanded adult stem cells (eASCs) (obtenues par liposuction)

- injection dans le trajet après fermeture de l'orifice primaire
- étude randomisée (Madrid)
- n= 49 (cg = 35; Crohn's = 14)
- pas d'effets secondaires

	guérison à 8 semaines		guérison à 1 an
colle de fibrine	3/25 (12%)	P < 0.001	3/25 (12%)
colle de fibrine + eASCs*	17/24 (71%)		15/24 (63%)

**répetition d'une dose de 60 millions de eASCs à 8 sem si fistule persistante*

Garcia-Olmo D et al, DCR 2009
Guadalajara H et al, Int J Colorectal Dis 2012

Expanded adult stem cells (eASCs) (obtenues par liposuction)

- injection dans le trajet après fermeture de l'orifice primaire
- étude randomisée (Madrid)
- n= 49 (cg = 35; Crohn's = 14)
- pas d'effets secondaires

	guérison à 8 semaines		guérison à 1 an	guérison à la fin du f-up (médiane=38mois)
colle de fibrine	3/25 (12%)	P < 0.001	3/25 (12%)	2/25 (8%)
colle de fibrine + eASCs*	17/24 (71%)		15/24 (63%)	7/21 (33%)

**répetition d'une dose de 60 millions de eASCs à 8 sem si fistule persistante*

Garcia-Olmo D et al, DCR 2009
Guadalajara H et al, Int J Colorectal Dis 2012

Expanded adult stem cells (eASCs) (obtenues par liposuction)

- Etude randomisée multicentrique (19) single blind
- n=200

	guérison à 6 mois (centre pionnier)	guérison à 1 an (tout centre)
colle de fibrine	18 %	37 %
colle de fibrine + eASCs*	83 %	52 %
eASCs seul*	55 %	57 %

**répetition d'une dose de 60 millions de eASCs à 8 sem si fistule persistante*

- auteur principal a un licence agreement avec Cellerix SA

Herreros D et al (Madrid), DCR 2012

Cellules mesenchymateuses stromales (eMSC)
(obtenues par ponction de la moelle osseuse)

administration iv[1]

- réponse clinique à 6 semaines chez 3/9 patients (- ≥70 CDAI)
- pas d'effets secondaires

administration intra-fistulaire

- 10 patients Crohn avec fistules réfractaires
- ciprofloxacine, ceftriaxone, metronidazol pendant 2 semaines pré-op
- injection toutes les 4 semaines (médiane: 4x/patient)
- 7/10: guérison complète, 3/10: amélioration (f-up 12 mois)
- (!) effet systémique:
  - réduction significative du CDI et PADI ($p<0.01$)
  - augmentation soutenue du nombre de cellules T régulatrices (mucosales et circulantes)

[1]*Duijvestein M et al (Leiden), Gut 2010*
[2]*Ciccocioppo R et al (Pavia), Gut 2011*

THE LANCET
Volume 389 - Number 10064 - Pages 1-126 - January 7-13, 2017 www.thelancet.com

Stem cells: intralesional injection

- Phase 3 multicenter randomised, double-blind controlled trial
- single injection of expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) vs. placebo in complex perianal fistulas in Crohn's disease
- Assessment by blinded GE + radiologist (MRI)
- stratification according to concomitant baseline treatment
- primary endpoint: combined remission @ week 24
  - clinical assessment of closure of all treated external openings that were draining at baseline
  - absence of collections >2 cm of the treated perianal fistulas in MRI
- 212 patients
- Results:
  - combined remission (ITT) Cx601 50% s. placebo 34%, p=0·024

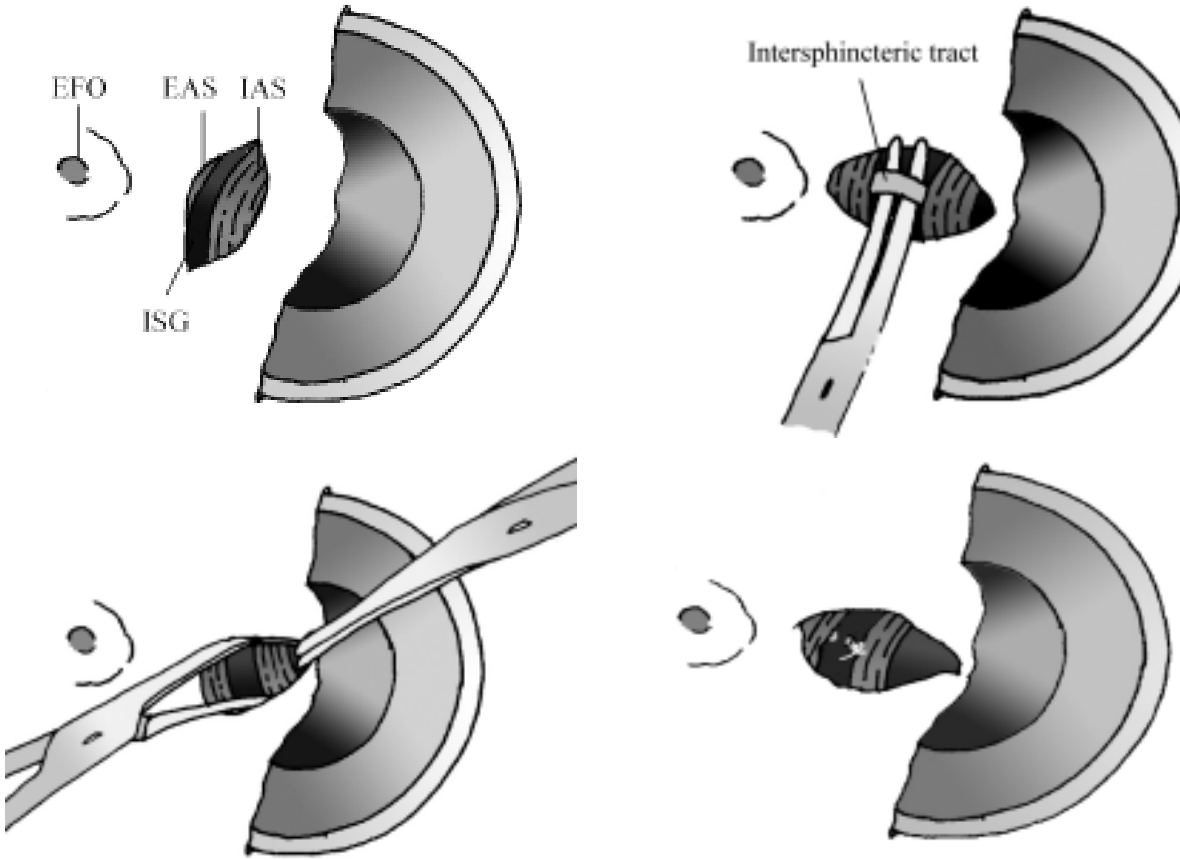
Panés J et al (ADMIRE) Lancet 2016

The LIFT procedure
(Ligation of Intersphincteric Fistula Tract)

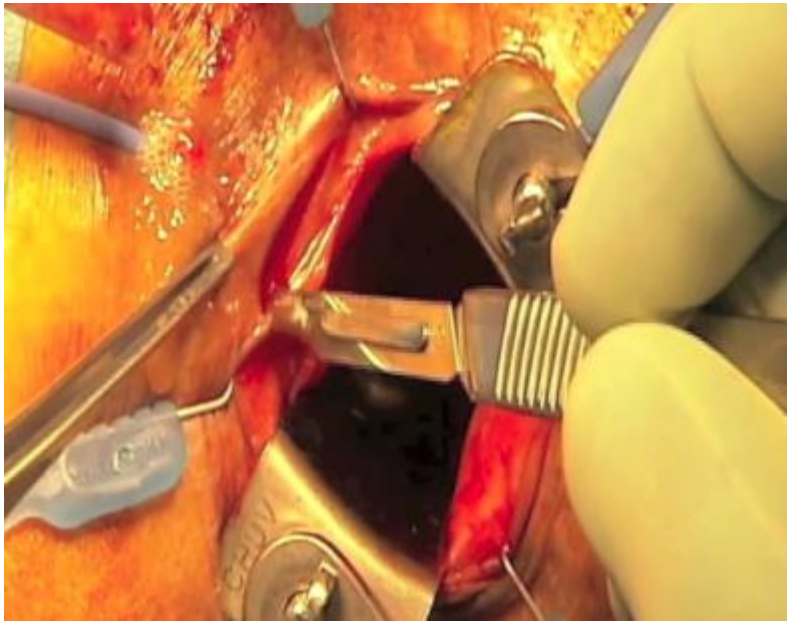
Total Anal Sphincter Saving Technique for Fistula-in-Ano; The Ligation of Intersphincteric Fistula Tract

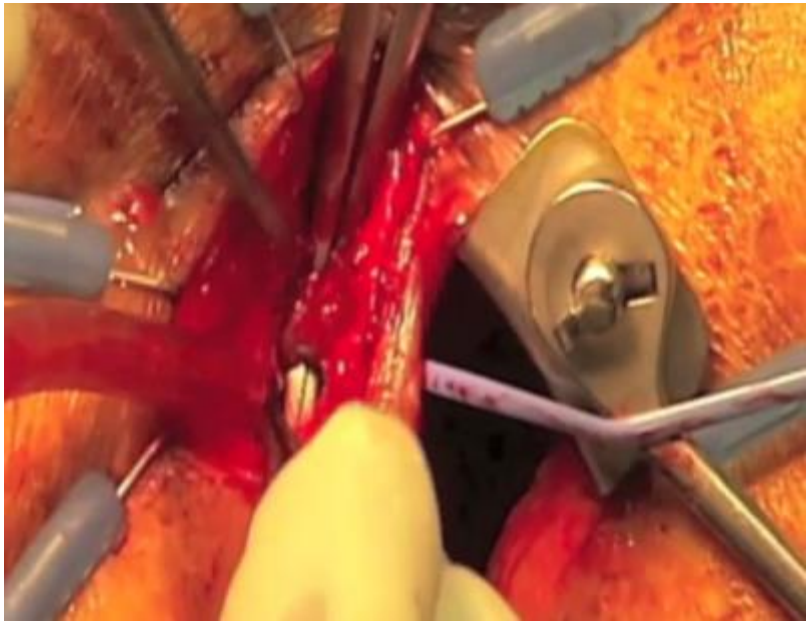
Arun Rojanasakul MD*, Jirawat Pattanaarun MD*,
Chucheep Sahakitrungruang MD*, Kasaya Tantiphlachiva MD*

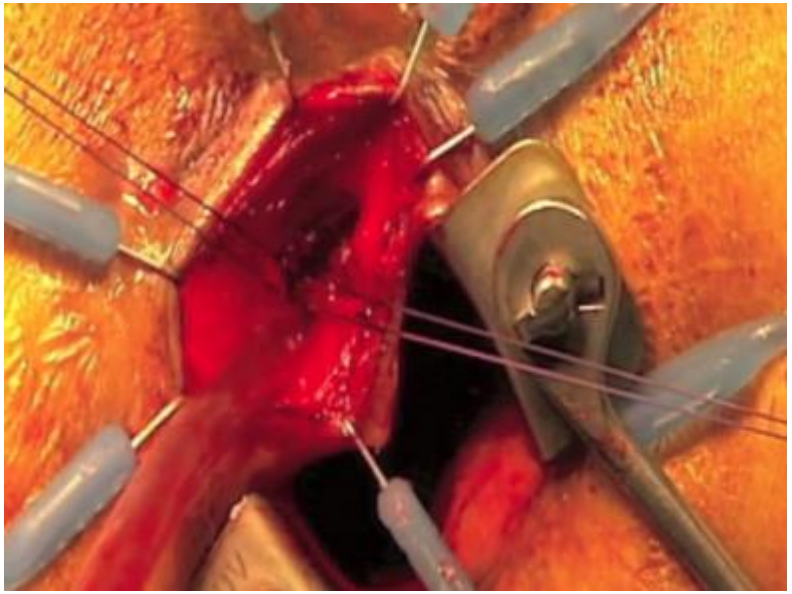
** Division of Colorectal Surgery, Chulalongkorn University*

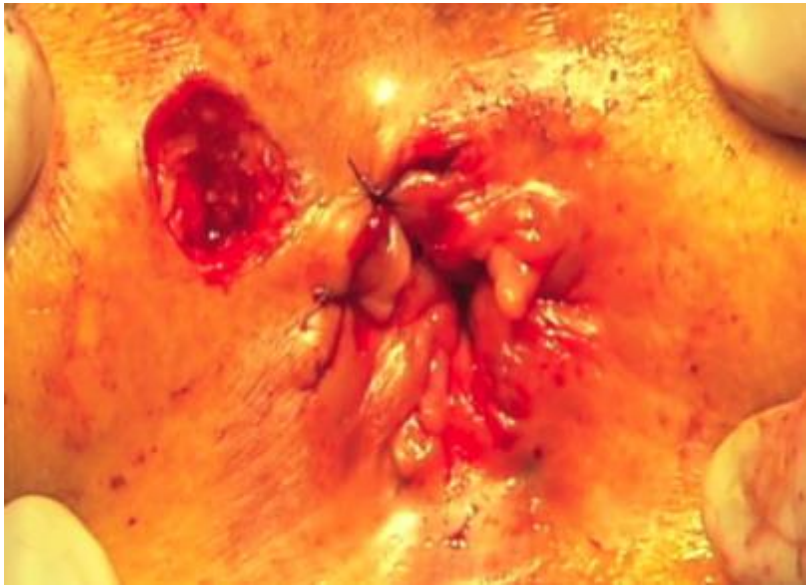


J Med Assoc Thai 2007; 90 (3): 581-6









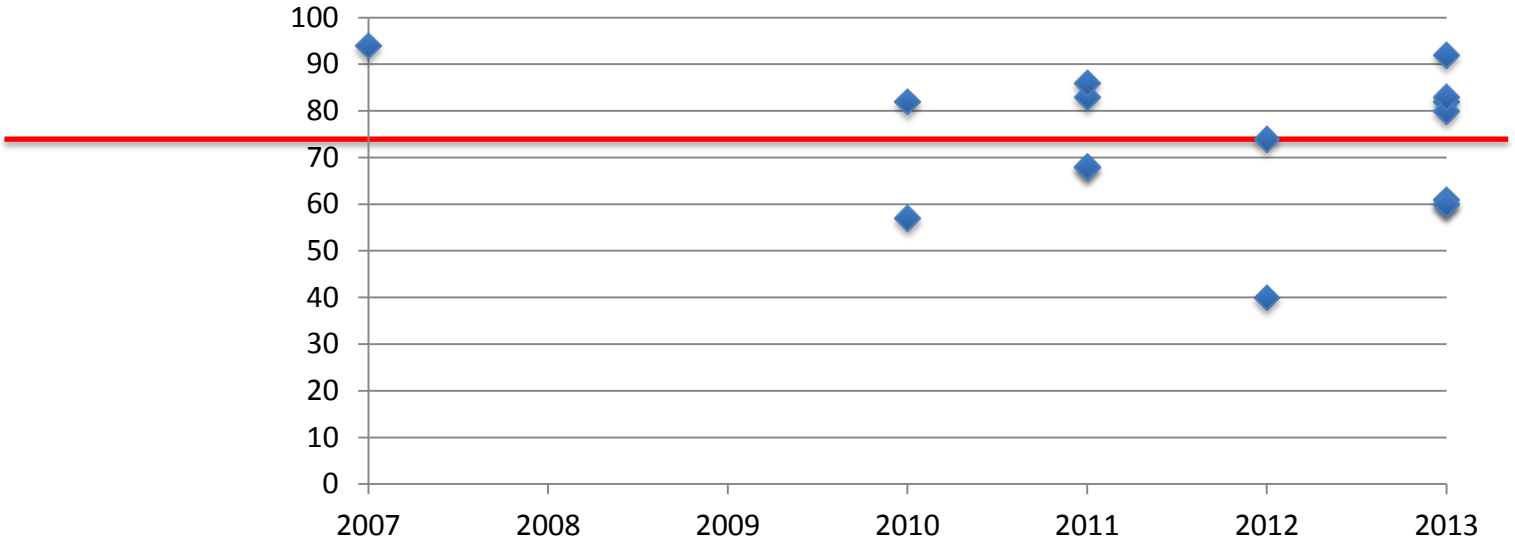
LIFT in Crohn's disease

- 15 patients
- 8/12 healed @ 12 months
- no fecal incontinecne
- Better results if fistula tract
  - lateral > median
  - long > short

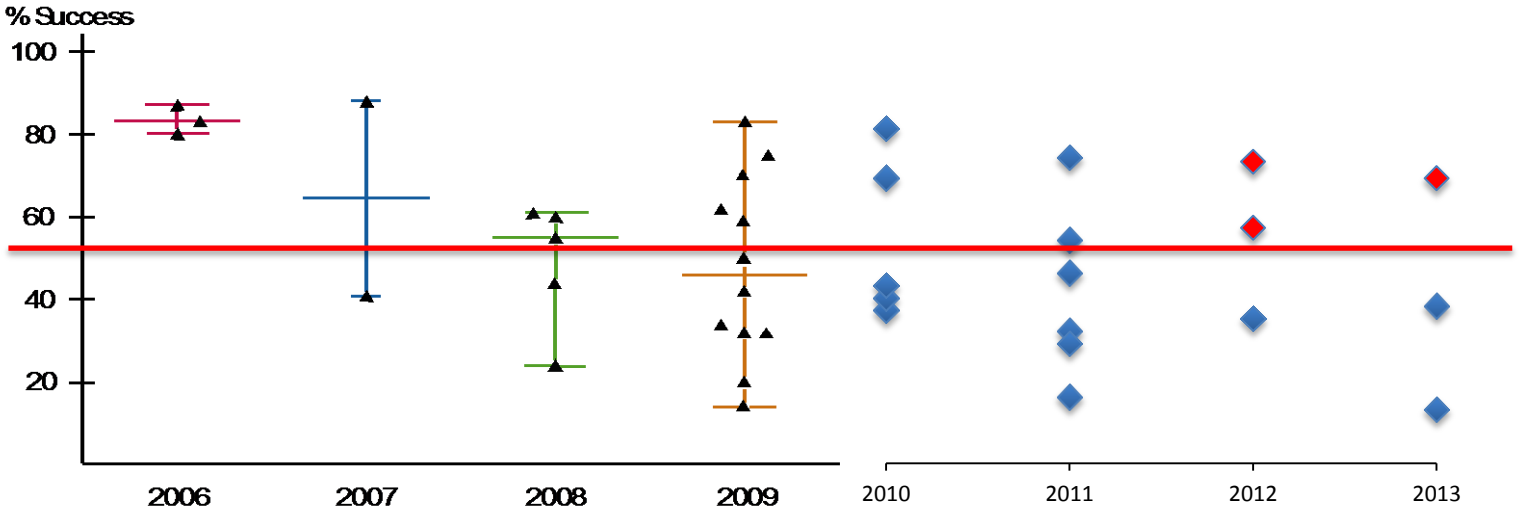
Gingold D, Fleshner P et al., Ann Surg 2014

Results according to year of publication

LIFT:
75%



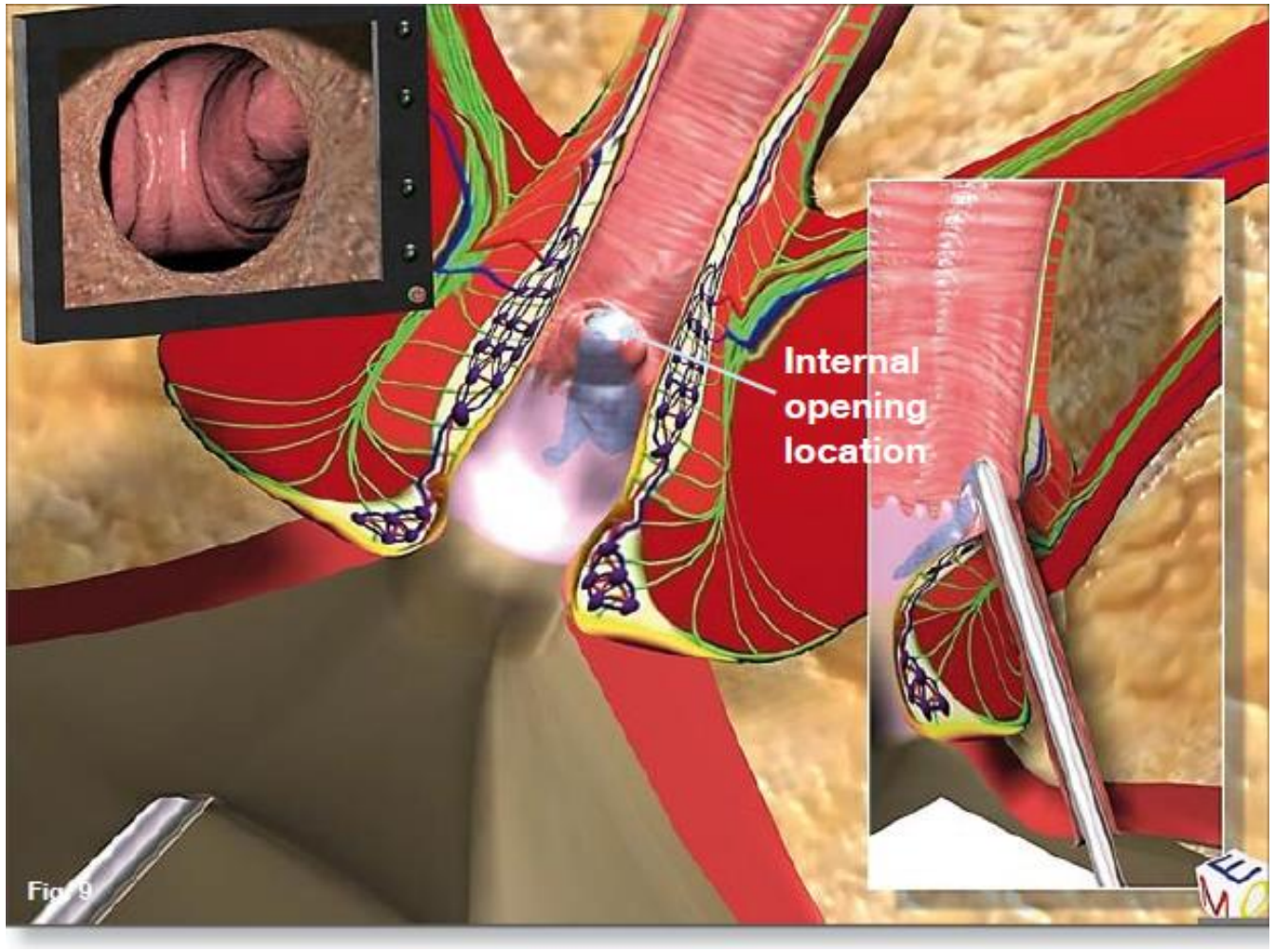
plug:
50%



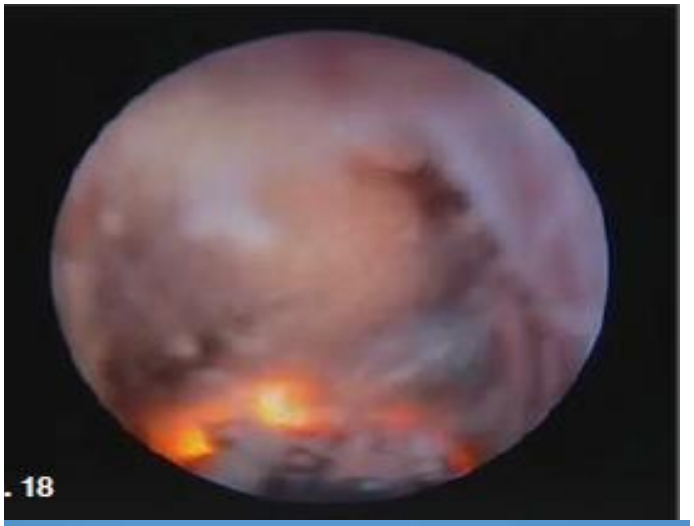
VAAFT

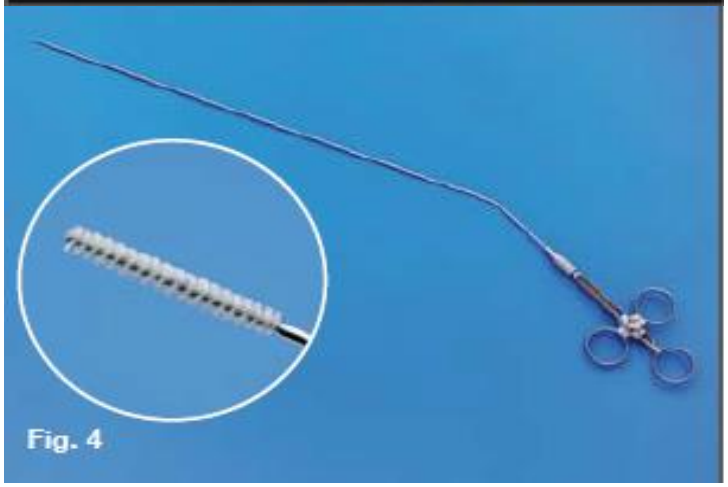
(Video Assisted Anal Fistula Treatment)

Rigid fistuloscopy
under glycine-mannitol perfusion

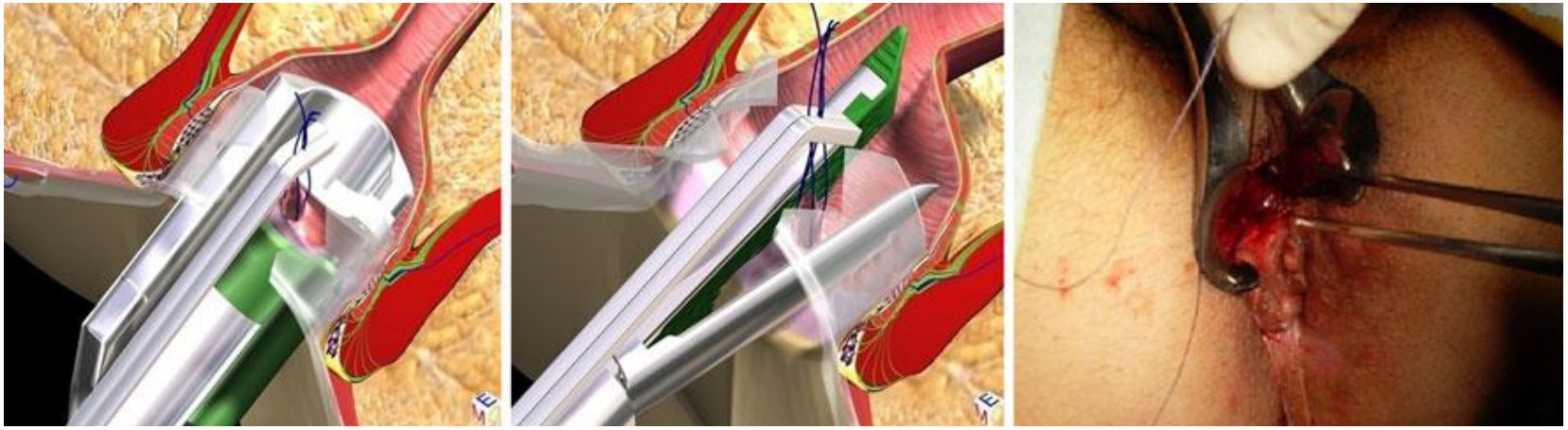


Fistula cleansing by fulguration, brushing and wash-out





Closure of the primary orifice by flap or stapling



Cyanoacrylate glue injection un the tract

Results VAAFT - Meinero

- 203 patients
  - 149 with h/o past fistula surgery
- F-up a 2, 4, 6 et 12 months
- success @ 1 year: 76%
  - in remission @ 2 years: 94%
- no continence disturbance

Meinero P et al, Dis Colon Rectum 2014

VAAFT with endorectal flap - Crohn

- 13 patients
- 2/13 VAAFT not completed
- 7/11 identification of prior occult sinuses
- 9/11 healed
- no impact on continence

Schwander O, Tech Coloproctol 2013

VAAFT - conclusions

- promising technique
- treatment under direct vision
- advantage (?) for
  - 1° orifice unclear
  - presence of sinuses, deep abcesses
- cost
- awaiting more evidence in CD

UK survey – perianal CD collaborators: what would do you do for CD anal fistulas?

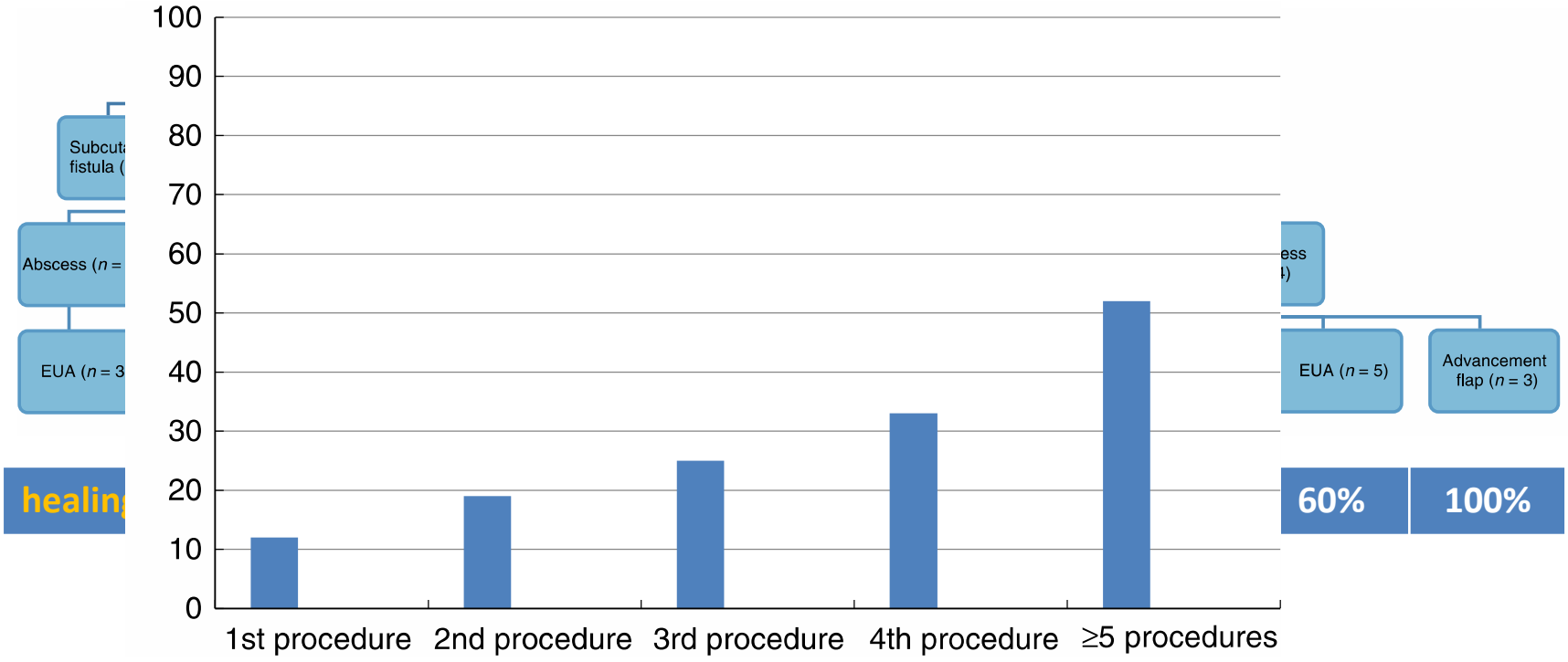
- Anti-TNF-α therapy: 64.2%
- Surgical definitive procedures
  - removal of seton only (70.7%)
  - fistulotomy (57.1%)
  - advancement flap (38.9%)
  - fistula plug (36.4%)
  - ligation of intersphincteric track (LIFT) (31.8%)

Lee MJ, Colorectal Dis 2016

Original article doi:10.1111/codi.13106

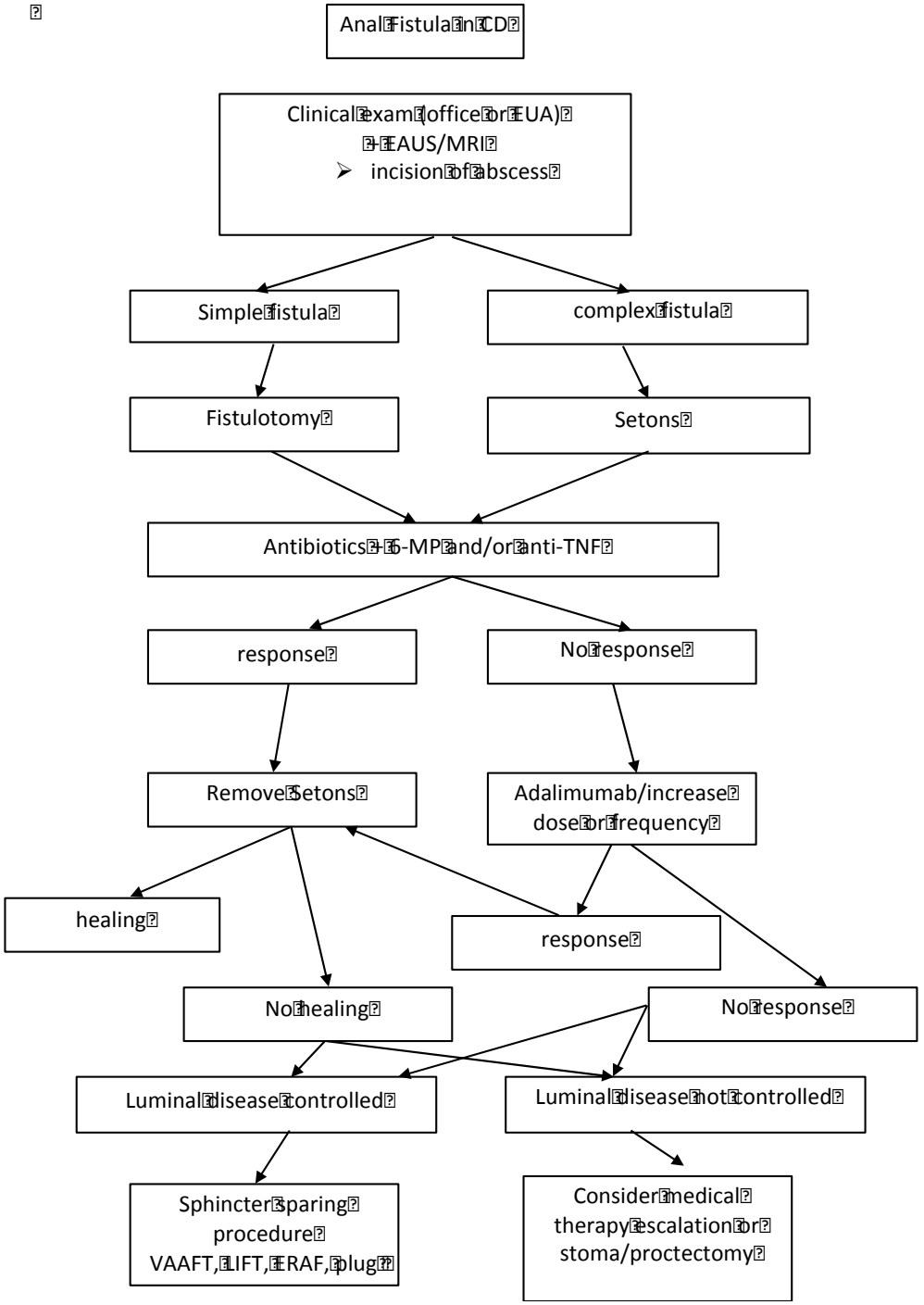
Long-term outcome after surgery for Crohn's anal fistula

- 4 centers in Sweden, 119 patients, 1998-2009
- ➢ median follow-up 7.1 years (1.0–17.5)



Graf W et al , Colorectal Dis 2015

algorithm


Anal Fistula in CD
Clinical exam (office or EUA)
+- EAUS/MRI
➢ incision of abscess
Simple fistula
complex fistula
Fistulotomy
Setons
Antibiotics +- 6-MP and/or anti-TNF
response
No response
Remove Setons
Adalimumab/increase dose or frequency
healing
response
No healing
No response
Luminal disease controlled
Luminal disease not controlled
Sphincter sparing procedure
VAAFT, LIFT, ERAF, plug??
Consider medical therapy escalation or stoma/proctectomy

conlcusions

- multidisciplinary approach
- drain sepsis, then medical therapy
- if medical therapy fails and fistula complex
  - discuss with patient
    - long term setons
    - sphincter sparing procedure, if luminal disease controlled
- if perianal disease uncontrollable:
  - stoma / proctectomy

18th ALPINE COLORECTAL MEETING

22th-24th January 2017
Villars, Switzerland

www.alpinecolorectal.org

Video Session: Transanal Surgery

Watch and wait strategy

Prevention of complications

Inherited colorectal cancer

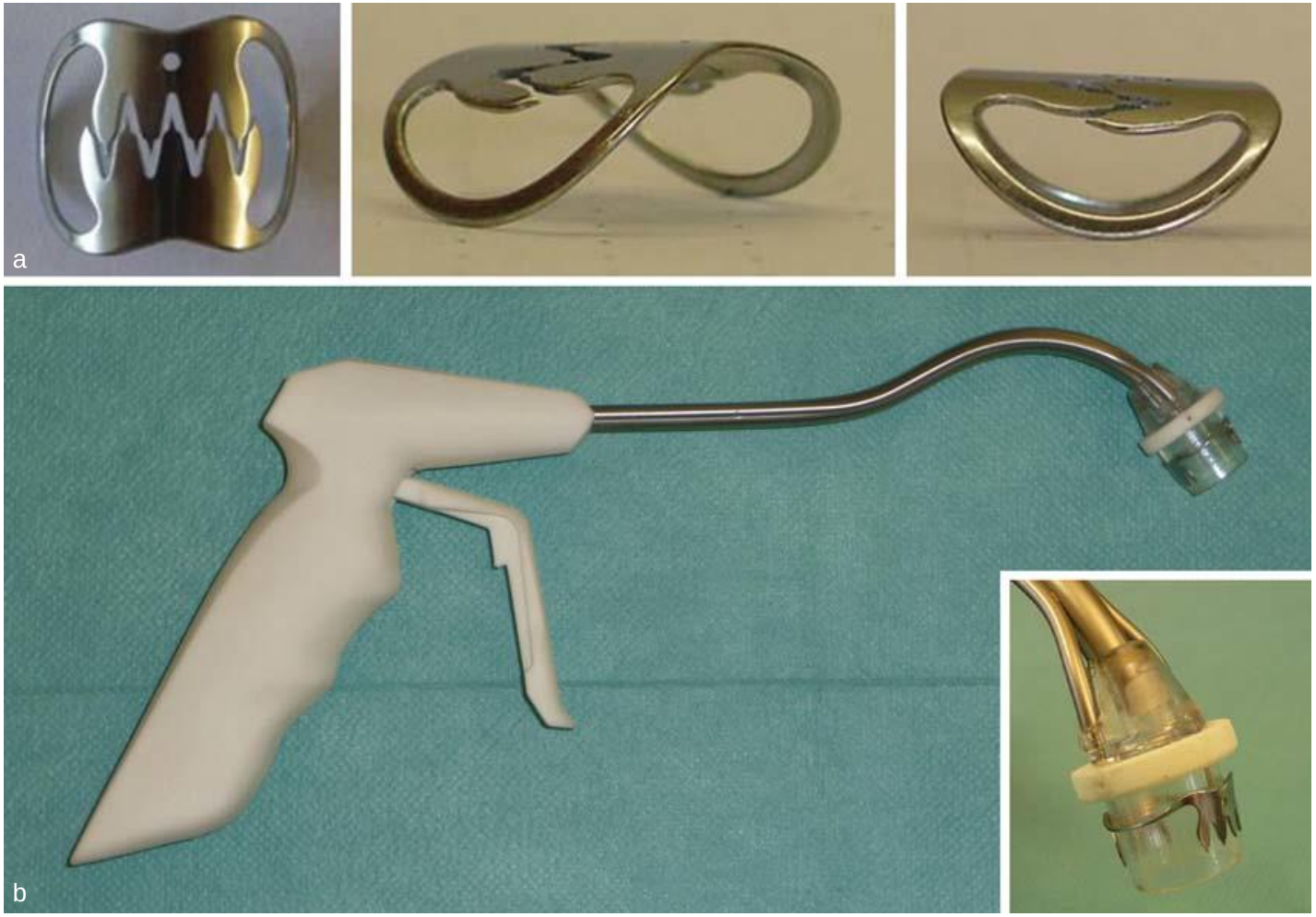
Debate on ventral mesh rectopexy

Hot topics in IBD

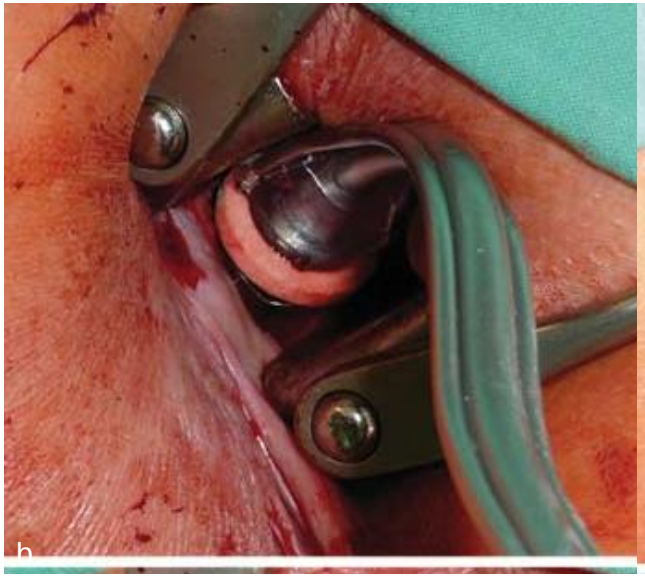
Trial update

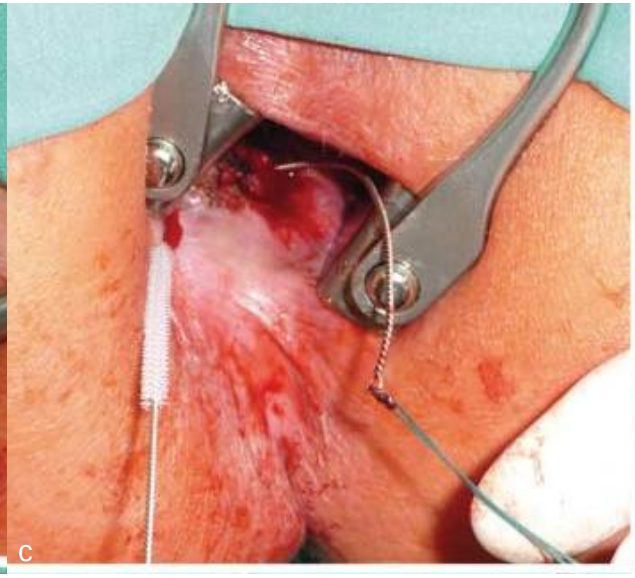

The End

Over The Scope Clip

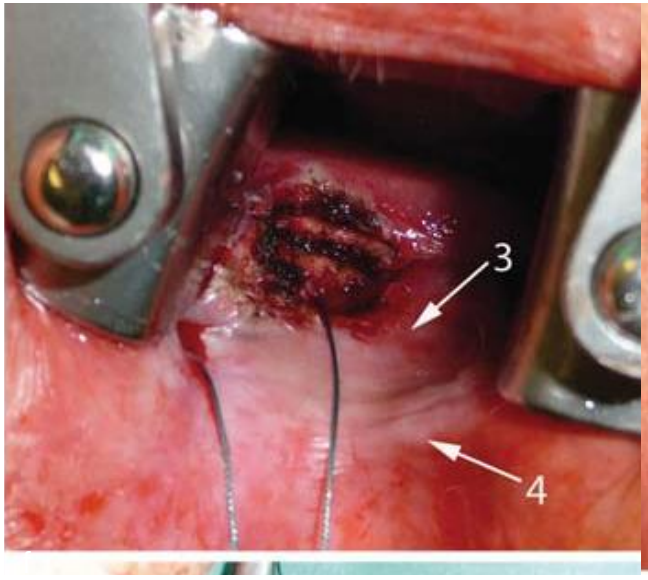


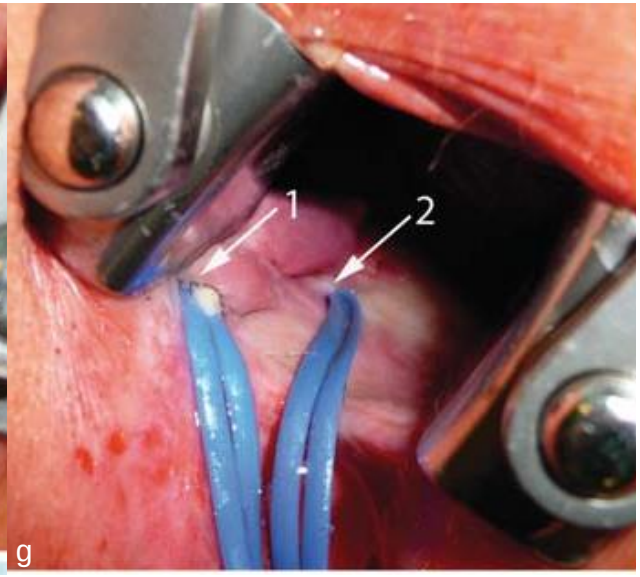
Prosst RL et al, Minimally Invasive Therapy 2012


b


c


d


3
4


1
2
g

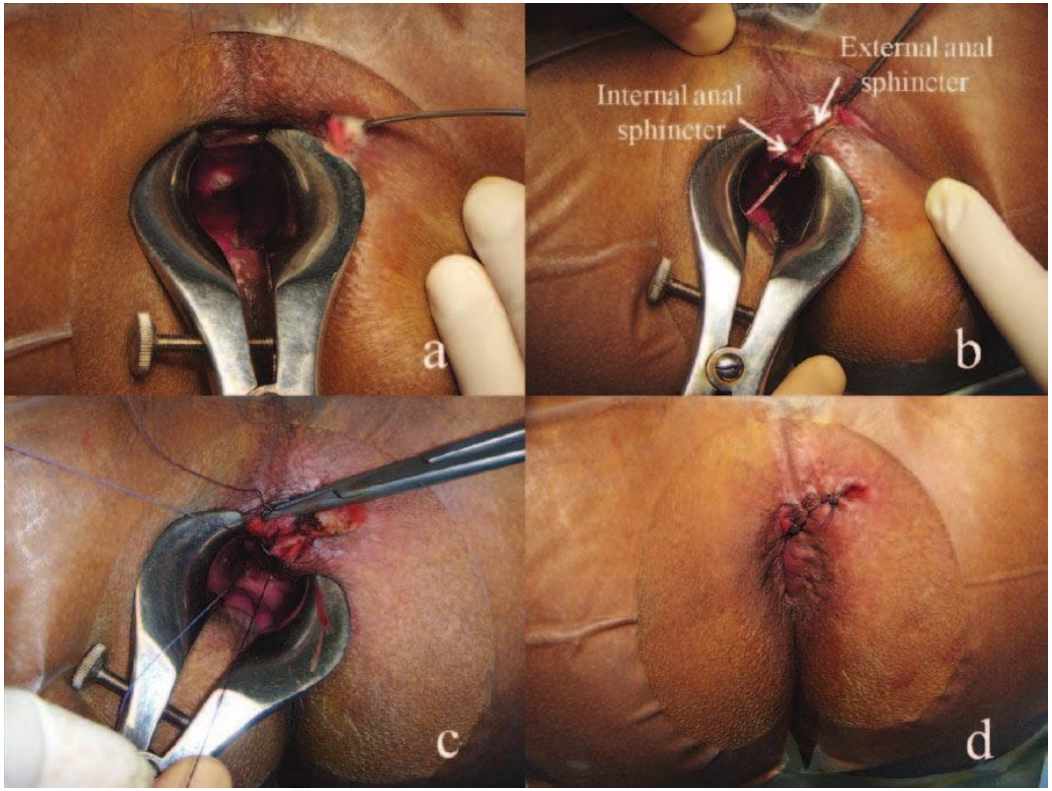

b


d

FIPS (Fistulotomy and Primary Sphincter repair)

FIPS (Fistulotomy and Primary Sphincter repair)

- Fistulotomie, currettage trajet/abcès profonds
- suture primaire end-to-end du sphincter



Résultats littérature

TABLE 5. Data from the literature on fistulotomy or fistulectomy with primary sphincteroplasty

Author	Year	Study type	Patients n	Complex fistulas n (%)	Recurrent fistulas, n (%)	Follow-up months	Sphincter dehiscence %	Success %	Fecal incontinence	
									Impaired %	Major %
Parkash et al[14]	1985	R	120	2 (1.7)	na	6–60	3.3	97.5	3.7	na
Lux et al[28]	1991	P	46	26 (56.5)	20 (43.5)	15.3	0	100	21.7	10.9
Christiansen et al[23]	1995	P	14	14 (100)	14 (100)	12–48	0	85.7	21.4	0
Lewis[29]	1996	R	32	32 (100)	nr	nr	nr	90.6	nr	nr
Gemsenjager[19]	1996	R	21	11 (52.4)	na	2–9	4.8	95.2	4.8	na
Roig et al[20]	1999	R	31	31 (100)	11 (35.5)	24	3.2	90.3	20.0	0[a]
Perez et al[17]	2005	P	35	35 (100)	16 (45.7)	32	0	93.8	12.5	0[a]
Perez et al[24]	2006	RCT	28	28 (100)	9 (32.1)	36	0	92.9	17.4	0[a]
Jivapaisarnpong[21]	2009	P	33	33 (100)	nr	14	6.1	87.9	0	0
Roig et al[18]	2010	R	75	75 (100)	na	13	1.3	89.3	18.3	6.7[a]
Kraemer et al[22]	2011	R	38	38 (100)	7 (18.4)	nr	2.6	97.4	9.4	6.3[a]
Total			473							
Average							2.1	92.8	12.9	3.0
Weighted average							2.3	93.8	11.6	4.1
Present study	2012	P	72	72 (100)	12 (16.7)	29.4	1.4	95.7	11.6	1.4[a]

R = retrospective; P = prospective; RCT = randomized clinical trial; FI = fecal incontinence; nr = not reported; na = not available.
[a]Patients with full continence prior to surgery.

86-100% 10-20% 0-10%

Ratto C. et al, DCR 2013

FIPS – résultats fonctionnels à long terme

- 70 patients opérés par FIPS (32% fistules récidivantes)
- manométrie pré-op, et post-op à 3 mois, 1, 3, 5 ans
- f-up 81 (48-120) mois, 0 patients perdus
- 32% incontinence pre-op (score Wexner)
- succès: 91.5%
- incontinence de novo: 17% (score Wexner <3)

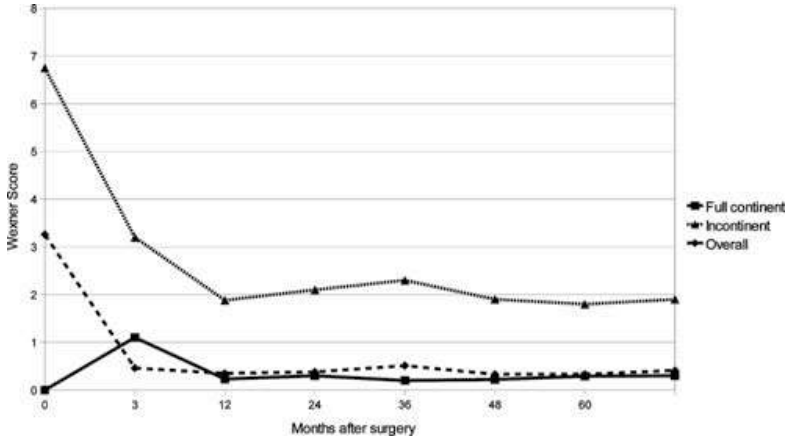


FIGURE 1. Continence Wexner Score as a function of time after surgery.

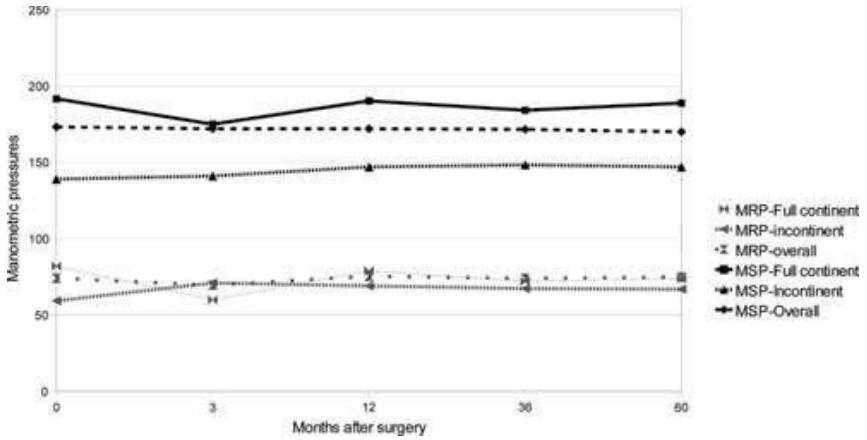


FIGURE 2. Sphincter pressures as a function of time after surgery.

Arroyo A et al., Ann Surg 2012