

# Perianalfistel: Minimal invasive Therapiekonzepte



**PD Dr. Dimitri Christoforidis**

EBSQ Coloproctology

Lugano, Suisse

35° Schweizerische Koloproktologie Tagung

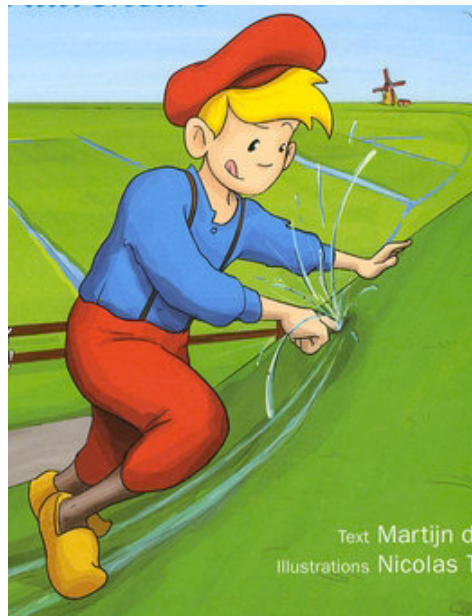
# Sphincter sparing techniques

- 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)

# My presentation

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# PLUGS

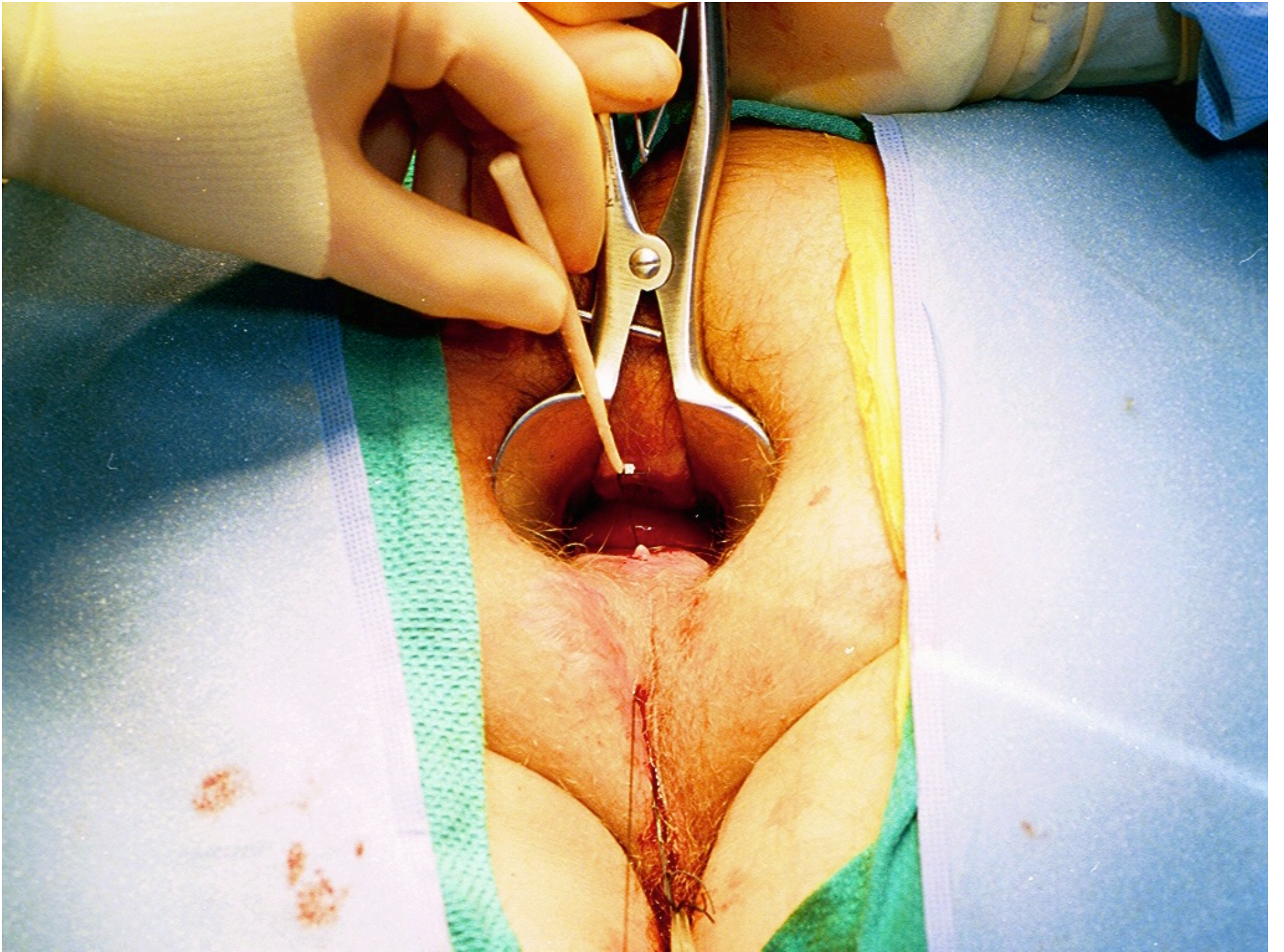


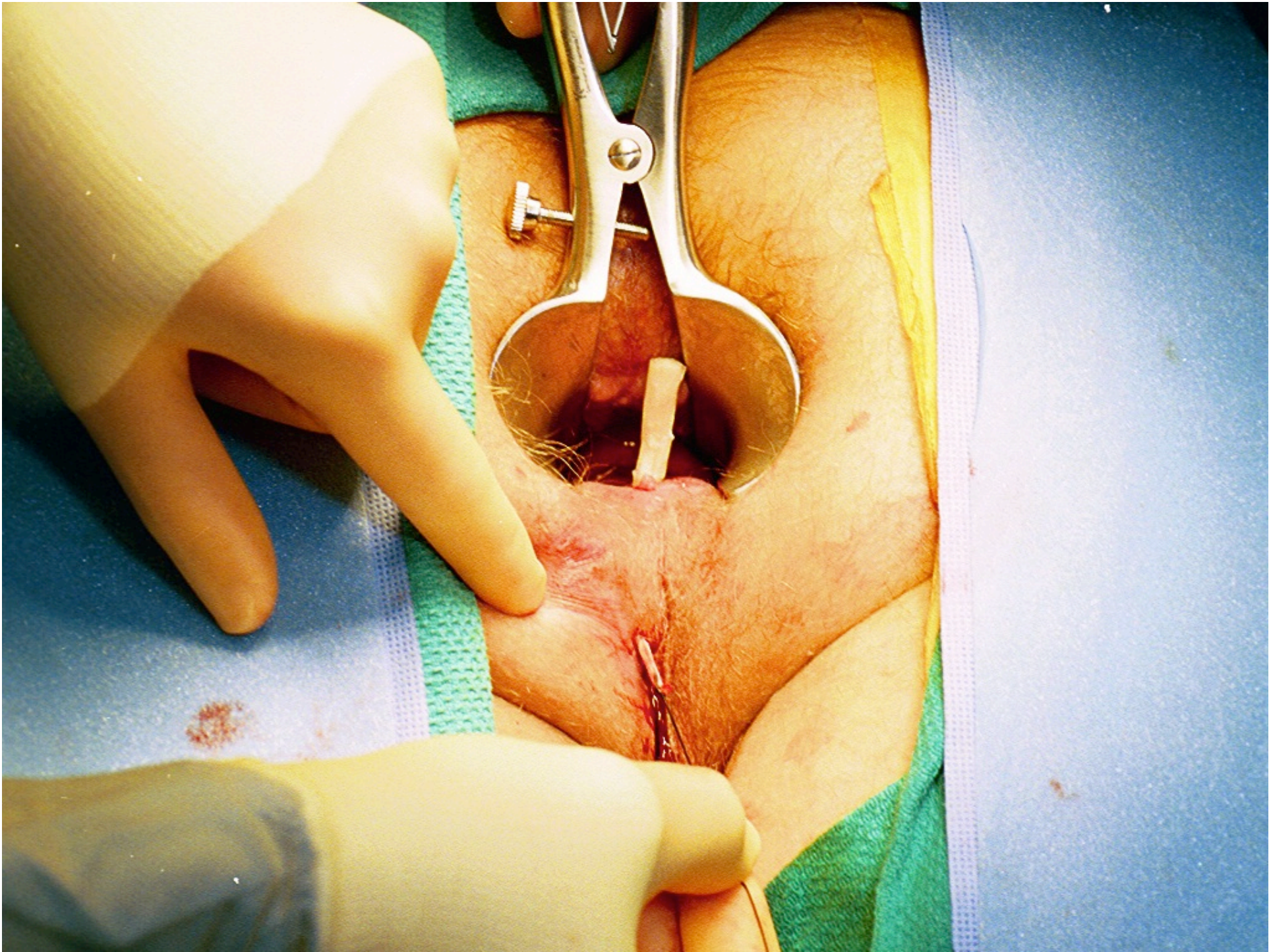
## Surgisis® Anal Fistula Plug™ (AFP)

*Armstrong DN et al.,*

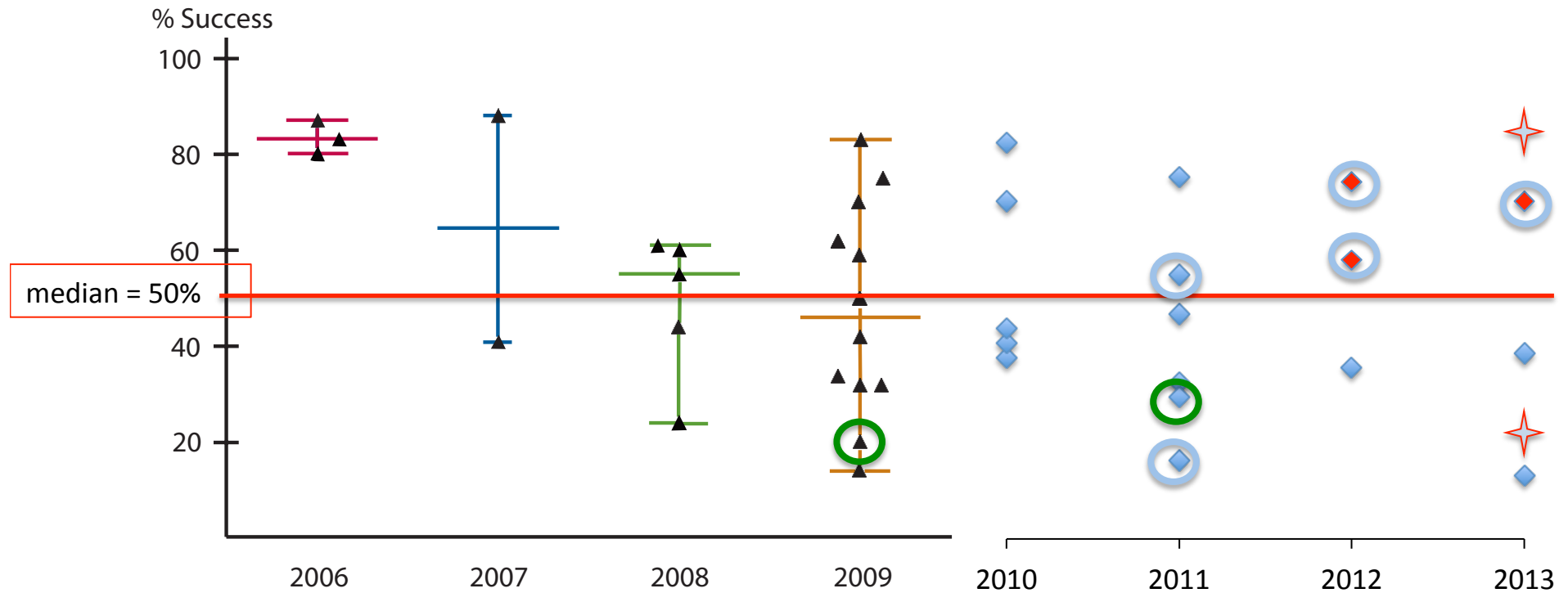
*Georgia Colon & Rectal Surgical Clinic, Atlanta*

- n=15 cg fistulas
  - f-up 3 mo; success: 87% *Johnson et al. DCR 2006*
- n=46 cg fistulas
  - f-up 12 mo; success: 83% *Champagne et al. DCR 2006*
- n=20 fistules Crohn
  - f-up 10 mo; success: 80% *O'Connor et al. DCR 2006*





# Published results



**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.

○ = RCT

○ = non-Cook plug

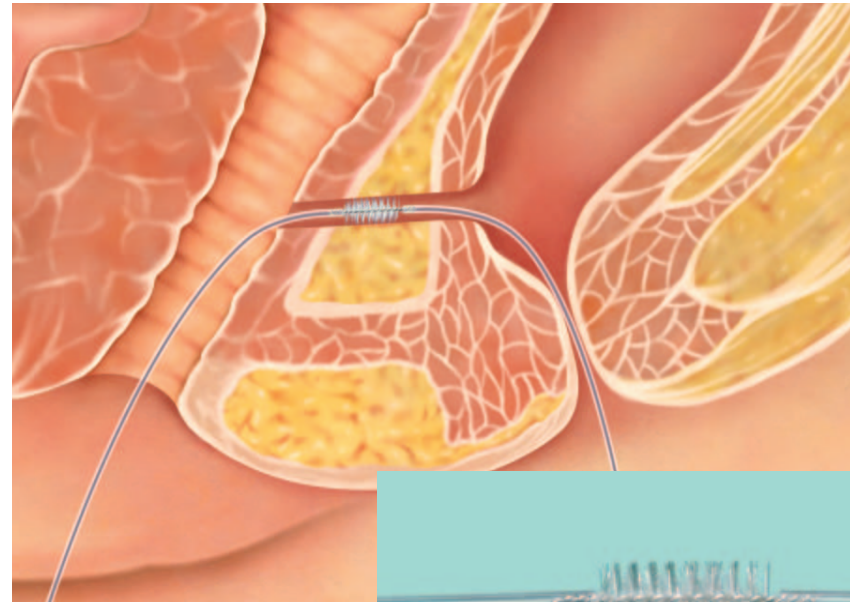
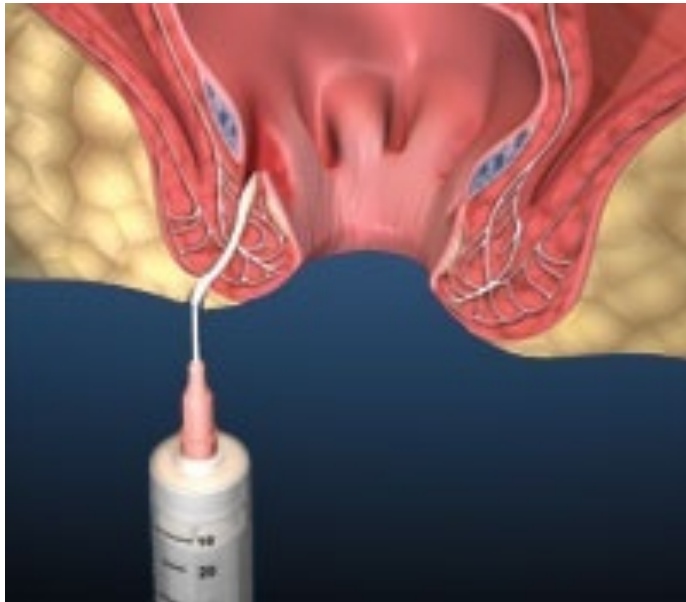


# Why such disparity in results?

1. learning curve/ technique?
2. quality of studies / f-up?
3. patient selection?

# preparation of the fistula track

- pre-op seton: non significant trend for better outcomes<sup>1-3</sup>
- no fistulectomy recommended (avoid enlargement of track)

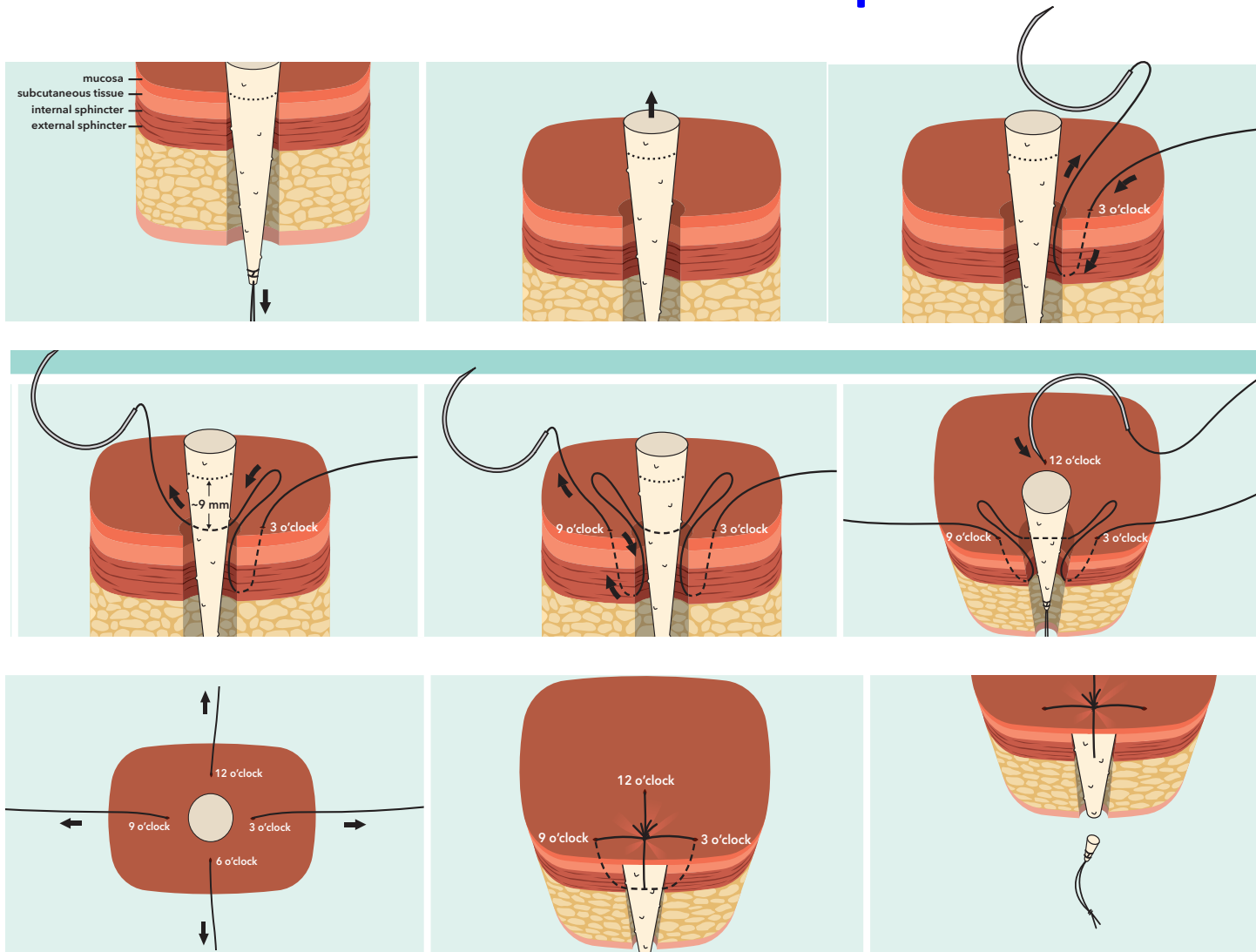


<sup>1</sup>Champagne LC DCR 2006

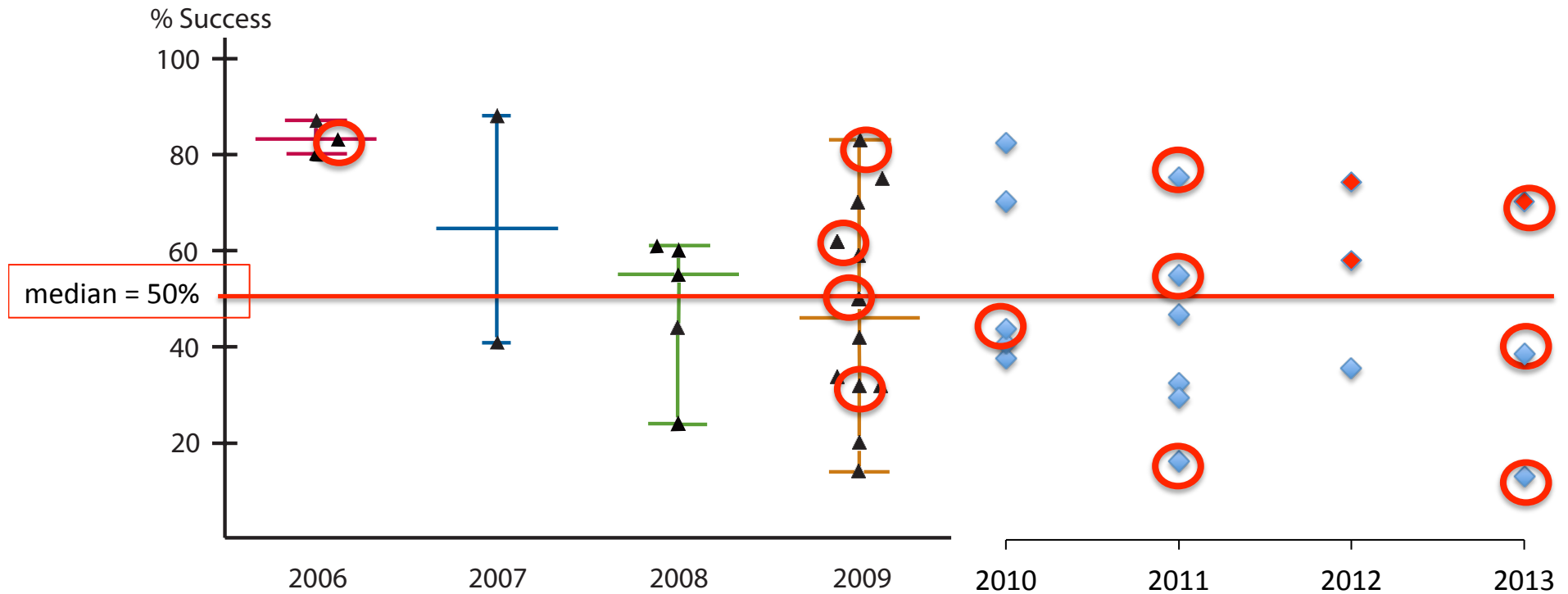
<sup>2</sup>Echenique I et al, Bol Assoc Med PR 2008

<sup>2</sup>Christoforidis D et al, DCR 2008

# fixation technique



## Results in studies with median f-up $\geq 12$ mois



**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*

# RCTs: plug vs. ERAF



## Randomized clinical trial

### Randomized clinical trial of anal fistula plug *versus* endorectal advancement flap for the treatment of high cryptoglandular fistula *in ano*

H. Ortiz, J. Marzo, M. A. Ciga, F. Oteiza, P. Armendáriz and M. de Miguel

Unit of Coloproctology, Department of Surgery, Hospital Virgen del Camino, Universidad Pública de Navarra, Pamplona, Spain  
Correspondence to: Dr H. Ortiz, C/Irunlarrea 4, 31008 Pamplona, Navarra, Spain (e-mail: hortizhu@cfnavarra.es)



## ORIGINAL CONTRIBUTION

### The Anal Fistula Plug Treatment Compared With the Mucosal Advancement Flap for Cryptoglandular High Transsphincteric Perianal Fistula: A Double-Blinded Multicenter Randomized Trial

Paul J. van Koperen, M.D., Ph.D.<sup>1</sup> • Willem A. Bemelman, M.D., Ph.D.<sup>1</sup>  
Michael F. Gerhards, M.D., Ph.D.<sup>2</sup> • Lucas W. M. Janssen, M.D., Ph.D.<sup>3</sup>  
Willem F. van Tets, M.D., Ph.D.<sup>4</sup> • Annette D. van Dalsen, M.D.<sup>5</sup>  
J. Frederik M. Slors, M.D., Ph.D.<sup>1†</sup>

- 1 Department of Surgery, Academic Medical Center, Amsterdam, the Netherlands
- 2 Department of Surgery, Onze Lieve Vrouwe Gasthuis, Amsterdam, the Netherlands
- 3 Department of Surgery, Zuwe Hofpoort Hospital, Woerden, the Netherlands
- 4 Department of Surgery, Sint Lucas Andreas Hospital, Amsterdam, the Netherlands
- 5 Department of Surgery, Isala Clinics, Zwolle, the Netherlands



*Ortiz H et al, Br J Surg 2009*

- cg, unique track high TS; +/- 50% recurrent
- 1 centre
- 43 patients randomized=> 32 received allocated treatment
- f-up: 1 year
- % success: **plug = 3/15** vs. ERAF 14/16 (p<0.0001)
  - study arrested prematurely
- critiques:
  - sample size calculation: **plug 65% vs. ERAF 82.5%**
  - interim analysis not planned
  - 3/12 plug failures = extrusions
  - centre with a long tradition and expertise with ERAF



*van Koperen C et al, DCR 2011*

- cg fistulas, mid/highTS
- multicentric double-blind
- 60 patients randomized (in OR)
- f-up: 11 months
  
- % success: **plug 29%** vs. ERAF 48% (p=0.126)
- no difference in continence, QoL, or post-op pain (COREFO, Wexner, Vaizey, SF-36)
  
- critiques:
  - sample size calculation: 2x23, **plug 80% vs ERAF 40%**
  - low ERAF success rates (?)

# Patient selection: Predictive factors of failure

- smoking<sup>1,4,6</sup> (retro, UV+MV)
- diabetes<sup>1</sup> (retro, UV)
- short fistula track (<4cm)<sup>3</sup> (retro, UV)
- 2° opening distant<sup>6</sup> (retro, MV)
- high TS (vs. low TS)<sup>2</sup> (retro, MV)
- posterior fistula (vs. other)<sup>4</sup> (retro, MV)
- anterior fistula\* (retro, MV)
- previous plug failure<sup>4,5</sup> (retro, MV)

<sup>1</sup>Schwander T et al, DCR 2009

<sup>2</sup>Christoforidis D et al, DCR 2008

<sup>3</sup>McGee MF et al, DCR 2010

<sup>4</sup>Ellis CN et al, DCR 2010

<sup>5</sup>Ky A et al, DCR 2008

<sup>6</sup>Han JG et al, DCR 2011

\*unpublished paper



## plug in Crohn's disease?

- Systematic review and data pooling
- anocutaneous fistulas only
- 20 studies (8 retro, 10 pro, 2 RCTs)
- F-up 3-48 months
- % success:
  - Crohn's:                   23/42       (54.8%)
  - non-Crohn's :           265/488   (54.3%)

# *The Next Generation*

*of Anal Fistula Repair*



polyglycolic acid : trimethylene carbonate  
(=Maxon®)

PERFORMANCE by design

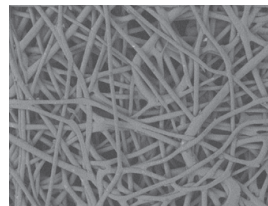
# COOK vs. GORE

- Cook: 12 patients, 16 insertions
- Gore: 10 patients, 11 insertions

Porous 3D matrix facilitates tissue generation and healing



Porcine Submucosa Plug Surface (50x)



GORE BIO-A® Fistula Plug Surface (50x)

## Anal Fistula Closure: Cook vs. Gore

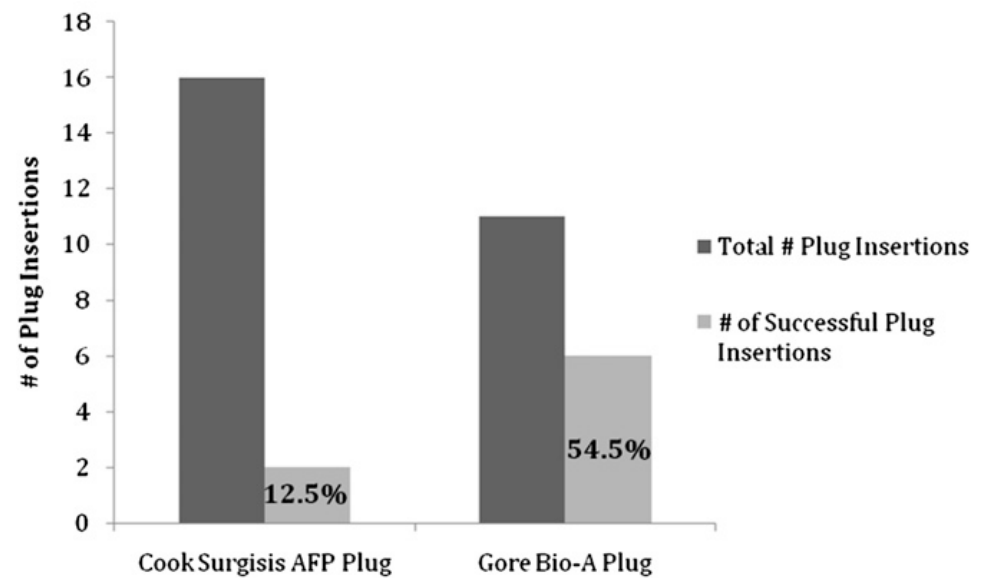


FIG. 1. Overall procedural success rate for Cook and Gore fistula plugs. Closure rates were higher using the Gore Bio-A® plug.

# Published results with the Gore™ plug

author	Journal	n patients	months f-up	% success (par patient)
Ratto C	Colorectal Dis 2012	11	5	8/11 (73%)
Favreau-Weltzer C	Colorectal Dis 2012	9		1/9 (11%)
de la Portilla F	DCR 2011	19	12	3/19 (16%)
Buchberg B	Am Surg 2010	10	2	6/10 (60%)
Omer A	Ger Med Sci 2012	40	6	22/40 (58%)
<b><i>total</i></b>		<b>89</b>		<b>40/89 (45%)</b>

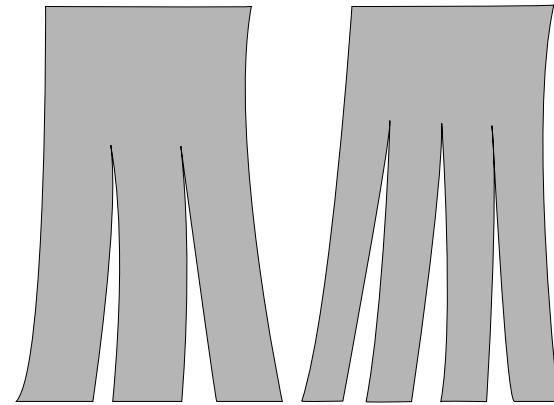
# German study

- 40 patients
- 3 centres, 5 surgeons (5-12 cases/surgeon)
- hospital duration: 4.9 +/-1.9 days
- oral preparation of the colon
  
- success: 22/40 (57.5%)
  - variation by surgeon: 0-75%
  - NPT ou « Kosmonautenkost » vs. normal nutrition :  
16/22 (73%) vs. 7/18 (39%)

# The « chinese » plug

- Acellular dermal matrix
- same insertion technique
- 30 patients with cg fistula
  - mean op duration
  - f-up:?
  - mean healing time: 10 days
  - success rate.

100%



## Long-term Outcomes of Human Acellular Dermal Matrix Plug in Closure of Complex Anal Fistulas With a Single Tract

Jia Gang Han, M.D. • Zhen Jun Wang, M.D. • Bao Cheng Zhao, M.D.  
Yi Zheng, M.D. • Bo Zhao, M.D. • Bing Qiang Yi, M.D. • Xin Qing Yang, M.D.

Department of General Surgery, Beijing Chaoyang Hospital, Capital Medical University, Beijing, People's Republic of China

- prospective database 2007-2010
- 114 patients with cg fistula
- oral colonic prep, abttt 24 h, 4 weeks rest
- follow-up 20 months
- success rate: 54%
- risk factors for failure (multivariate analysis)
  - smoking
  - long distance 2° opening – anal verge
  - « non-expert surgeon »\*

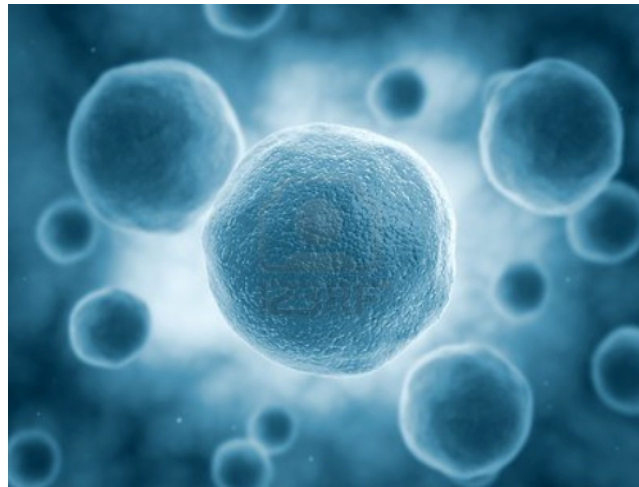
\*1 « expert surgeon » treated 18/114, 2 colorectal but non-expert treated 96/114 patients

# PLUG - CONCLUSIONS

- easy to do
- variable success rate – disappointing (<50%)
- new plugs do not seem to be any better
- may be worth trying once



stem cells



## Expanded adult stem cells (eASCs) (obtained by liposuction)

- closure of 1° opening, intra fistular injection
- RCT (Madrid)
- n= 49 (cg = 35; Crohn's = 14)
- no complications

	healing at 8 weeks	healing at 1 year	healing at final f-up (median 38mo)
fibrine glue	3/25 (12%)	3/25 (12%)	2/25 (8%)
fibrine glue+ eASCs*	17/24 (71%)	15/24 (63%)	7/21 (33%)

P < 0.001

*\*repeat injection of 60 million eASCs at 8 weeks if fistula persisted*

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

# Expanded adult stem cells (eASCs) (obtained by liposuction)

- Multicenter RCT (19) single blind
- n=200

	healing at 6 mo (pioneer centre)	healing at 1 year (all centres)
fibrin glue	18 %	37 %
fibrin glue + eASCs*	83 %	52 %
eASCs alone*	55 %	57 %

*\*repeat injection of 60 million eASCs at 8 weeks if fistula persisted*

- main author has licence agreement with Cellerix SA

# Mesenchymal stroma cells (eMSC) (obtained by medullary aspiration)

## *iv administration*<sup>1</sup>

- clinical response after 6 weeks in 3/9 patients (-  $\geq 70$  CDAI)
- no complications

## *intra-fistular administration*<sup>2</sup>

- 10 Crohn's patients with refractory fistulas
- ciprofloxacin, ceftriaxone, metronidazole for 2 weeks pre-op
- injection every 4 weeks (median: 4x/patient)
- 7/10: complete healing, 3/10: improvement (f-up 12 months)
- (!) additional systemic effect :
  - significant reduction of CDI and PADI ( $p < 0.01$ )
  - sustained increase in number of regulatory T cells (mucosal and circulating)

<sup>1</sup>Duijvestein M et al (Leiden), Gut 2010

<sup>2</sup>Ciccocioppo R et al (Pavia), Gut 2011

# Conclusions stem cells

- disappointing results with eASC
- very preliminary results (promising?) with eMSCs for Crohn's fistulas

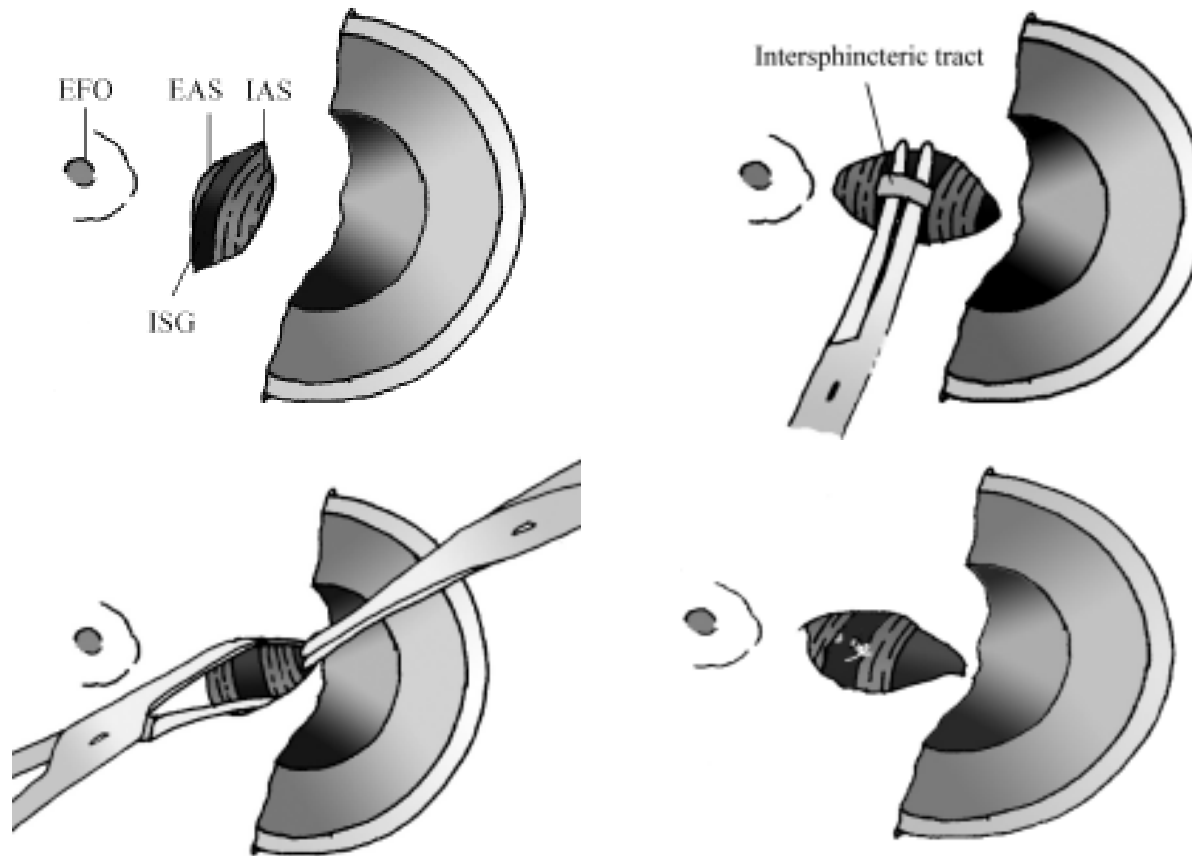
LIFT

(Ligation of Intersphincteric Fistula Track)

# 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*

# new technique?

## *Goligher (Leeds, 1967)*

- fistulotomy of the IS for drainage and facilitated access for fistulectomy
  - healing in 25/25 patients
  - incontinence: 8 gas, 4 liq stool, 7 solid stool

## *Matos (St. Mark's, 1993)*

- intersphincteric approach for fistulectomy and closure of the IS from the inside
  - healing: 7/13
  - incontinence: 3 gas, 1 liquid



# Résultats LIFT littérature

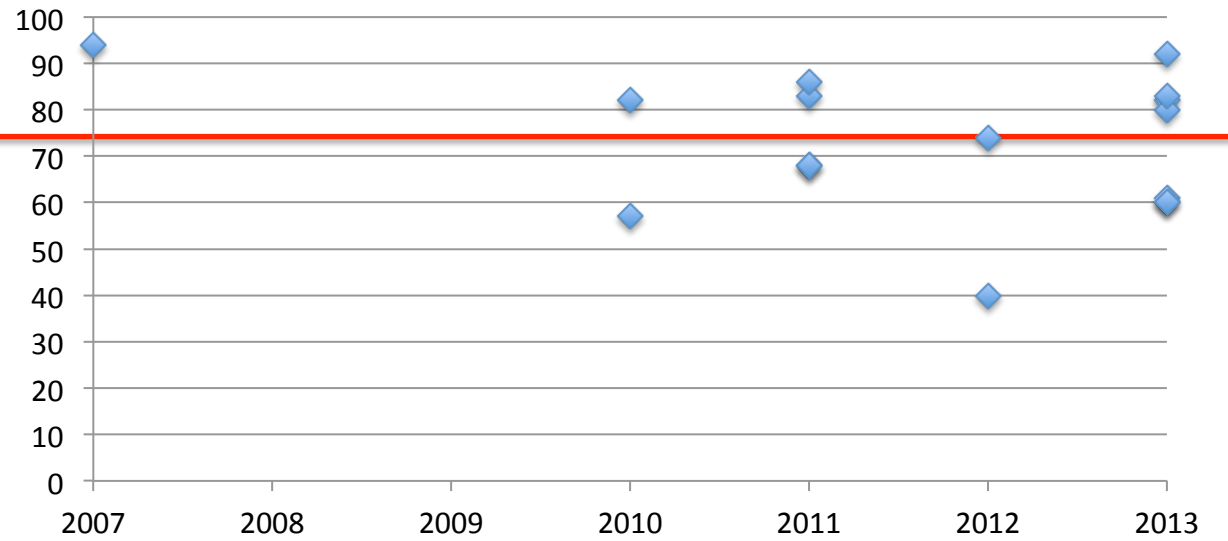
Author	journal	n patients	fup (mo)	success rate	2° success rate	incontinence
Rojanasakul A (Thailand)	J Med Ass Thai 2007	18	≤ 6	94%	94%	0
Shanwani A (Malaysia)	DCR 2010	45	9	82%	82%	0
Bleier J (Minneapolis)	DCR 2010	39	4 (35 pat)	57%	69%	0
Ooi K (Melbourne)	Colorectal Dis 2011	25	5	68%	82%	0
Sileri P (Rome)	Tech Coloproctol 2011	18	>4	83%	89%	0
Tan KK (Singapore)	DCR 2011	93	6	86%	93%	
Aboulian A (UCLA CA)	DCR 2011	25	6	68%	72%	0
Abcarian AM (Chicago)	DCR 2012	40	4	74%		0
Wallin UG (Minneapolis)	DCR 2102	93	19	40%	57%	CCF FI = 1
Liu WY (UCLA CA)	DCR 2013	38	26	61%		0
Chew MH (Sydney)	Int J Colorect Dis 2013	29	4	63%	88%	0
van Onkelen (Rotterdam)	Colorectal Dis 2013	22 (low TS)	19.5	82%	100%	unchanged
Campbell ML (Tampa FL)	Am Surg 2013	20	3	80%		0
Lehman JP (Sweden)	Colorectal Dis 2013	17 (rec)	13.5	60%		0
Sirikurnpiboon S (Thai)	WJ Gastroint Surg 2013	41		83%		
Mushaya C (Australia)	Am J Surg 2013 (RCT)	25	19	92%		0
<b>Yassin NA (St. Mark's)</b>	<b>Colorectal Dis 2013 (review)</b>	<b>498 (13)</b>	<b>4-19.5</b>	<b>71 % (40-95)</b>		<b>6% (minor)</b>
<b>Vergara F (Mexico)</b>	<b>W J Gastro 2013 (review)</b>	<b>592 (18)</b>		<b>75% (40-95)</b>		

# personal results

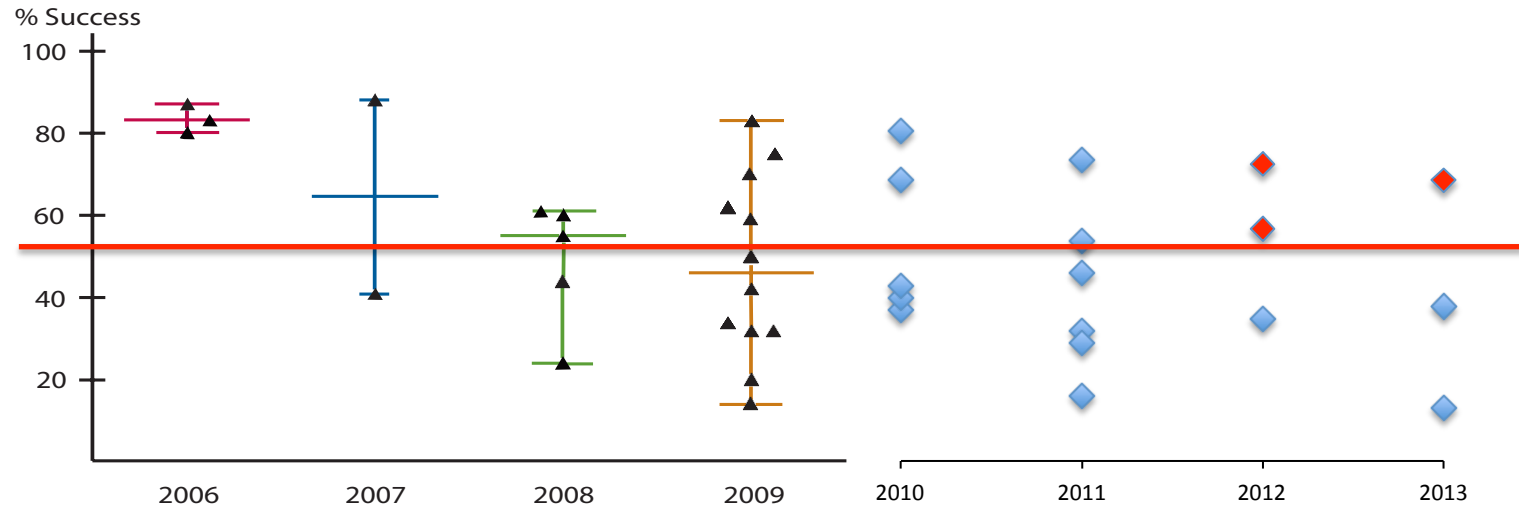
	CHUV	Lugano	total
n patients	12	13	25
median f-up	3 months	6 months	
1° success	5/12	5/13	10/25 (40%)
2° success	6/12	12/13	18/25 (72%)
incontinence	none	1 patient gas	

# Published results over time

LIFT:  
75%



plug:  
50%

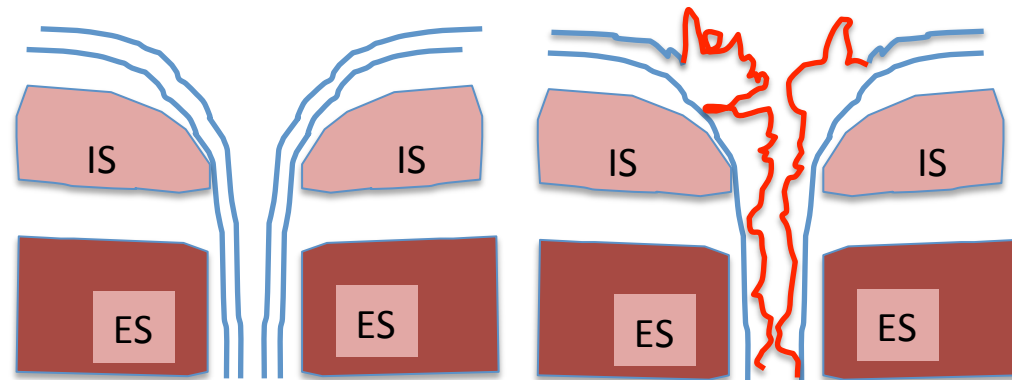
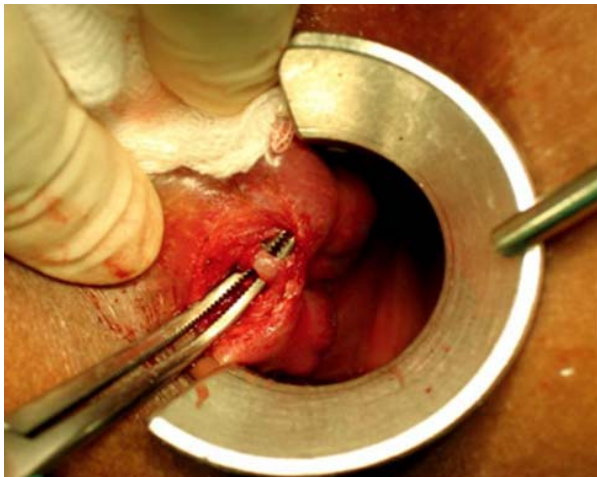


# LIFT in Crohn's patients

- 15 patients
- 8/12 patients healed at 12 months
- no FI
- lateral fistula > midline
- longer fistula > short

# risk factors for LIFT failure

- obesity<sup>1</sup> retro, UV
- long track<sup>2</sup> retro, UV
- previous failed fistula surgery<sup>3</sup> retro, UV



<sup>1</sup>Sirikurnpiboon S wt al., *W J Gastrointest Surg* 2013

<sup>2</sup>Liu WY et al., *DCR* 2013

<sup>3</sup>Abcarian AM et al., *DCR* 2012

## Variation 1: LIFT + ERAF

- 41 patients, high cg fistulas
  - LIFT then ERAF
  - 5 days bedrest, liquid diet, iv cefurx+ flagyl
  - f-up 15 months
- % success:
- I°: 21/41
  - II° (including fistulotomy for IS recurrence): 29/41 (71%)
- continence:
- FISI improved in 6, same in 34, worse in 1 patient

## Variation 2: LIFT « plus »

- retrospective study
  - 21 classic LIFT : debridement of fistula
  - 20 LIFT « plus »: fistulectomy of extrasphincteric part
- high TS fistulas
- % success:
  - LIFT: 17/21 (81%)
  - LIFT plus: 18/21 (85%)
- obesity = failure risk factor:
  - BMI group success: 22(3.9) vs. failure 30.5 (3.5),  $p < 0.001$

## Variation 3: LIFT + Surgisis mesh (BioLIFT)

- 31 patients (18 failed plugs\*, 4 Crohn's)
- LIFT, wide dissection of IS space
- fixation of a Surgisis mesh on the levators and ES overlapping the fistula site by 1-2 cm, partial closure of the incision
- follow-up 15 months (12-30)
- healing in 29/31 (94%)
  - 2 failures:
    - 1 IS fistula => fistulotomy (overall healing rate 97%)
    - 1 horseshoe fistula => cutting seton
- no worsening of continence

\* author's success rate with the plug: 81%

*Ellis N, DCR 2010*



# (BioLIFT)

- 13 patients with 16 fistules (4 recurrences post LIFT)
- f-up: 26 (12-51) weeks
- 1° success: 11/16 (69%)
- 2° success: 13/16 (81%)
- continence:
  - no patient
  - manometry rest/squeeze: no différence

## Variation 4: LIFT + plug

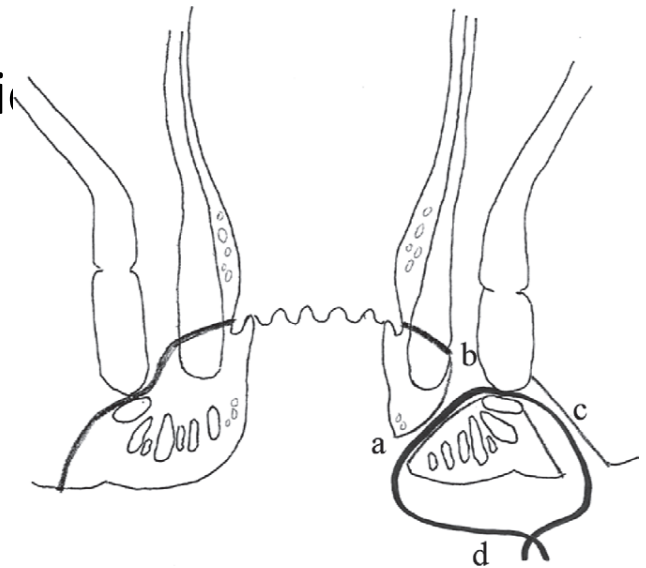
- 21 patients, TS fistulas
- LIFT + acellular dermal matrix plug
- median f-up 14 (12-15) months
- healing time 2° opening: 2 weeks; surgical incision: 4 weeks
- success rate: 20/21 (95%)
- 1/21 rare incontinence in gas
  
- 36 patients, f-up >3 months, success 94%
- RCT started: LIFT vs. LIFT + plug clinical trial number NCT01478139

*Han JG et al. (Beijing) Colorectal Dis 2013*

*Cui JJ, Han JG et al. (Beijing), Zhonghua Wei Chang Wai Ke Za Zhi. 2012*

## Variation 5: LIFT + seton

- 20 patients with complex cg fistulas
- LIFT
  - fistulectomy up to the ES
  - seton between fistulectomy and IS incision
  - removal of seton after 3 weeks
- f-up: 18 months
- 1° success rate : 19/20 (95%)
- no incontinence (FISI, mano)



# Conclusions LIFT

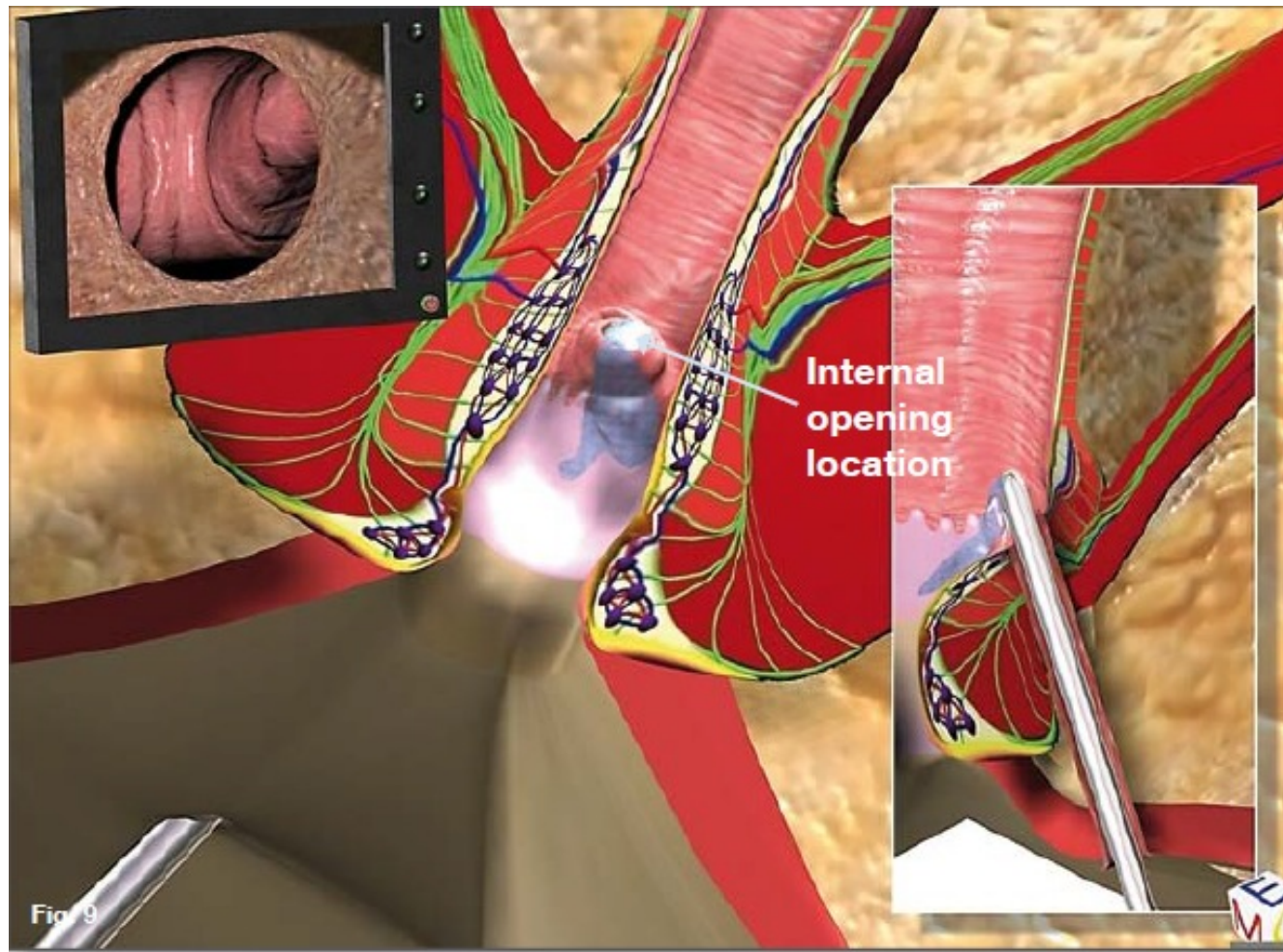
- promising technique
  - good healing rates
  - minimal effect on continence
  - failures
    - often IS => fistulotomy
    - no bridges burnt for other techniques (ERAF)
- many variations
- evidence still scarce

# VAAFT

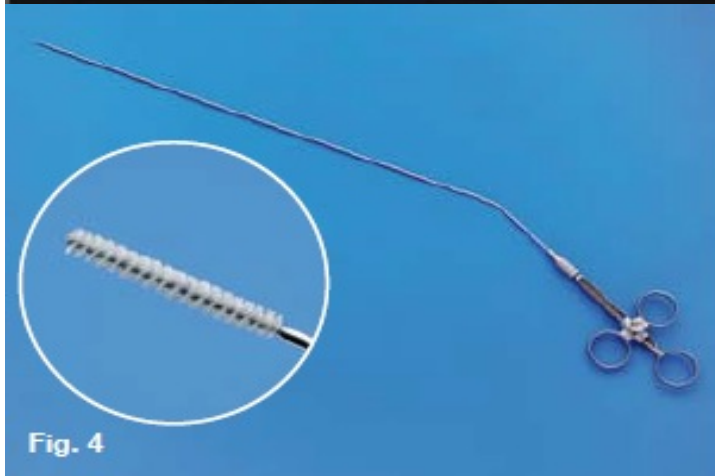
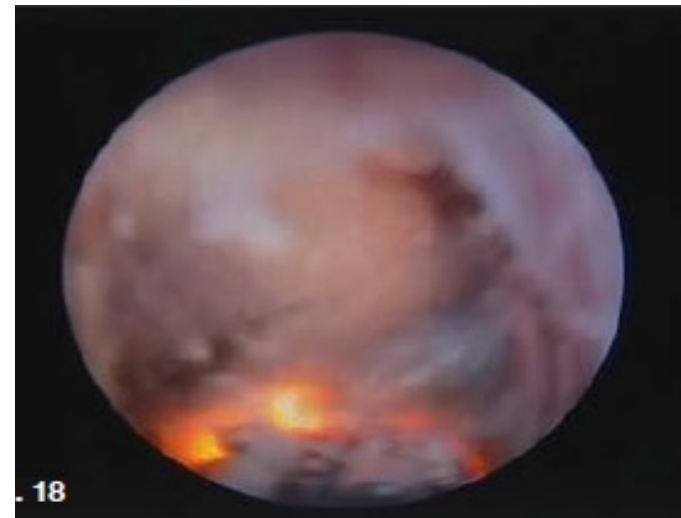
(Video Assisted Anal Fistula Treatment)



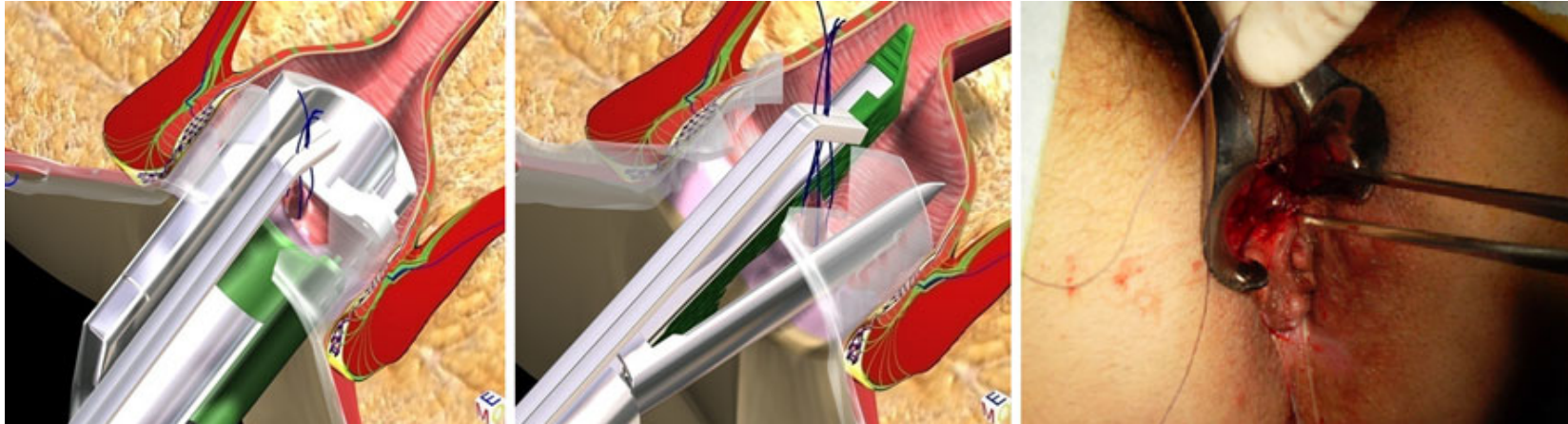
# Rigid fistuloscopy under perfusion of glycine-mannitol solution



# endoscopic cleansing of the fistula (fulguration, brushing, lavage)



closure of the 1° opening by stapling or ERAF



injection of cyanoacrylate glue under the closure





# Results VAAFT

- 203 patients
  - 149 previous surgery
- F-up at 2, 4, 6 and 12 months
- success at 1 year: 76%
  - fistula free after 2 years: 94%
- no de novo incontinence or continence worsening

*Meinero PC, Mori L Tech Coloproctol 2011  
Meinero P et al, oral poster ESCP Belgrade 2013*

## VAAFT + ERAF – Crohn's fistulas

- 13 patients with M.Crohn
- 2/13 VAAFT not completed
- 7/11 identification of blind sinus
- 9/11 healed
- no incontinence

# Conclusions VAAFT

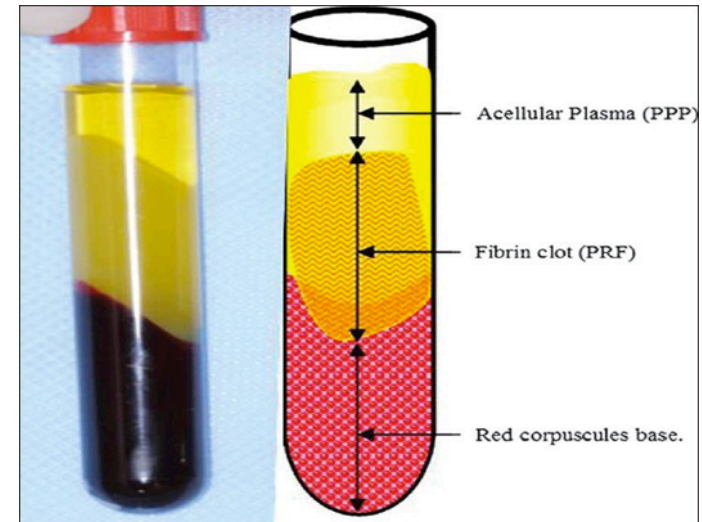
- promising technique
- treatment of fistula under vision
- advantage (?) in cases where:
  - 1° opening not identified
  - presence of blind sinus / active abcess
- costs (equipement, staplers)
- curently: one man show  
(= inventor with license agreement with Karl Storz)

# Platelet rich plasma



# Autologous Platelet Rich Plasma

- used in facial and esthetic surgery, stomatology, sports medicine
  - 10 patients, high TS fistulas
  - ERAF + PRP
  - f-up 26 months
  - success: 9/10
- 
- 27 patients, high TS fistulas
  - f-up median: 6.5 months
  - 1° success: 23/27 (85%)



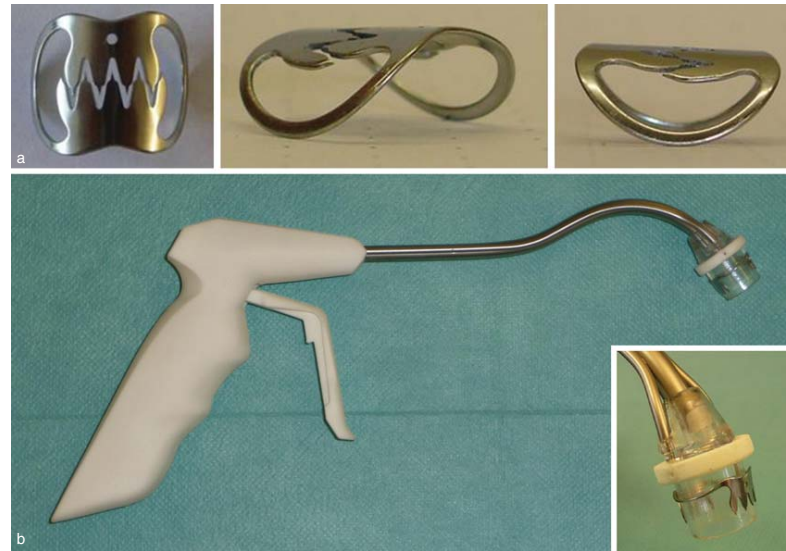
*van der Hagen SJ et al., Colorectal Dis 2011*

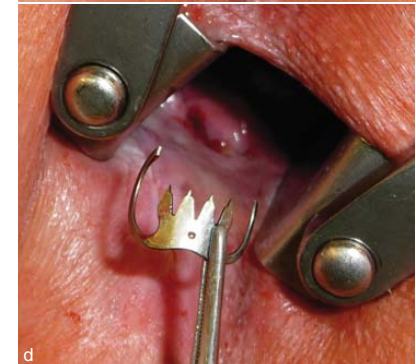
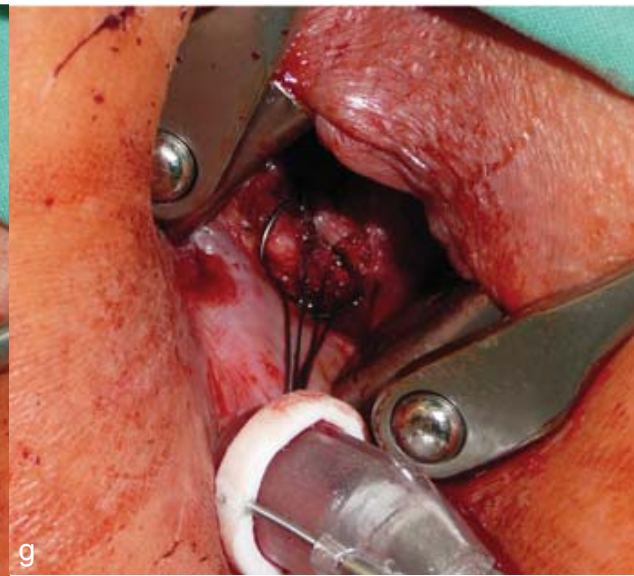
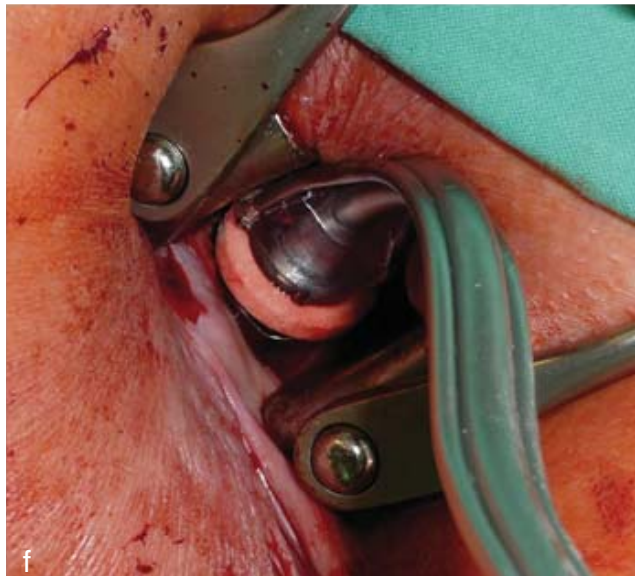
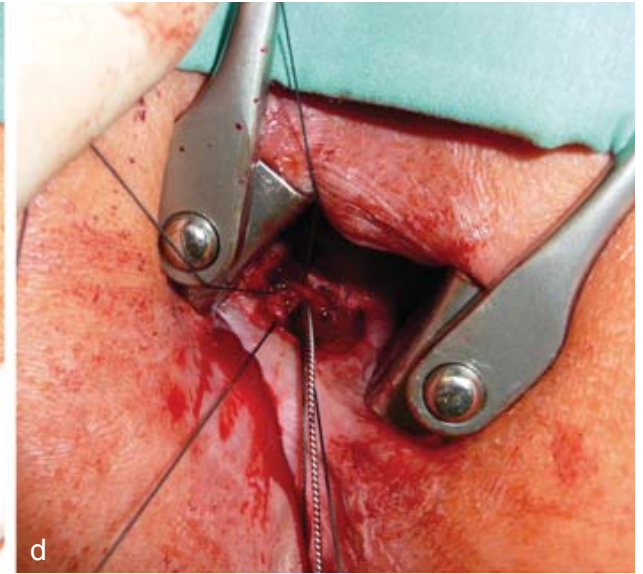
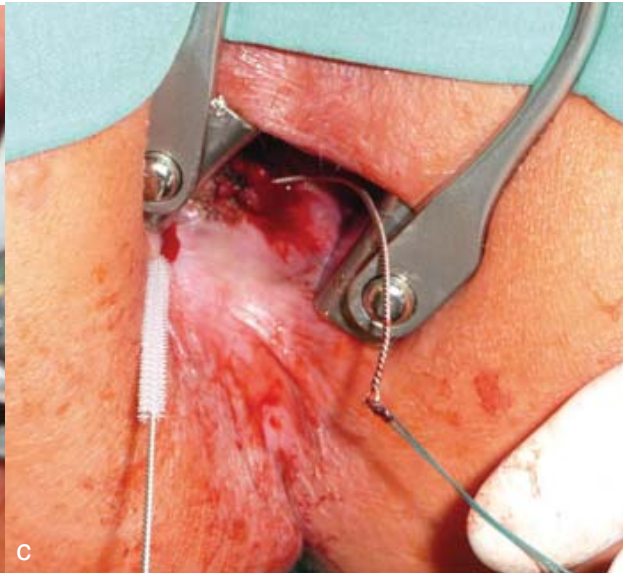
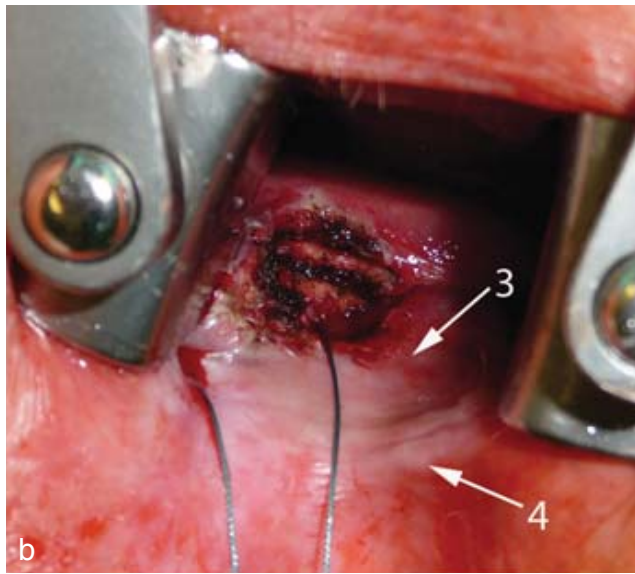
*Queralto M (Toulouse F) et al., oral poster ESCP Belgrade 2013*

# ERAF + platelet rich plasma

- 25 patients, cg fistula
- 3 hospitals, 6 years, retrospective study
- procedure:
  - excision of external opening, debridement of track
  - mucosal advancement flap
  - injection of autologous PRP (preparation in OR)
- f-up: 27 (4-7) months
  - recurrence (after 100% I° healing): 4/25
  - incontinence: 16% >6/24
- RCT started

# Over The Scope Clip







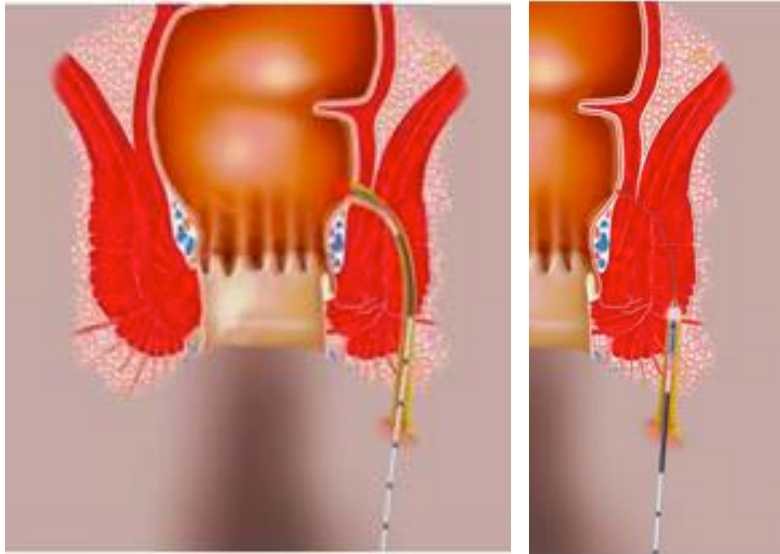
# OSTC for anal fistula

- 10 patients, high cg TS fistulas
- seton >6 weeks, full bowel prep, prophyl abx
- brushing of fistula track
- op time 30 (20-45) min
- no surg complications, pain « normal »
- f-up 6 months: success rate: 9/10
- clip loss: 1 at 3 days, 5 at 10-30 days, 1 removed

# FiLac (Fistula Laser closure)



# FiLac (Fistula Laser closure)



- 35 patients
- cg TS fistulas
- op duration: 20 (6-35) min
- follow-up 20 (3-36) months
- 25/35 (71%) success
- 8/35 never closed
- 2/35 reccurred at 3 and 6 months
- no incontinence

# FiLac

Author	n	type fistula	f-up (mo)	success	incontinence
Giamundo P Colorectal Dis 2013	35	TS	30 (3-36)	25/35 (71%)	0/35
Wilhelm A* Tech Coloproctol 2011	11	TS + IS	7.4 (2-11)	9/11 (82%)	1/11 (minor soiling)
Ozturk E OP ESCP 2013	42 (60?)	10 hTS 38 ITS 12 IS	12	85%	

\*closure of 1° opening with ERAF

# Conclusions anal fistulas

- several new techniques +/- sponsored by the industry
- plug: simple but disappointing
- LIFT, VAAFT: promising
- low quality literature, we need:
  - standardisation (technique, per-op care)
  - prospective registrees
  - RCTs

# personal algorithme

- endoanal US and seton for  $\geq 2$  months (mini-vessel loop)
- no bowel prep, prophylactic abx only
- technique:
  - 1° choice: LIFT (linear +/- simple track)
  - very high track, blind sinuses, active retroanal abscess: => fistulectomy + ERAF
  - multirecurrent fistulas: fistulotomy and primary shincter repair

*The  
End*