EMERGING TECHNOLOGY IN FISTULA MANAGEMENT

(VAAFT, Stem cells, FiLaC)

Sabry A. Badr (MD. PhD.)

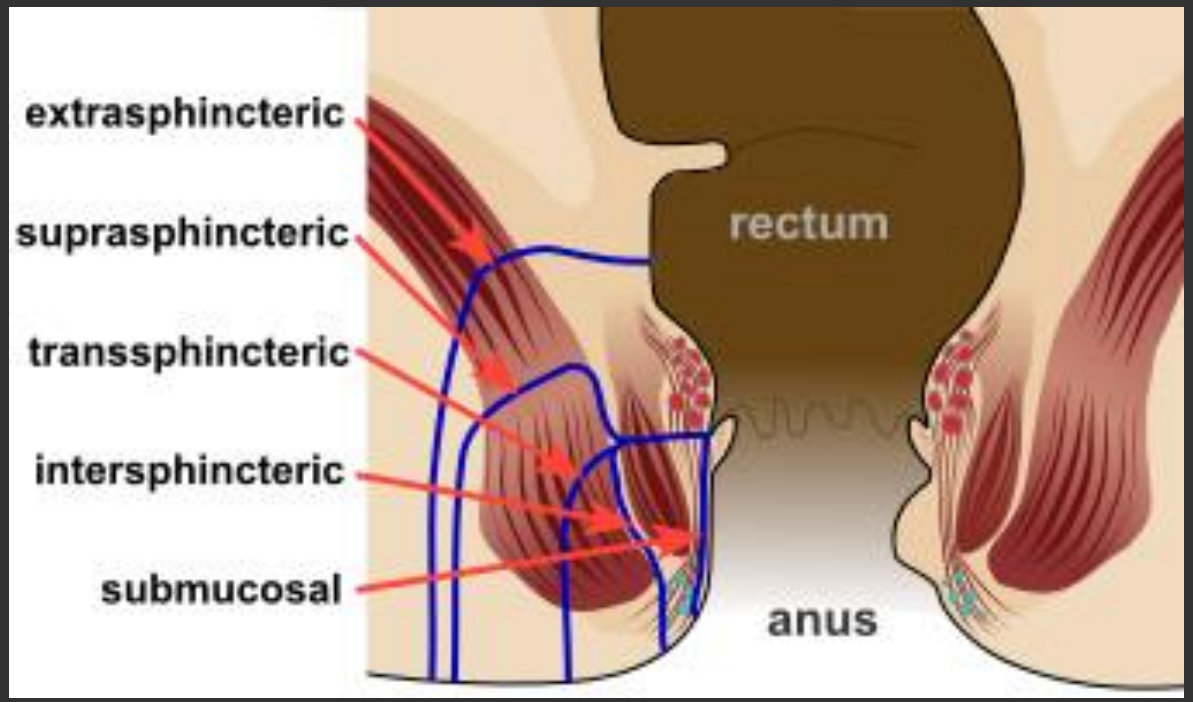
Professor of General Surgery, Mansoura University, Egypt

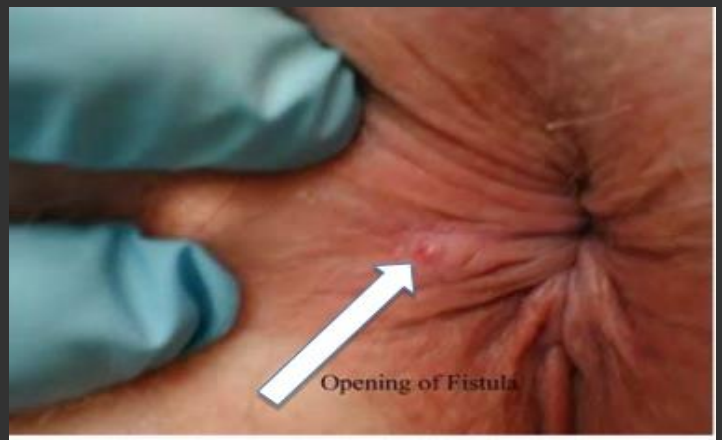
Disclosure

- None to be declared.

Fistula in Ano:

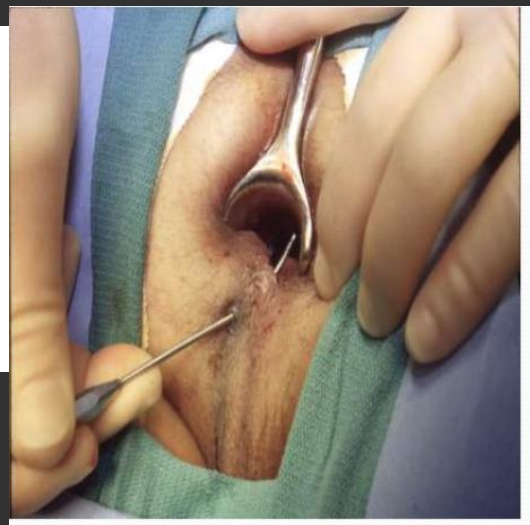
- Abnormal connection between epithelial surface of anal canal and perianal skin

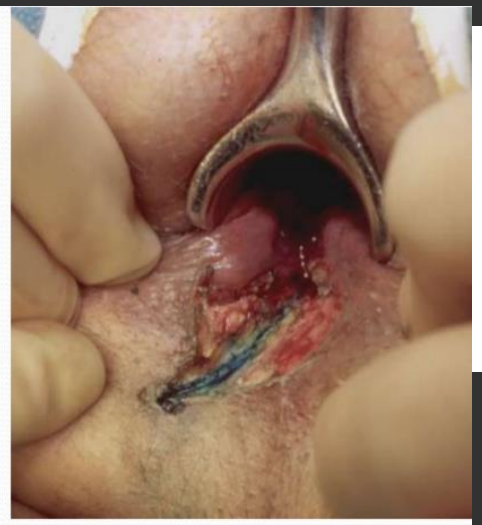




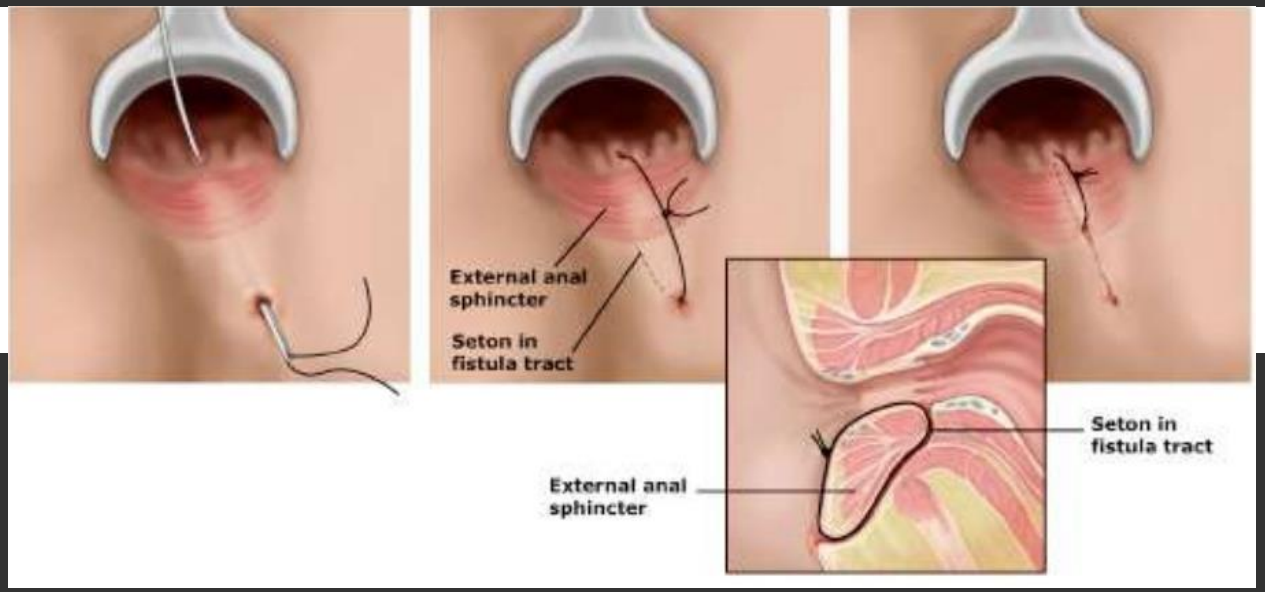
Fistula treatment options:

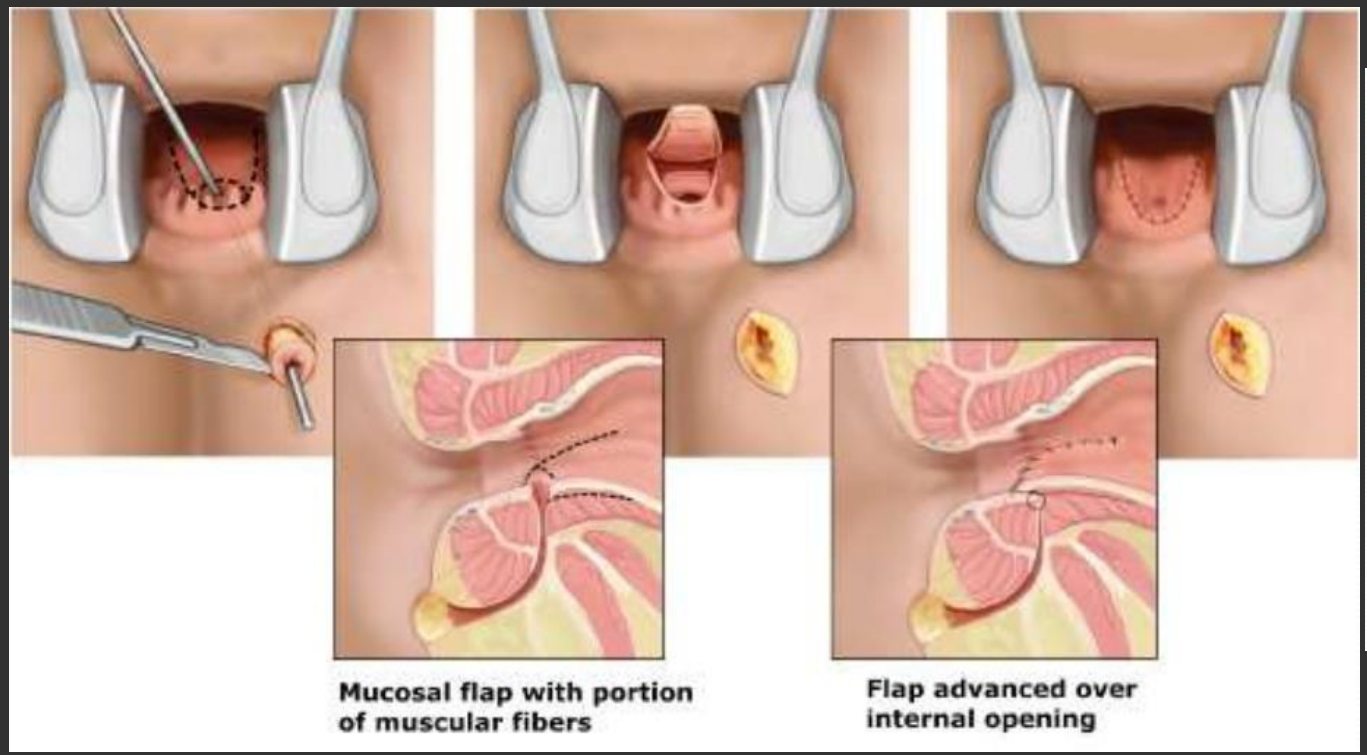
1. Fistulotomy.
2. Fistulectomy
3. Staged fistulotomy, fistulectomy
4. Mucosal advancement flaps
5. Plugs and adhesives
6. LIFT procedure
7. Fistula clip closure
8. PERFACT procedure (proximal superficial cauterization, emptying regularly fistula tracts and curettage of tracts)





Fistulotomy





Fibrin plugs

Evolution of Fistula management

World Journal of Surgery
May 2012, Volume 36, Issue 5, pp 1162–1167 | Cite as

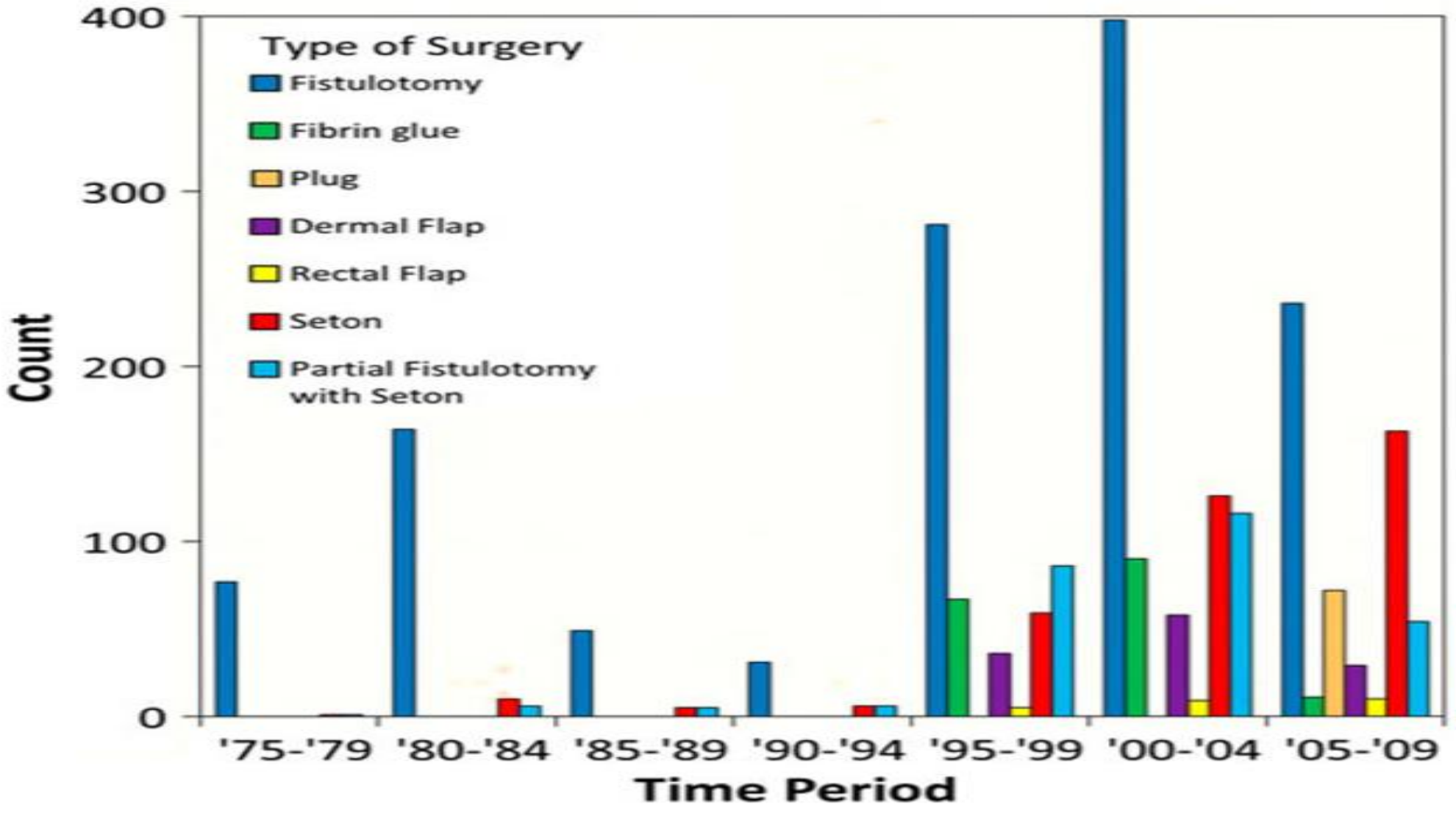
Evolution of Treatment of Fistula in Ano

Authors | Authors and affiliations

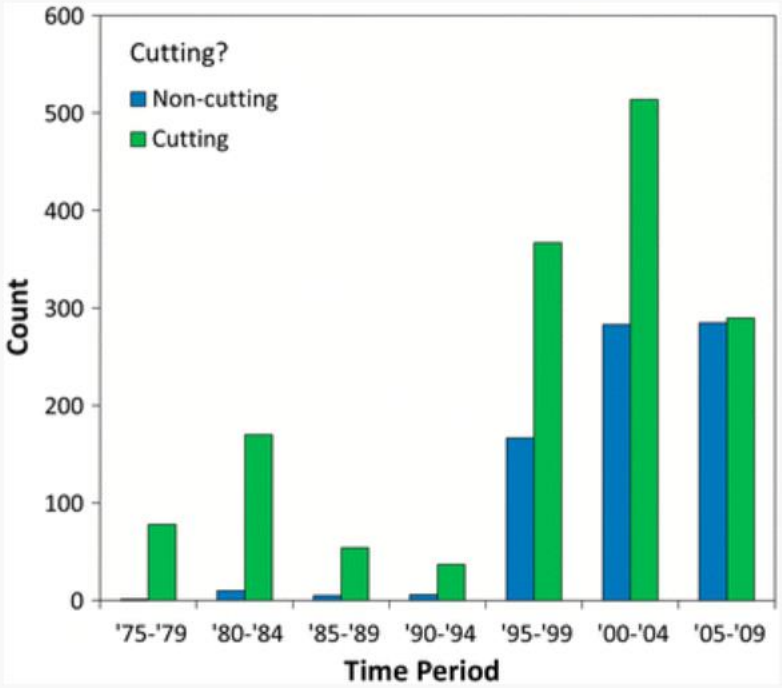
J. Blumetti, A. Abcarian, F. Quinteros, V. Chaudhry, L. Prasad, H. Abcarian

Article
First Online: 24 February 2012

Evolution of Fistula management



Evolution of Fistula management



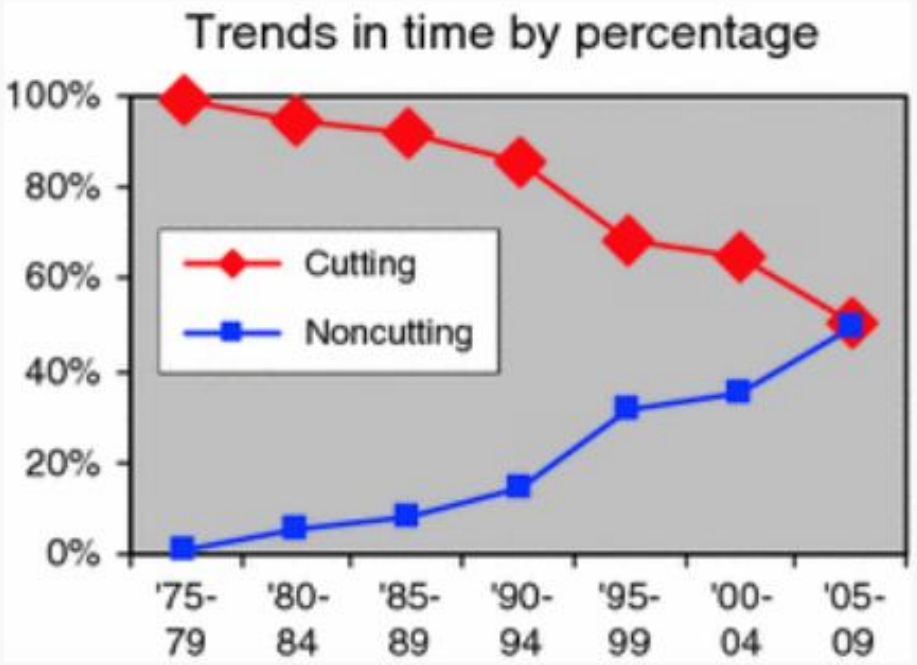
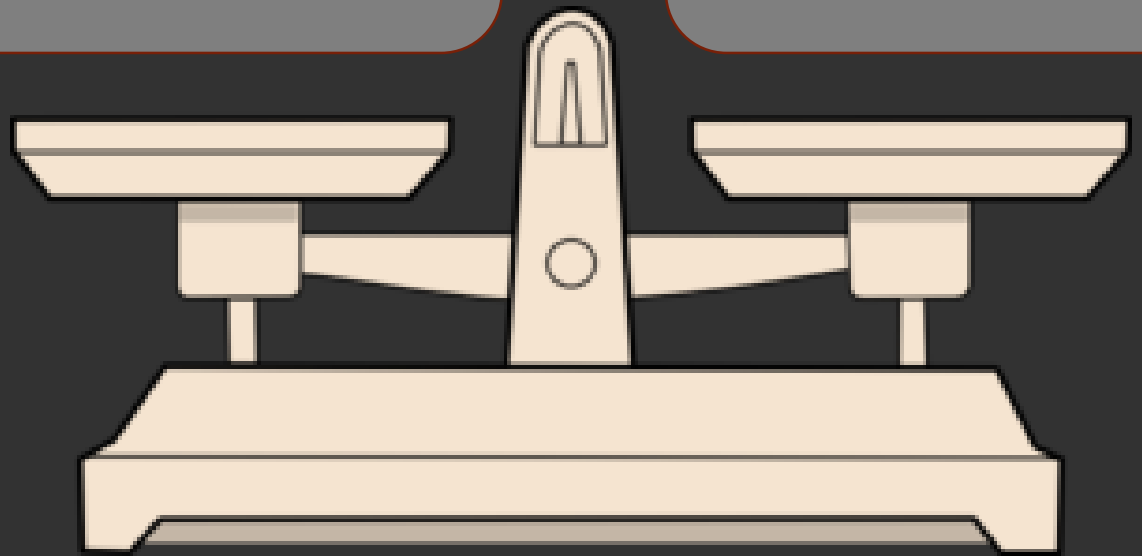


Fig. 2
Number and time distribution of cutting versus noncutting operations

Principles of fistula treatment:

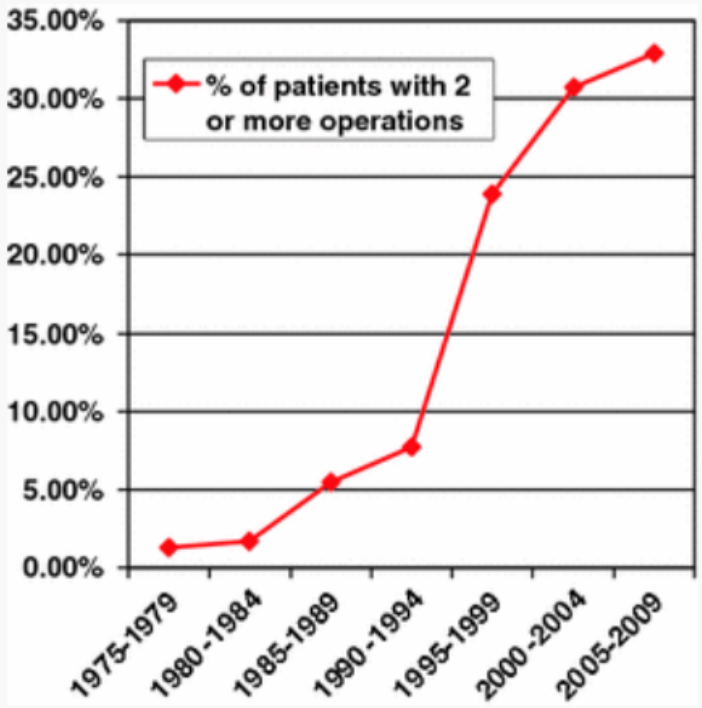
Eradicate the Fistula
"healing"

Preserve Continence



All Emerging techniques lean towards sphincter preservation

Evolution of fistula treatment



The incidence of re-operation rose :

1.5% → 32.9%

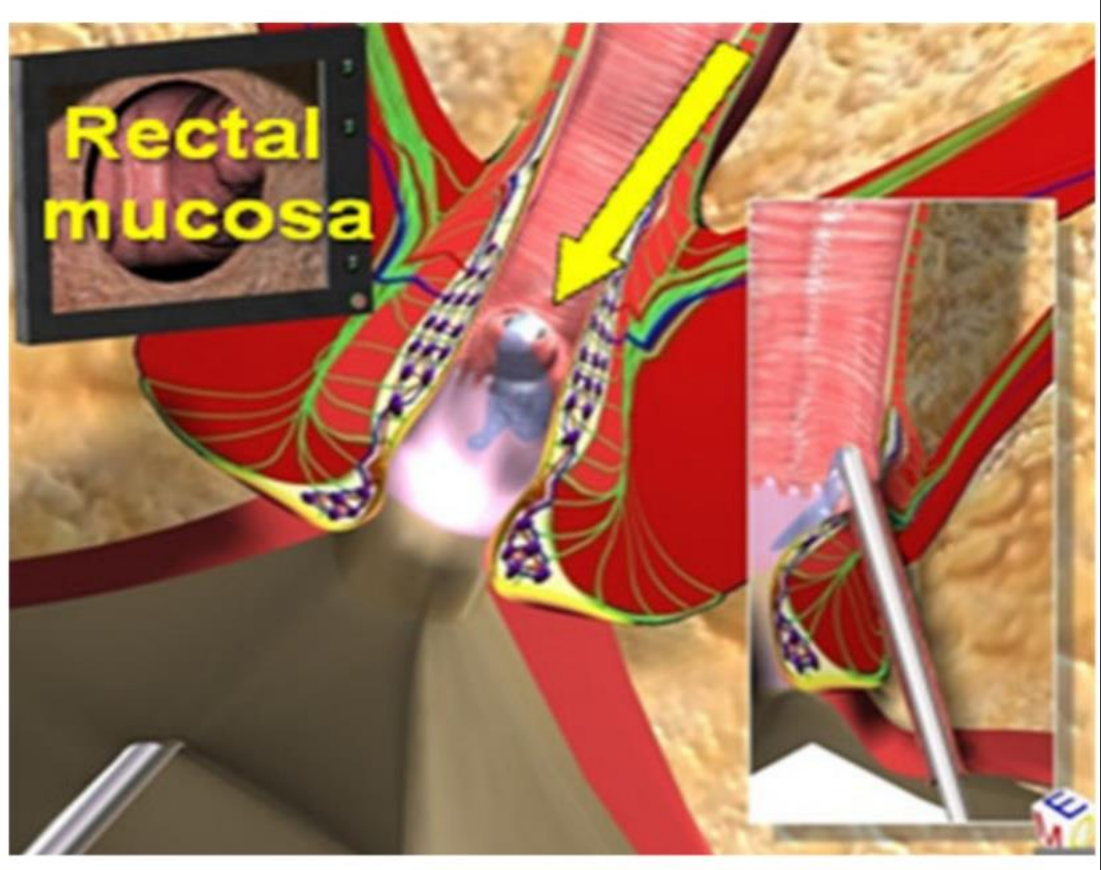
"In these litigious times, recurrence or persistence of a fistula is surely preferable to incontinence."

Herand Abcarian

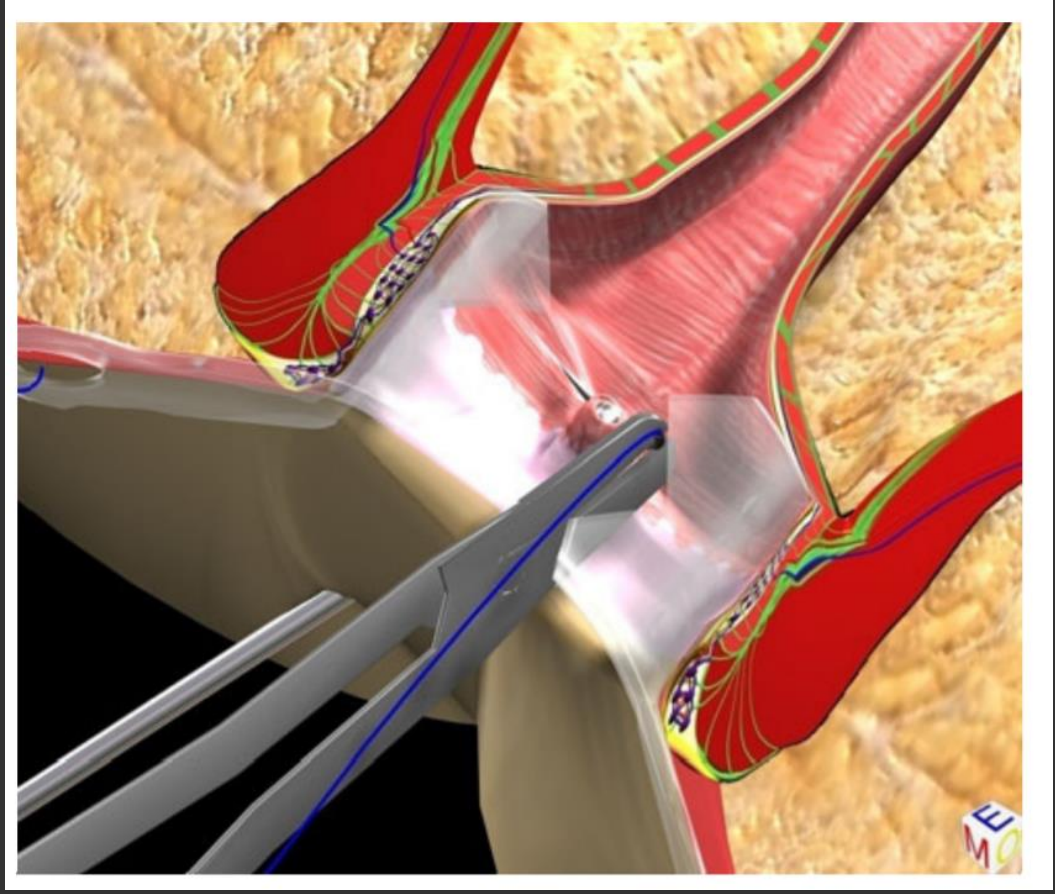
VAAFT (Video Assisted Anal Fistula Treatment)

VAAFT (Technique)

Diagnostic phase: localization of I.O.



Therapeutic: Closure of I.O. and fulguration of the tract



VAAFT (Results)

- 98 patient
- All cryptc
- 94 patien
- Classifica
  - 74 Hig (75.5%
  - 9 extr
  - 6 supr
  - 9 hors

- 72 patients achieved primary healing **(73.5%)** within 2-3 months.
- 26 patients → No healing (26.5%)
- 19/26 accepted re-VAAFT:
  - 9/19 healed
  - 6/19 recurrence
  - 4/19 still under observation.
- Overall healing rate **87.1%**

- Median follow up 13 months (range 6-60 m)

Further reports with similar results

ISSUES AND ARTICLES | ABOUT THIS JOURNAL | FOR AUTHORS | SUBSCRIBE

ORIGINAL ARTICLE

Minerva Chirurgica 2018 April;73(2):142-50

DOI: 10.23736/S0026-4733.18.07390-X

language: English

Video-assisted anal fistula treatment in the management of complex anal fistula: a single-center experience

Alessandro STAZI [1], Paolo IZZO [2], Francesco D'ANGELO [3], Monica RADICCHI [1], Manuele MAZZI [1], Federico TOMASSINI [3], Luciano IZZO [2], Stefano VALABREGA [2]

[1] Department of General Surgery, Colorectal Pelvic Center, Madonna delle Grazie Clinic, Velletri, Rome, Italy; [2] Pietro Valdoni Department of Surgery, Sapienza University, Rome, Italy; [3] Department of Surgical and Medical Sciences and Translational Medicine, Sapienza University, Rome, Italy

Techniques in Coloproctology
June 2016, Volume 20, Issue 6, pp 389–393 | Cite as

An experience with video-assisted anal fistula treatment (VAAFT) with new insights into the treatment of anal fistulae

Authors | Authors and affiliations

I. Seow-En, F. Seow-Choen, P. K. Koh

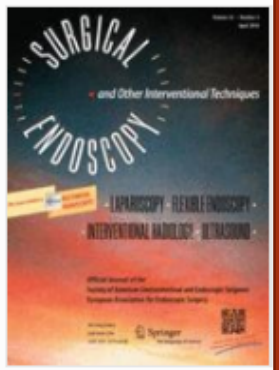
Short Communication
First Online: 08 April 2016

9 | 588 | 5

Primary Healing
77%
Overall after re-VAAFT
92.3%

Primary Healing
70.7%
Overall after re-VAAFT
83%

Pooled results and meta-analysis

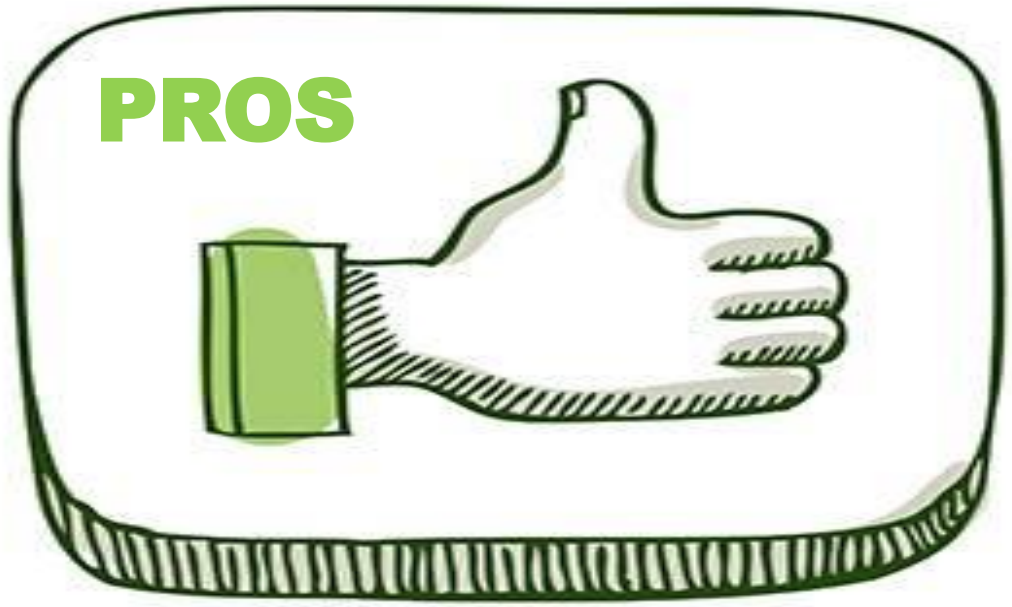


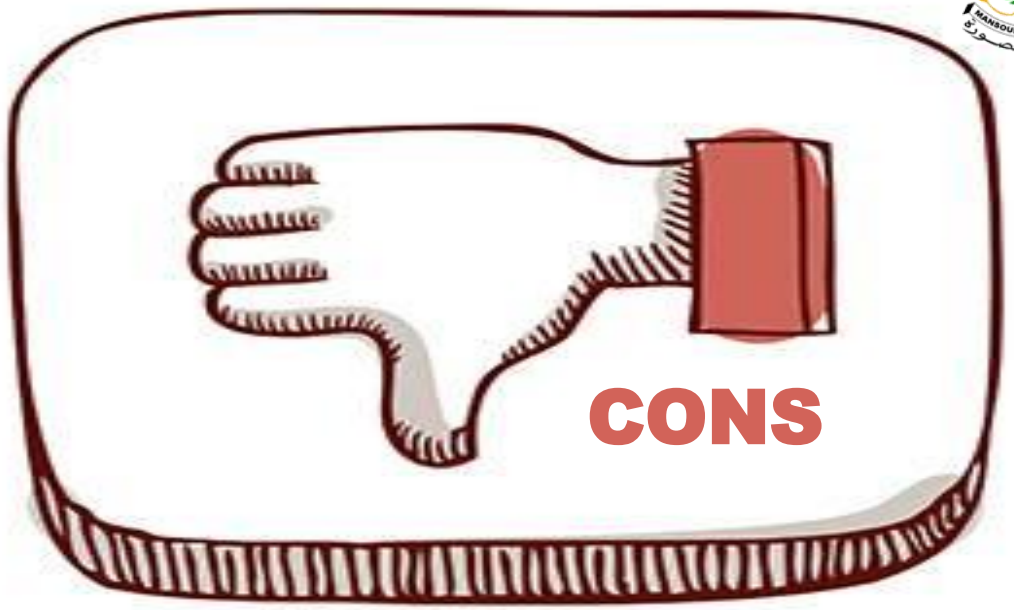
- 11 studies (788 patients, 66.5% complex fistula, 18.4% had prior surgery)
- Weighed mean for Internal opening detection in **93.3%** of the patients.
- Weighed mean of recurrence **17.7%**
- Weighed mean of complications **4.3%** (all minor)
- **No continence affection** reported in any study.
- Median follow up **9** months

Sameh Hany Emile 1
Hossam Elfeki 1 2
Mostafa Shalaby 1
Ahmad Sakr 1

1. Colorectal Surgery Unit, Department of General Surgery, Mansoura Faculty of Medicine, Mansoura University Hospitals, Mansoura City, Egypt
2. Department of Surgery, Aarhus University Hospital, Aarhus, Denmark

VAAFT summary

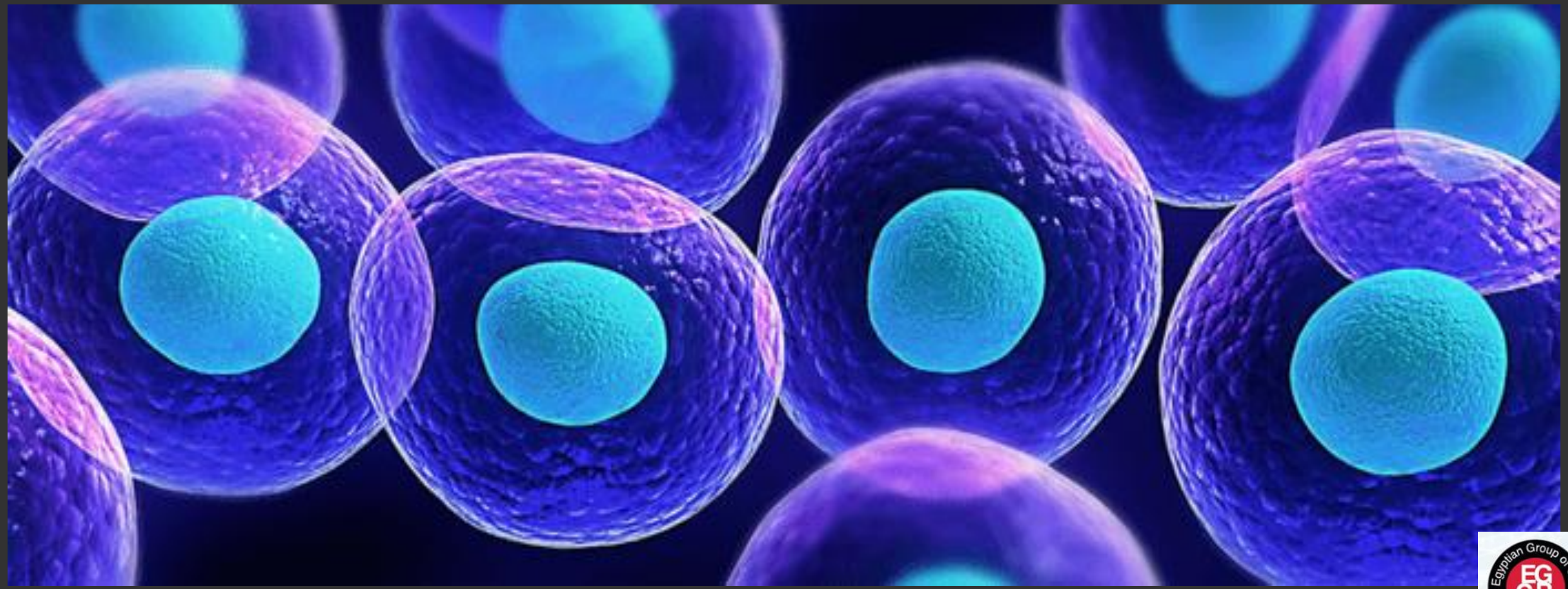




- Continence preservation.
- Visualization of the I.O. and secondary tracts.
- Promising healing rates.
- Early return to activity

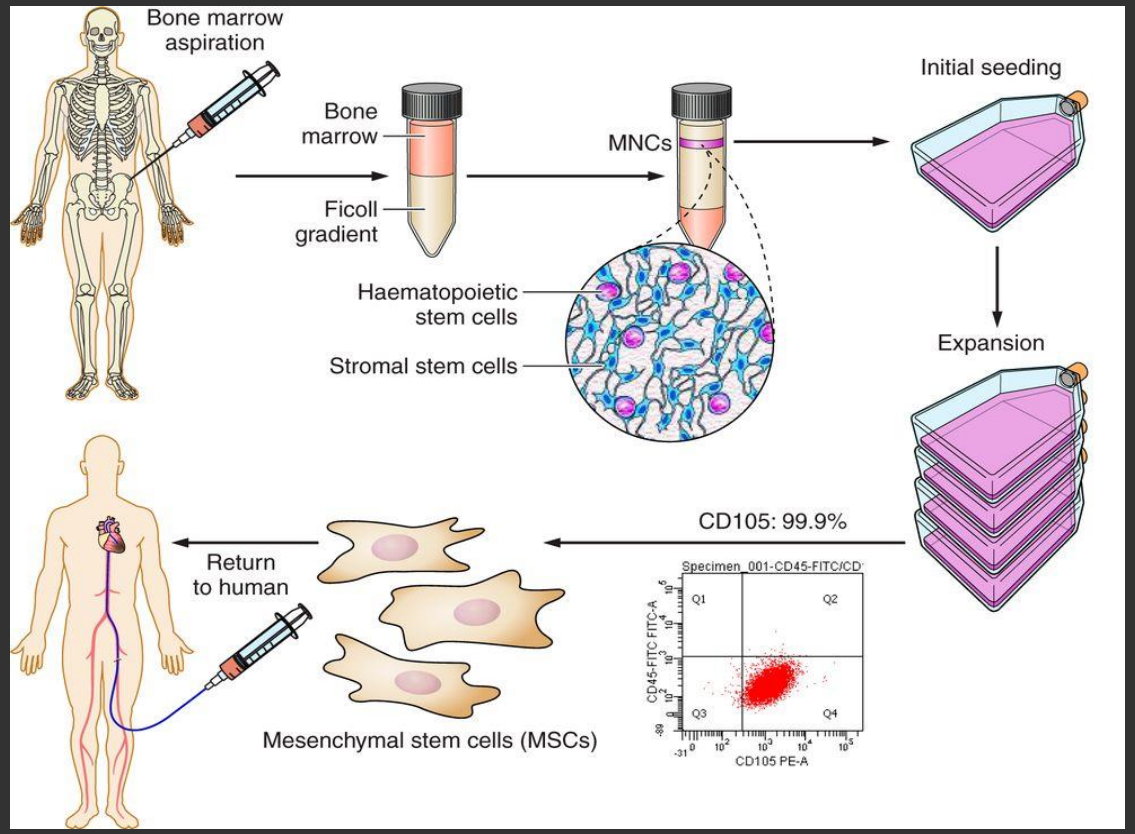
- Relatively expensive technology.
- No RCTs.
- Longer operative time.
- Learning curve ??

Stem Cells

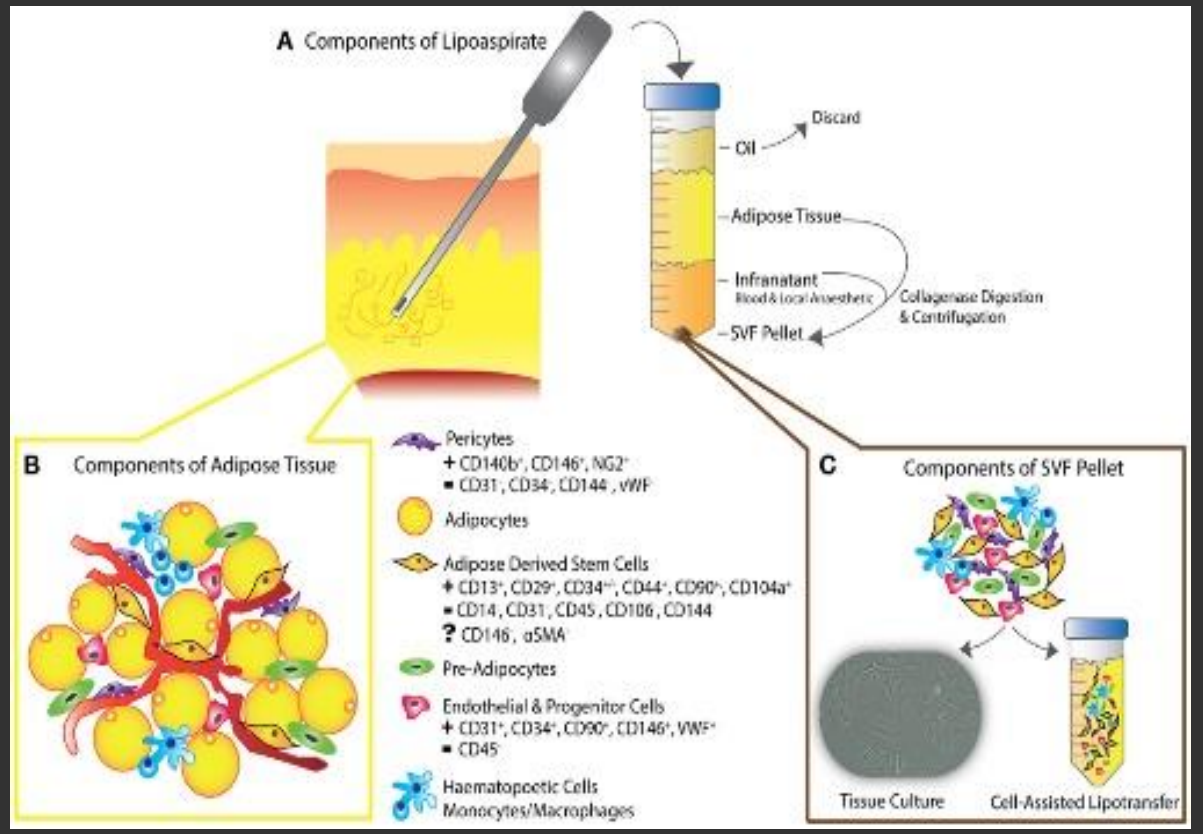


Source of Stem Cells

Bone marrow (mesenchymal)

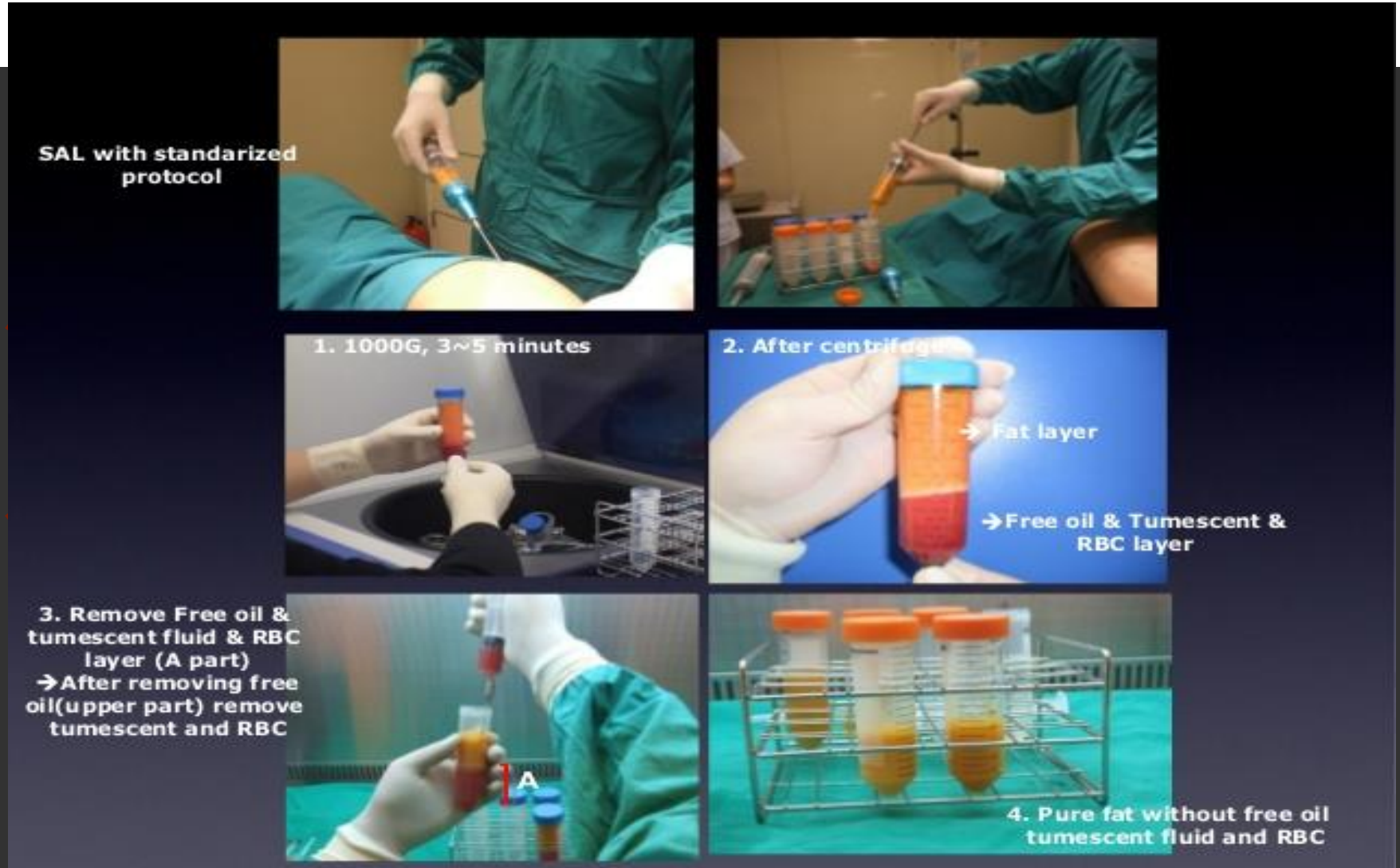


Adipose tissue (Fat)



Stem Cells (technique simplified)

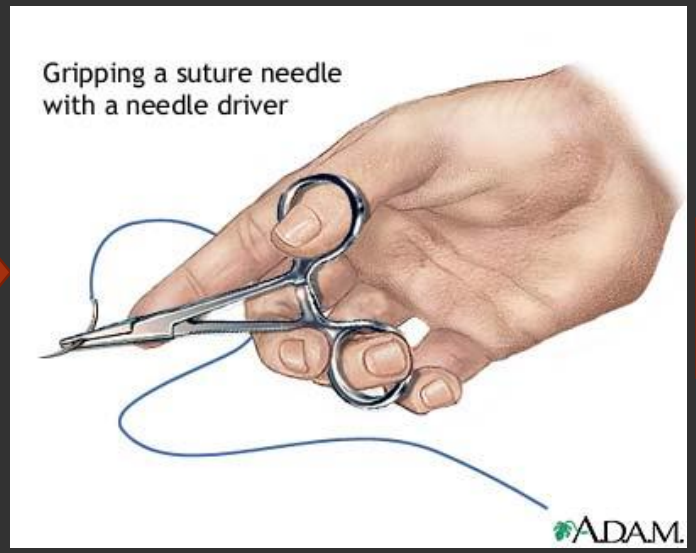
- Liposuction or Aspiration
- Centrifugation
- Pure fat without tumescence



Stem cells (continued)

Curette and clean

Closure of Internal opening



Injection of stem cells

The ASC suspension is injected through a long, fine needle into the tract walls; not deeper than 2 mm.

Stem cells (literature)

- Most of the studies were on Crohn's fistula, Also some reports on complex fistulas, recurrent fistulas and rectovaginal fistulas.
- All kinds of reports:
  - Phase I/II/III clinical trials.
  - Retrospective.
  - Systematic reviews & meta analysis.
- Adipose or bone marrow derived.
- Autologous or Allogenic.
- Local or systemic injection (IBD).

Stem cells (pooled analysis)

Table 1. Published Clinical Trials and Large Ongoing Phase III Trials Using Stem Cells for the Treatment of Crohn's Perianal Fistula

Authors, Year	Study Design	Source of Cells	Results
Garcia-Olmo et al, 2005[10]	Phase I clinical study (n = 4)	ASC (autologous)	Complete closure: 50% of patients 75% fistulas
Garcia-Olmo et al, 2009[11]	Open-label, multicenter, phase II study (n = 14)	ASC + fibrin glue (autologous)	Fistula healing: 71% vs 14%
Ciccocioppo et al, 2011[13]	Prospective study (n = 10)	MSC (autologous)	Reduction in CDAI, PDAI, and pain/discharge PDAI scores
Mannon et al, 2011[17]	Open-label Phase II study (n = 10)	MSC (allogeneic) IV	Reduction in CDAI and fistula drainage
Guadalajara et al, 2012[12]	Retrospective follow-up of Garcia-Olmo phase II study (n = 5)	ASC + fibrin glue (autologous)	58% sustained fistula closure at end of follow-up by mean 3 years
Cho et al, 2013[18]	Open-label, multicenter, dose escalation phase I study (n = 10)	ASC (autologous)	Healing in 50% receiving ≥2× 107 cells/mL
Lee et al, 2013[15]	Open-label, multicenter, phase II study (n = 42)	ASC (autologous)	Fistula closure in 82% PP, 67% ITT analysis
de la Portilla et al, 2013[19]	Open-label pilot study (n = 24)	ASC (allogeneic)	Complete closure: 56.3%
Ciccocioppo et al, 2015[14]	5-year follow-up of 2011 study (n = 10)	MSC (autologous)	37% fistula relapse free 4 years later
Cho et al, 2015[16]	1-year follow-up from 2013 study	ASC (autologous)	Complete closure maintained in 75% at 2 years ITT analysis
Garcia-Olmo et al, 2015[20]	Retrospective, open label (n = 3 with CD)	ASC (allogeneic and autologous)	Healing in 2/3 CD fistula patients
Molendijk et al, 2015[1]	Double-blind, placebo-controlled study, phase II	MSC (allogeneic)	Healing up to 85%

NOTE. Source: Clinicaltrials.gov.
ASCs, adipose-derived stem cells; CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; ITT, intention to treat; IV, intravenous; MSCs, mesenchymal stem cells/mesenchymal stromal cells; PDAI, Pouchitis Disease Activity Index; PP, per protocol; SC, stem cells.

- 12 clinical trials, phase I/II
- 8 used Adipose derived and 4 Mesenchymal SC.
- All autologous except 2 studies allogenic.
- Healing rates varies from 50%-85% (≈65%)

Create Citation Alert

Stem cells (pooled analysis)

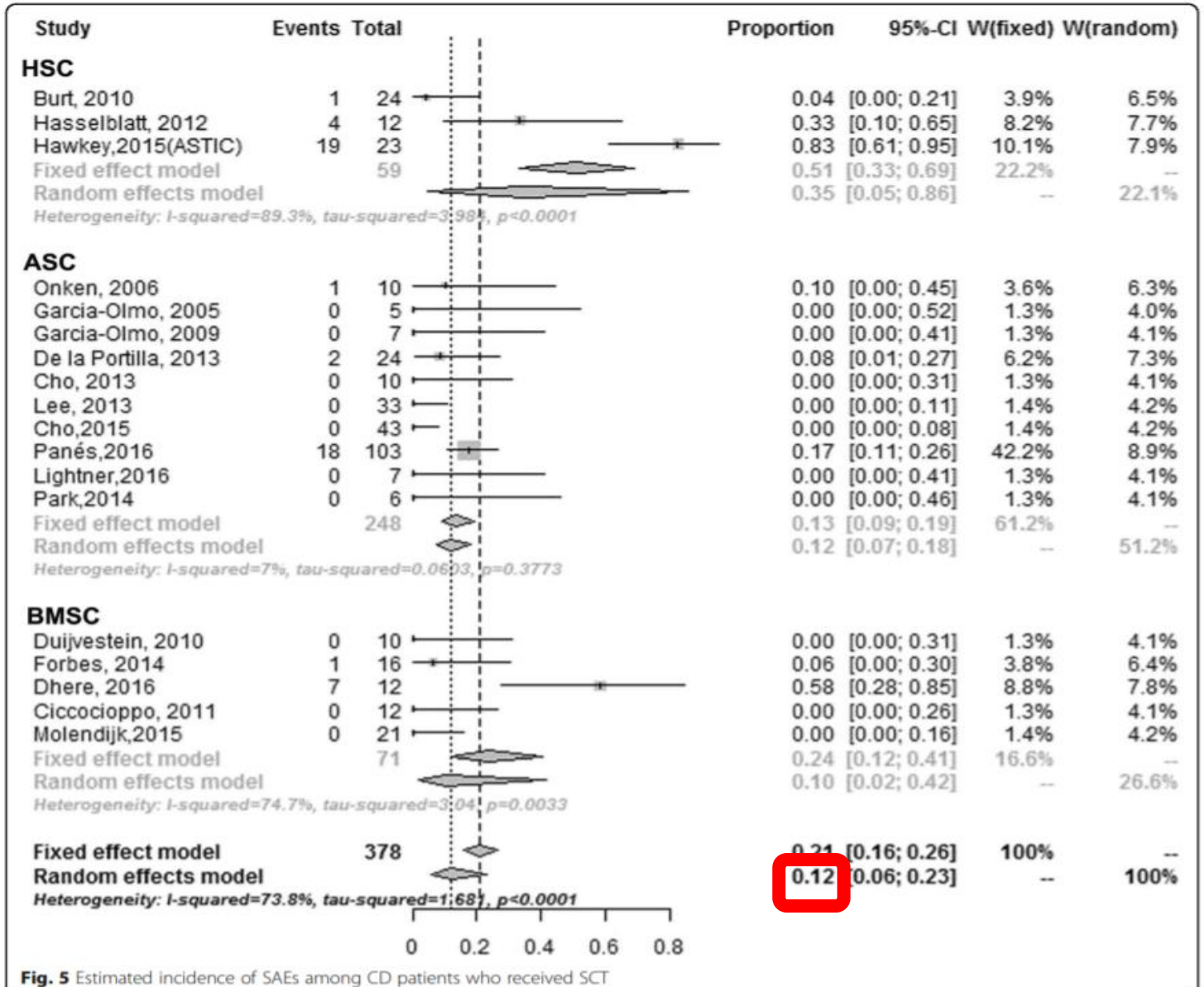


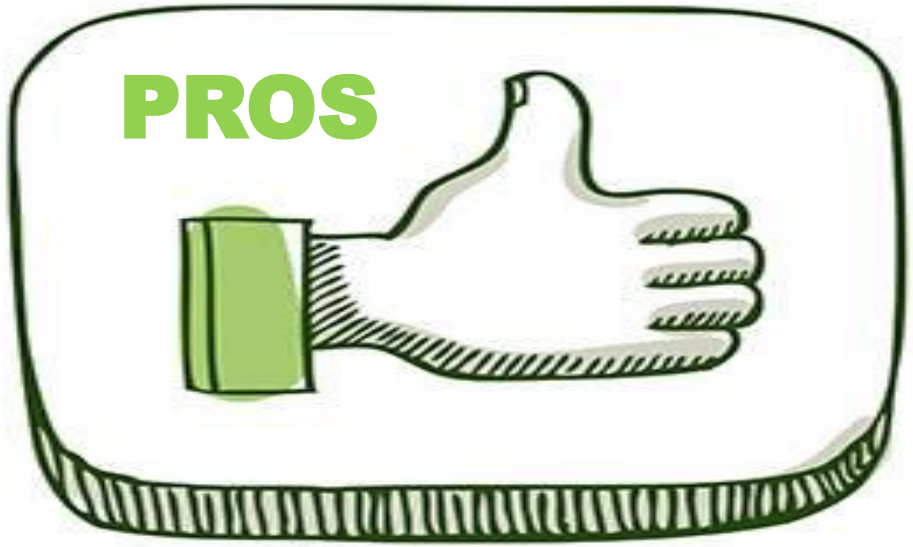
Fig. 5 Estimated incidence of SAEs among CD patients who received SCT

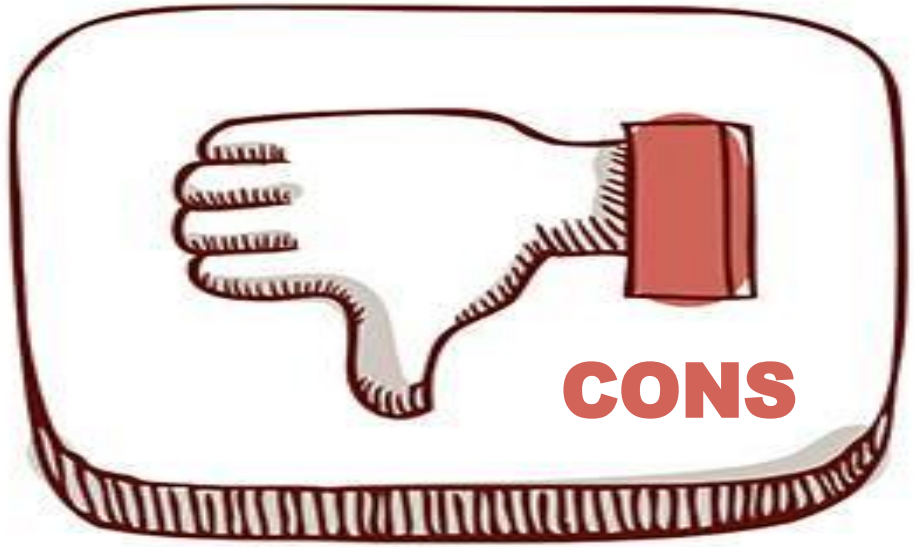
- 21 Studies, 514 patients.
- Follow up >12 months.
- Different source and techniques for SC injection.
- 57% healing rates.
- 16% clinical recurrence.
- 12% Severe adverse events.

Stem cells (pooled analysis)

- Eleven studies (3 clinical trials), 365 patients.
- 9 used adipose derived SC, 2 used mesenchymal SC.
- 6 studies defined healing by clinical definitions and 5 studies included MRI in their healing definition.
- Healing rates varies between 27% - 88%
- There were no significant increases in adverse events; $p = 0.81$
- MSCs were associated with improved healing as compared with control subjects at 24 to 52 weeks (OR = 2.37 (95% CI, 0.90–6.25); $p = 0.08$; $I^2 = 27.5\%$.

Stem cells



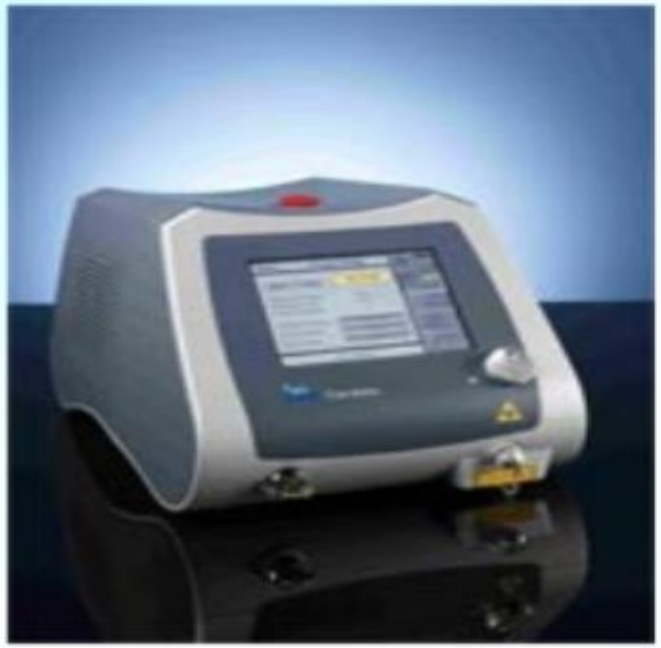


- Sphincter saving.
- Minor adverse effects.
- Promising results; particularly in Crohn's disease.
- No fancy technology involved.

- Long term follow up ??
- No standardized technique.
- Lack of adequate evidence regarding optimal SC origin, culturing, dosing, mode of delivery, site & frequency of injection.

FiLaC ™ (Fistula laser Closure)

FiLaC (Fistula Laser Closure)

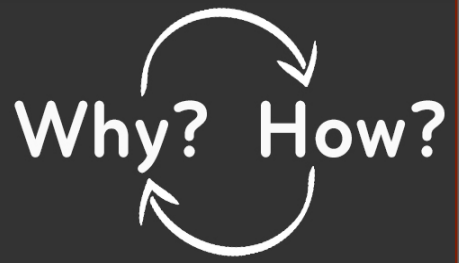


Diode Laser, 1470 nm

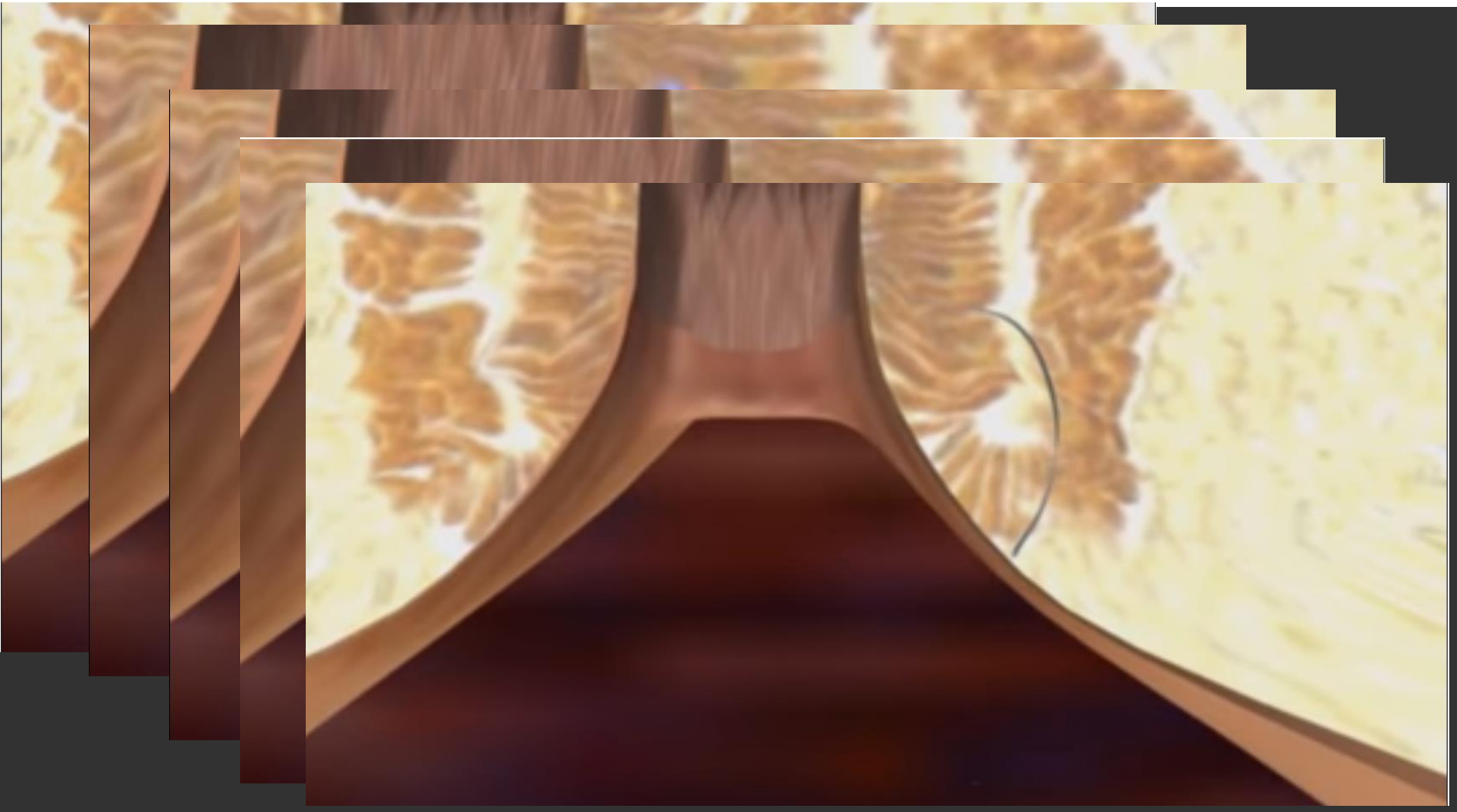
Radial Fiber: acting a 360°

FiLaC ™ (Fistula laser Closure)

1. Shrinkage and denaturation effect confined to the lumen.
2. Easily controllable depending on energy, wave length and duration.
3. Hence, reproducible.



FiLaC ™ (Technique)



Pull out at a speed of **1 mm/ second**

FiLaC ™ (Results)

Number of patients	35
Gender (M:F)	20:15
Age (years)	48 (27–76)
Type of fistula	
Intersphincteric	8 (23)
Low trans-sphincteric	8 (23)
Mid	12 (34)
High	6 (17)
Suprasphincteric	1 (3)
Multiple fistulous tracks	3
Previous fistula surgery	25
Previous draining (loose) seton	16
Operative time (min)	20 (6–35)

Results	*n* (%)
Cured	25 (71.4)
Failed	8 (22.8)
Recurrence	2 (5.8)

- 35 patients, different types, including 25 recurrence.
- 71.4 % healing rate.
- 20 minutes operative time.
- Median follow up 20 month (3-35)
- No incontinence.
- No intra operative complications.

Laser ablation for fistula (Results)

Variable	*Result*
Median age, years (range)	41 (23–83)
Male/female	37/13
Types of fistulas	
Intersphincteric	10
Transsphincteric	34
High transsphincteric	6
Median energy consumption, joules (range)	1,176 (320–6,843)
Intersphincteric	705 (320–1,780)
Transsphincteric	1,190 (720–3,450)
High transsphincteric	2,360 (1,174–6,843
Median number of days required to return to normal activities (range)	3 (2–22)
Median follow-up, months (range)	12 (2–18)
Success rate (%)	41/50 (82%)

- 50 patients (40 Trans-sphincteric).
- 82 % healing rate.
- Median follow up 12 month (2-18)
- No incontinence.
- No complications.

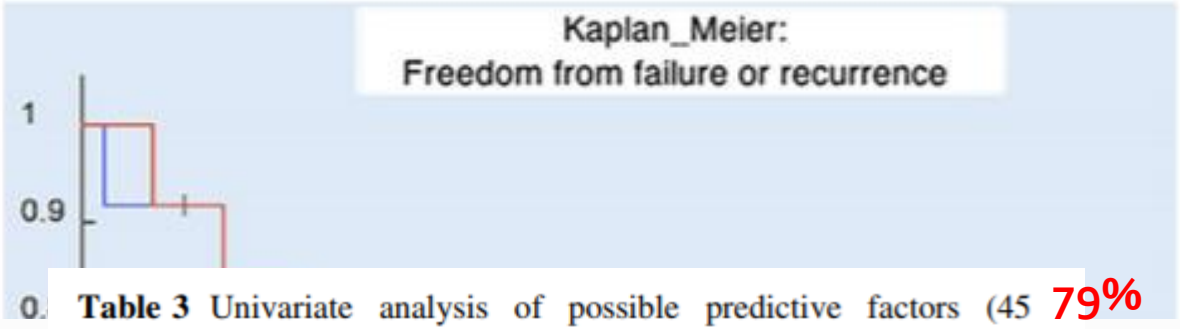
FiLaC ™ (Results)

Table 1 Patient and fistula characteristics

Number of patients	45
Gender (M, F)	21:24
Age (years)	46 (18–78)
Previous fistula surgery	35 (78)
Previous loose seton	24 (53)
Type of fistula	
Intersphincteric	7 (15)
Low transsphincteric	7 (15)
Mid transsphincteric	19 (42)
High transsphincteric	10 (22)
Suprasphincteric	2 (4)

Table 2 Results of the FiLaC™ at a median follow-up of 30 (range 6–46) months

Results	*n* (%)
Cured	32 (71.1)
Failed	11 (24.4)
Recurrence	2 (4.4)



79%

Table 3 Univariate analysis of possible predictive factors (45 patients)

Factor	Success ($n = 32$)	Failure ($n = 13$)	*p*
Sex			0.6[a]
Males ($n = 21$)	15 (71.4 %)	10 (28.6 %)	
Females ($n = 24$)	17 (70.8 %)	7 (29.2 %)	
Age (years)			
Median (range)	45 (18–76)	47 (27–78)	0.45[b]
Previous surgery for fistula			0.6[b]
Yes ($n = 35$)	25 (71.4 %)	10 (28.6 %)	
No ($n = 10$)	7 (70 %)	3 (30 %)	
Seton use prior to FiLaC™			0.20[c]
Yes ($n = 24$)	19 (79 %)	5 (21 %)	
No ($n = 21$)	13 (62 %)	8 (38 %)	

[a] Mann–Whitney *U* test
[b] Fisher's exact test
[c] Chi-square test

Non significant

62%

Median 30 months (6-46) follow up

Trend ??

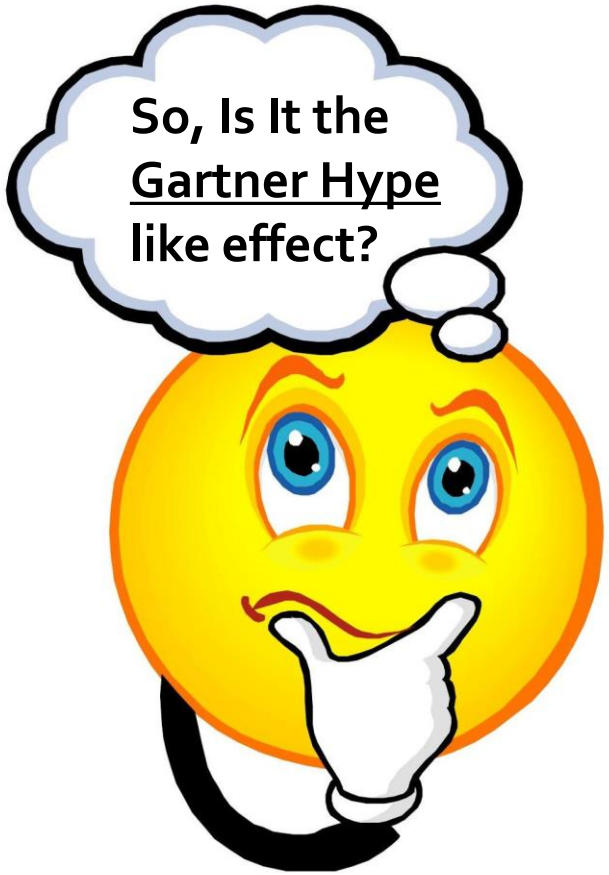
Fig. 2 Kaplan–Meier analysis of freedom from failure/recurrence

Laser ablation for fistula (Results)

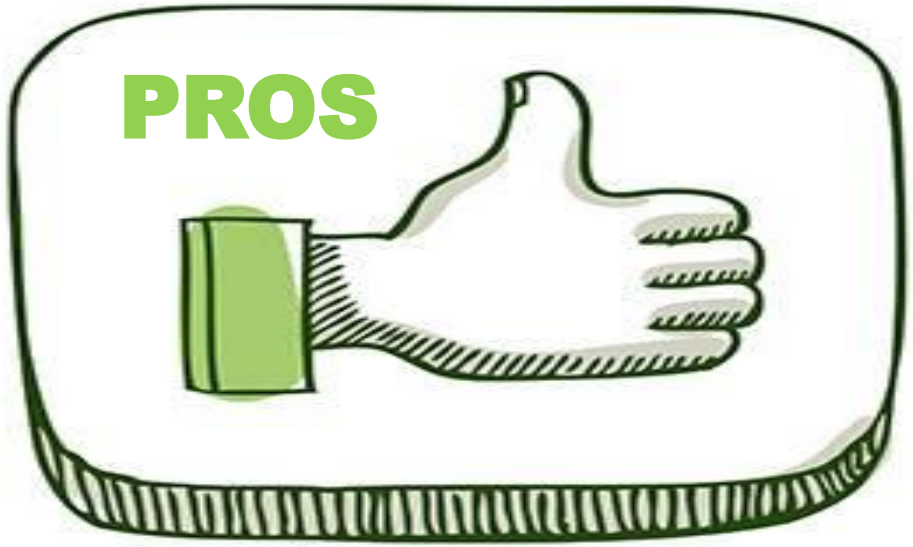
Characteristic	Data						
Study	No. of patients	Recurrent perianal fistula patients, n (%)	Treatment type	Energy, watts	Morbidity, n (%)	Follow-up period, mean, mo	Success rate, %
Wilhelm[1]	11	NA	FiLaC + conventional closure of the internal orifice	13	0	7.4	82
Giamundo et al[4]	35	25 (71)	FiLaC + loose seton as a bridge to laser therapy in some patients	10–13	17 (49)	20	71
Oztürk et al[2]	45	NA	FiLaC + loose seton as a bridge to laser therapy in some patients	15	0	12	82
Giamundo et al[3]	50	35 (78)	FiLaC + loose seton as a bridge to laser therapy in some patients	12	NA	30	71
Wilhelm et al[20]	117	16 (14)	FiLaC + external and internal orifices were excised, followed by the preparation of a flap + loose seton as a bridge to laser therapy in some patients	13	3 (3)	25	64
Present study	103	53 (52)	FiLaC only	12	0	28	40

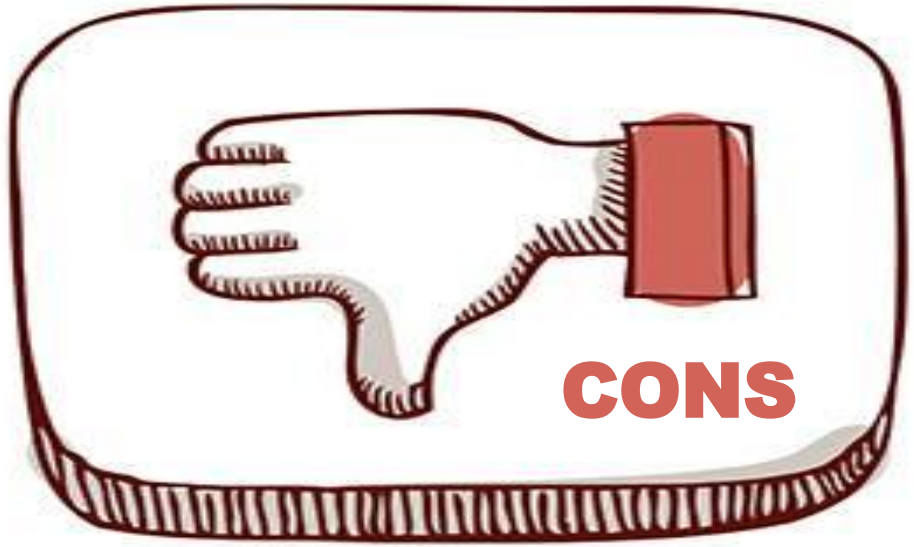
NA = not available; FiLaC = fistula-tract laser closure.

Laser ablation for fistula (Results)



Laser ablation





- Sphincter saving.
- No adverse effects.
- Promising results.
- Early return to activity.
- Easy to learn and reproduce.

- Relatively expensive.
- No RCTs.
- Current evidence on cryptoglandular fistulas, No available evidence on Crohn's.
- ? Early to judge.

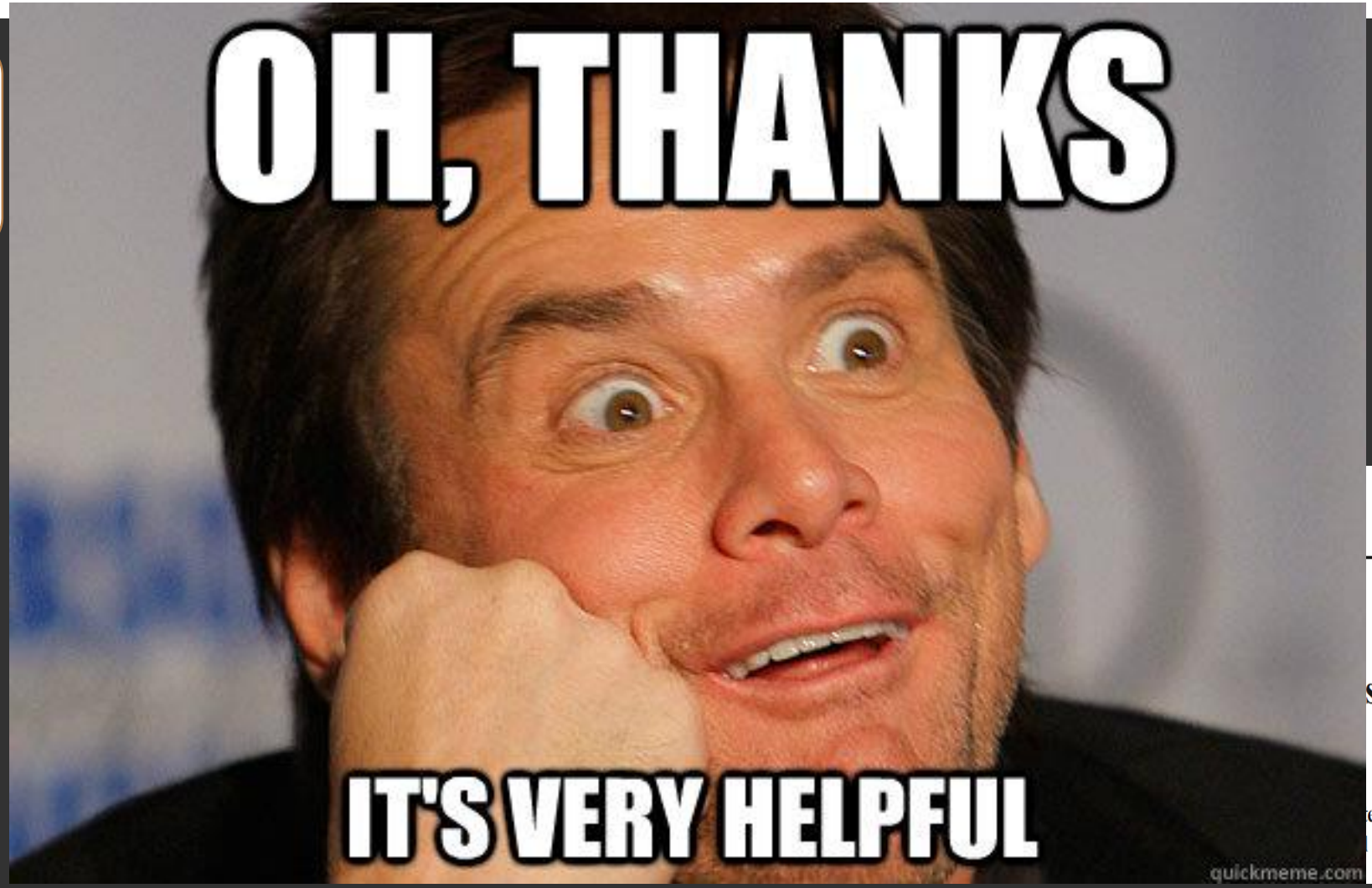
So, what do the available guidelines say?

So, what do the guidelines say?

VAAFT

Stem cells

Laser



Deutsche Gesellschaft für Koloproktologie

2017

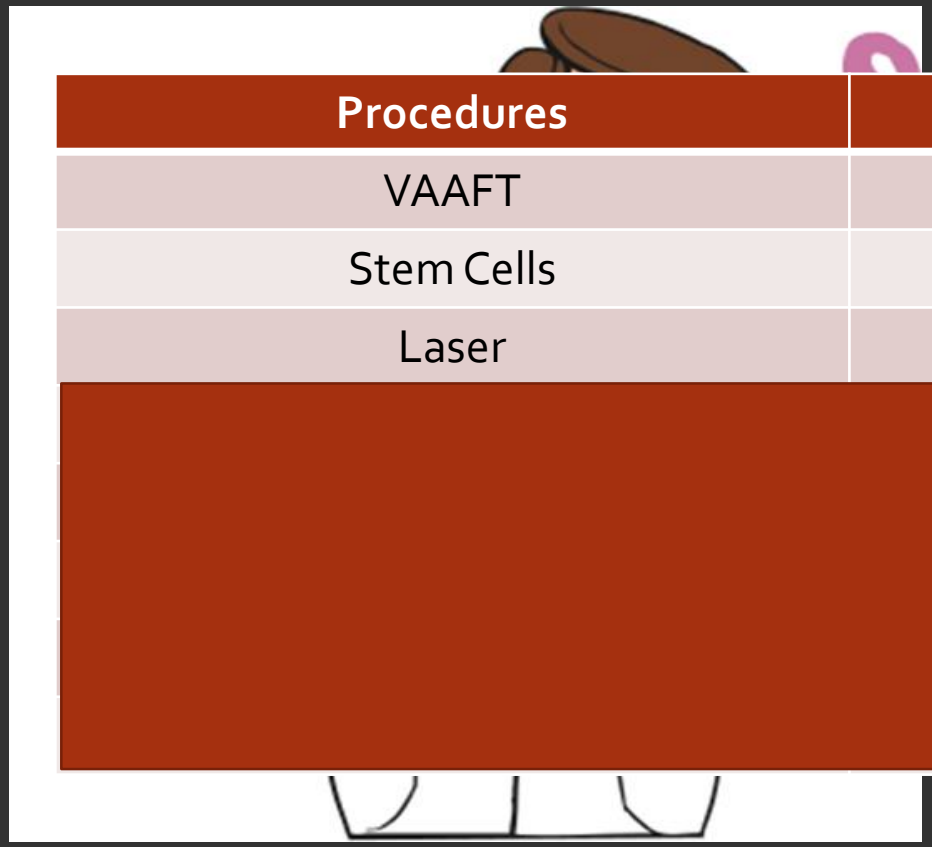
CrossMark

stula (second

efan Post[5] ·
Strittmatter[9]

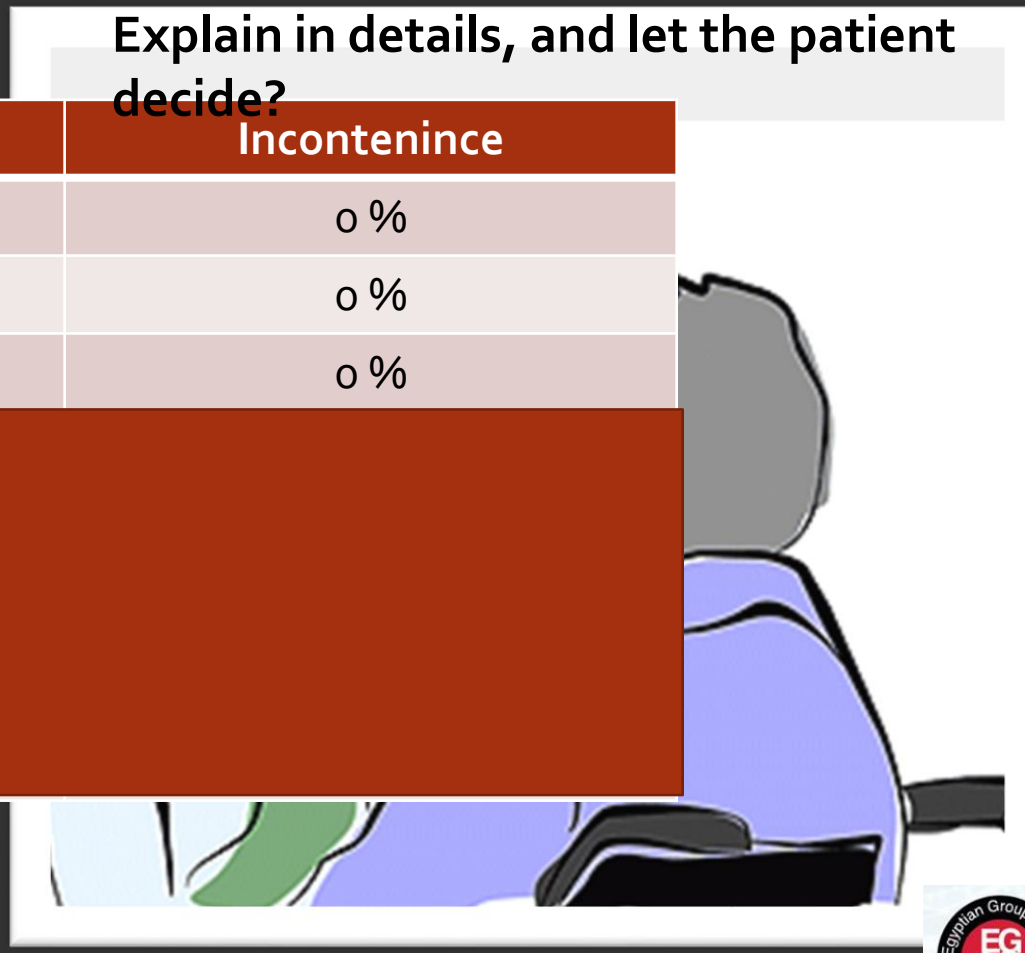
Egyptian Group of Colon & Rectal Surgeons
EGCRS

So, How to decide?



Explain in details, and let the patient decide?

Procedures	Healing	Incontenince
VAAFT	70-77%	0 %
Stem Cells	27-88%	0 %
Laser	40-82%	0 %



Summary

- *The more you cut, the better healing rates, but the more complication and incontinence.*
- *Emerging procedures lean towards sphincter preservation at the expense of healing rates.*
- *VAAFT, Stem cells and Laser showed very promising healing rates and very low complications.*
- *Time will prove/disprove the Gartner hype cycle like effect.*
- *Still no helpful guideline recommendation or consensus regarding these procedures.*
- *Treatment should be tailored according to weighing benefits and risks for every patient, explain in details and let the patient decide.*

Thank You


MANSOURA UNIVERSITY
جامعة المنصورة


Egyptian Group of Colon & Rectal Surgeons
EGRCS