Swiss Coloproctology Study Group Bern 2019

Recurrent Anal Fistula

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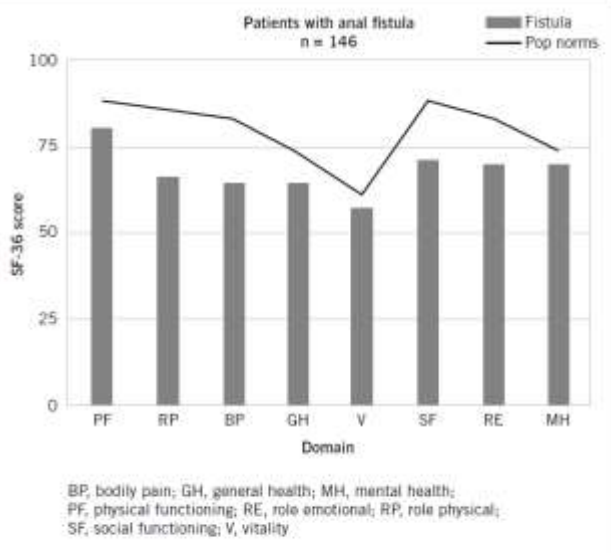
Imperial College London

St Mark's Hospital and Academic Institute

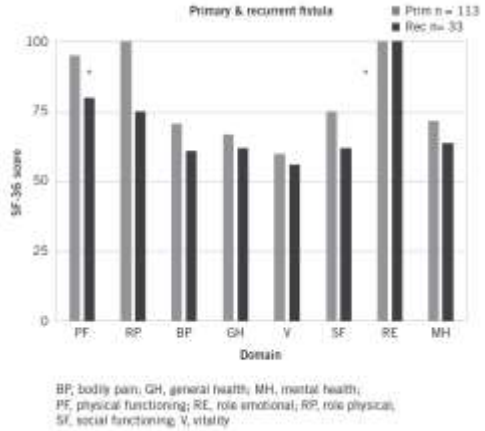
The questions I have to answer today

- What makes fistulas not heal
- Which is the best operation to achieve healing

Quality of life when you have an anal fistula



Having anal fistula has an effect of quality of life



It is worse when the fistula is recurrent

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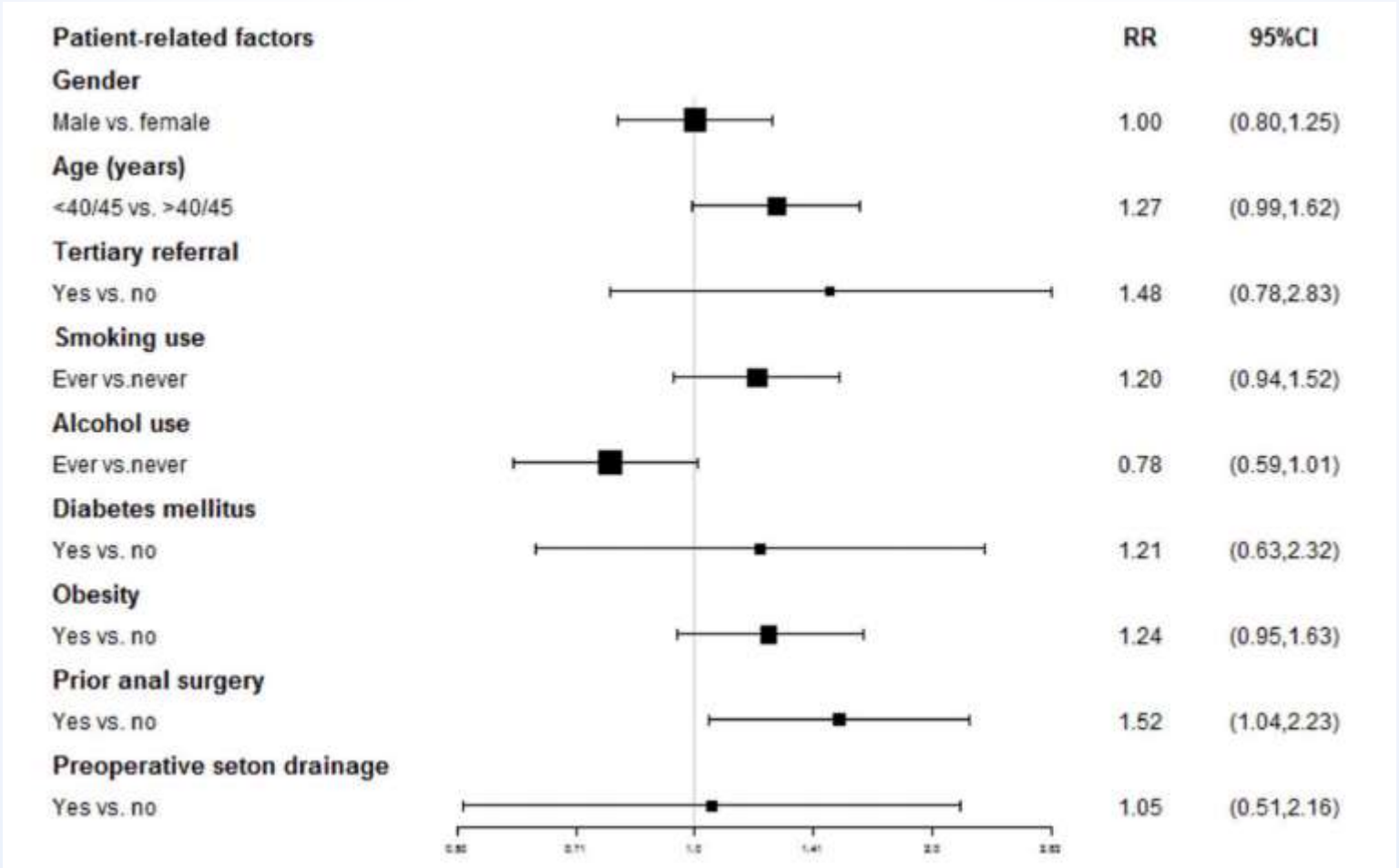
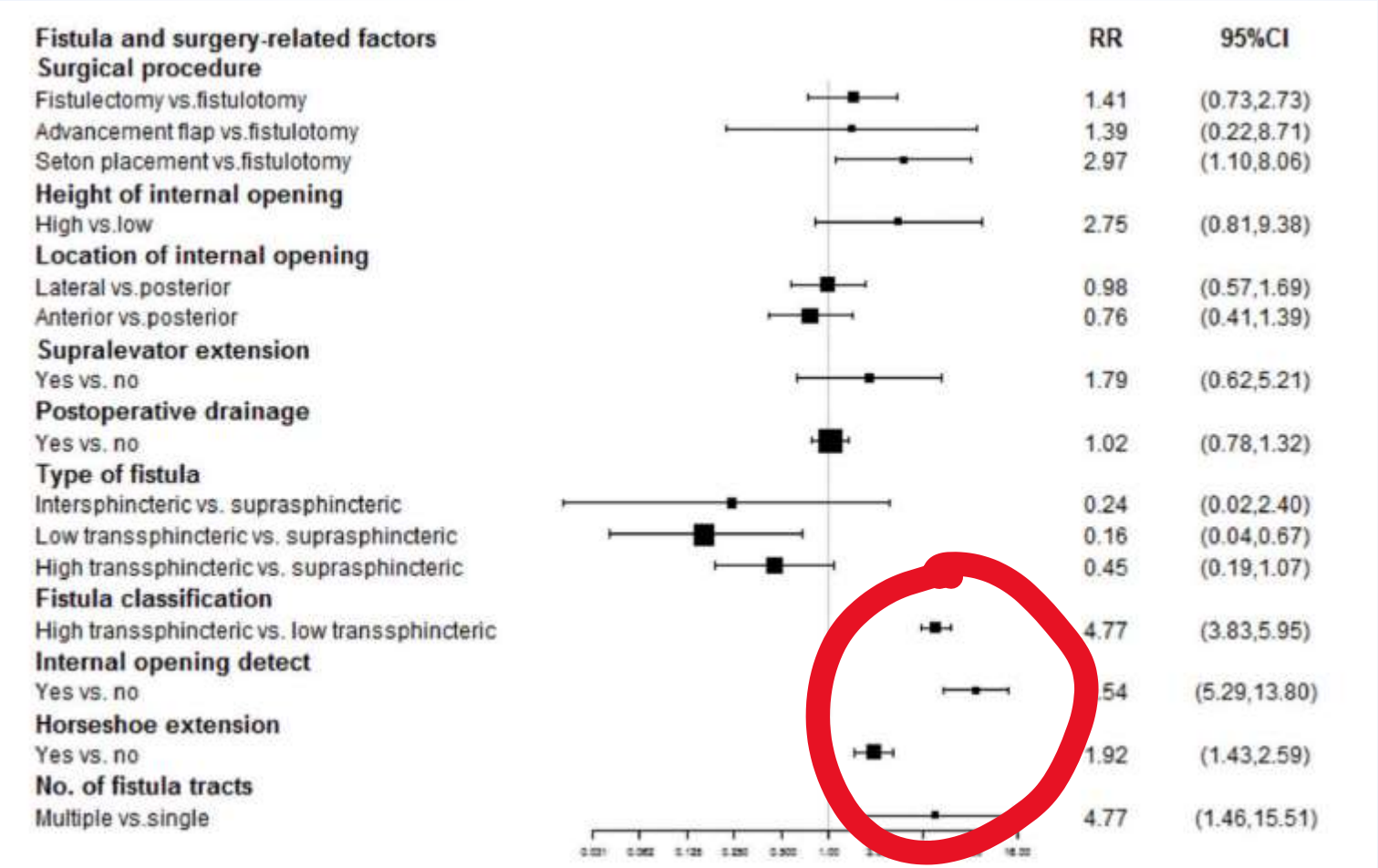

Patient-related factors
RR
95%CI
Gender
Male vs. female
1.00
(0.80,1.25)
Age (years)
<40/45 vs. >40/45
1.27
(0.99,1.62)
Tertiary referral
Yes vs. no
1.48
(0.78,2.83)
Smoking use
Ever vs.never
1.20
(0.94,1.52)
Alcohol use
Ever vs.never
0.78
(0.59,1.01)
Diabetes mellitus
Yes vs. no
1.21
(0.63,2.32)
Obesity
Yes vs. no
1.24
(0.95,1.63)
Prior anal surgery
Yes vs. no
1.52
(1.04,2.23)
Preoperative seton drainage
Yes vs. no
1.05
(0.51,2.16)

factors influencing healing

Variable	Category	No Cure N (%)	Cure N (%)	P-value
Operation type	Lay Open	5 (11%)	39 (89%)	**<0.001**
	Seton	20 (90%)	2 (9%)	
Type fistula tract	Intersphincteric	2 (25%)	6 (75%)	**0.04**
	Low TS	2 (13%)	13 (87%)	
	Mid/High TS	17 (49%)	18 (51%)	
Time to referral (grouped)	< 1 year	2 (12%)	15 (88%)	**0.03**
	1-2 years	5 (38%)	8 (62%)	
	> 2 years	15 (50%)	15 (50%)	

Fisher's exact test



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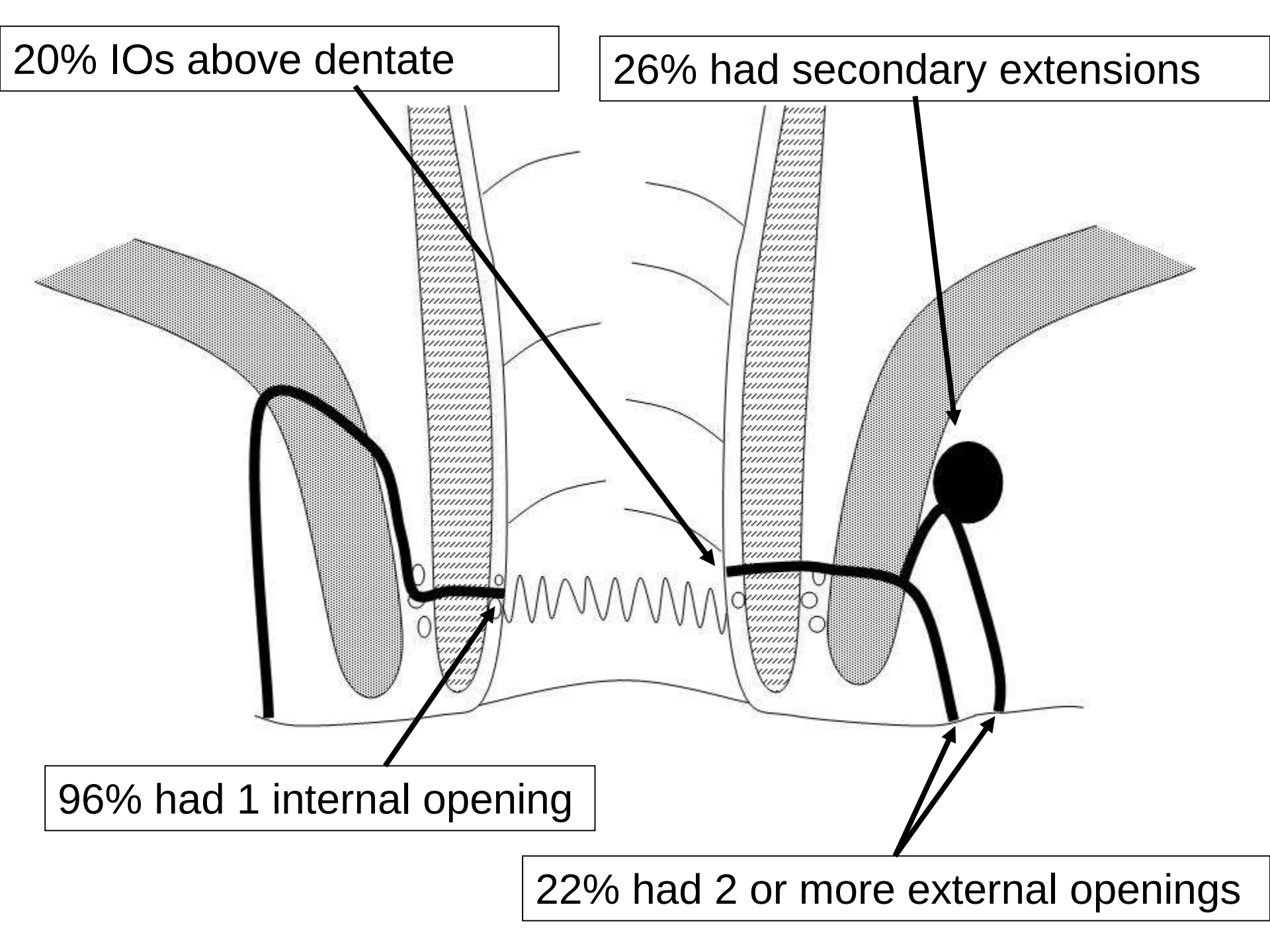
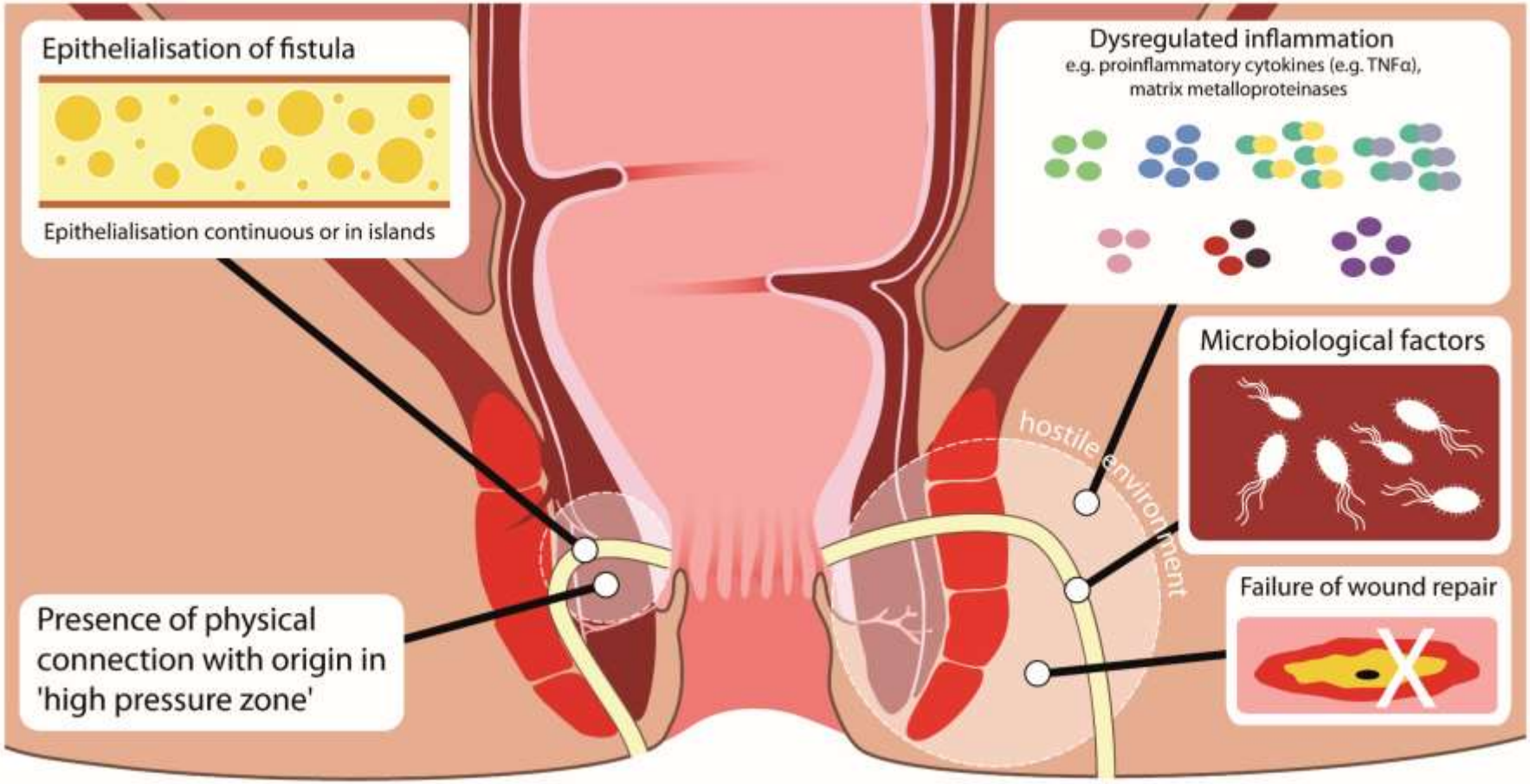

20% IOs above dentate
26% had secondary extensions
96% had 1 internal opening
22% had 2 or more external openings

But its not that simple



and unknown unknowns

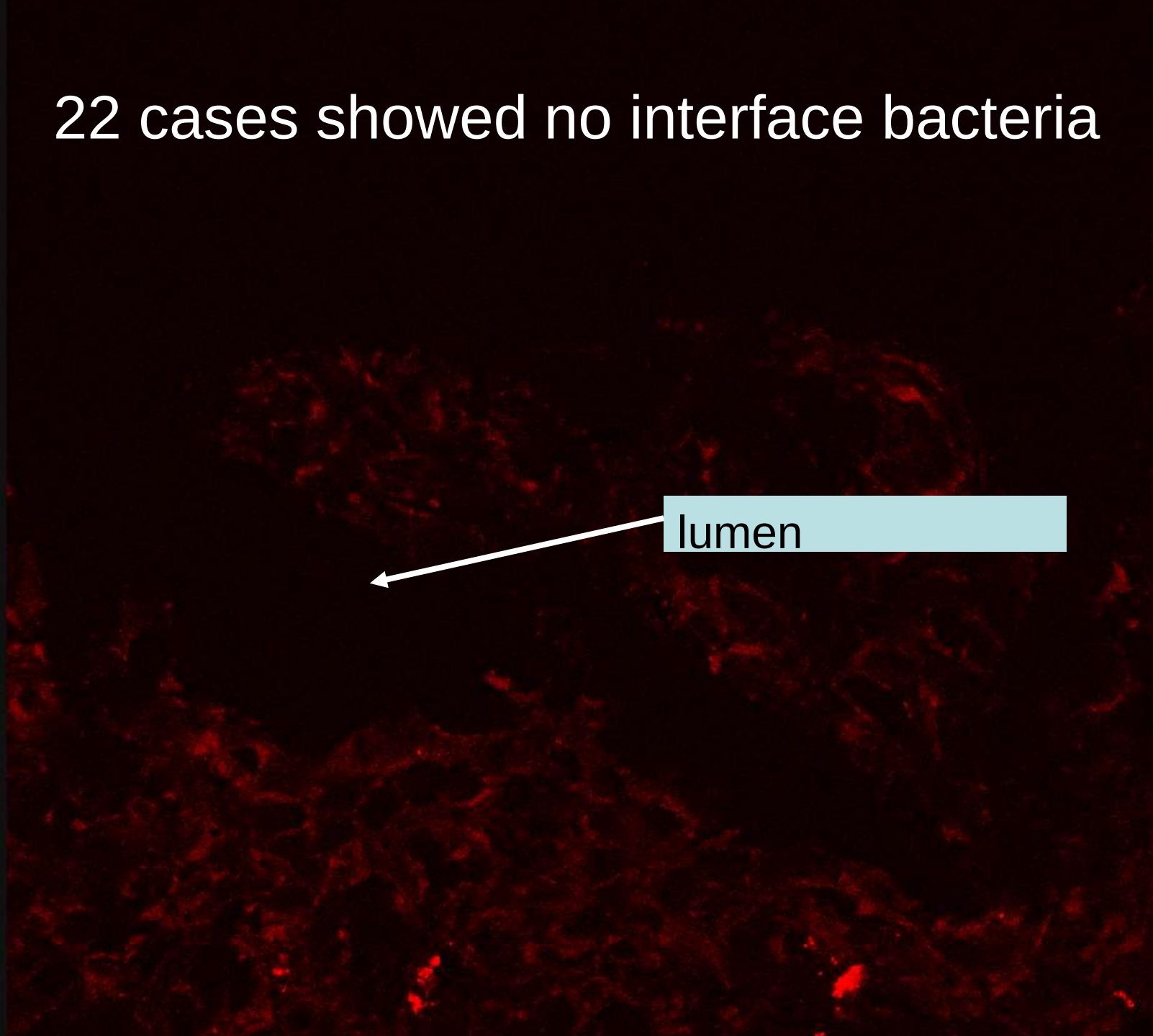
Tozer et al. ENiGMA. Gut 2018

Is infection the driving force behind fistula?

Examining idiopathic fistula tracts

- 23 tract samples
  - 1 with florid bacteria (+ve control, 43yo f IPD)
  - 22 with zero bacteria found (4 unwashed, 14 confirmed on Gram stain)

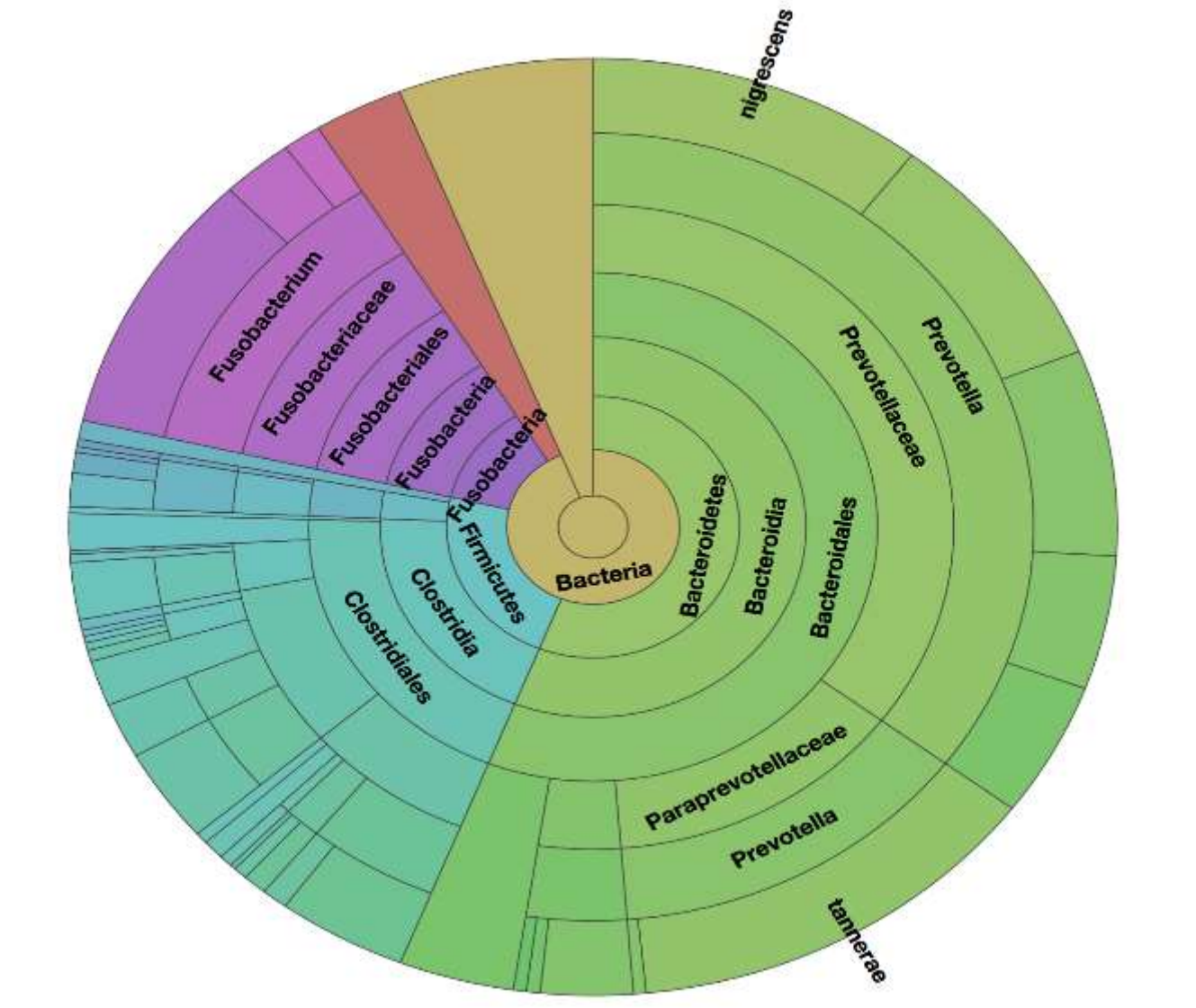
22 cases showed no interface bacteria



comment

- bugs are there but were missed for technical reasons
  - potentially absent biofilm/epithelium
  - because of wash in theatre/lab
- bugs do not drive anal fistula

16S Bacterial Metagenomics



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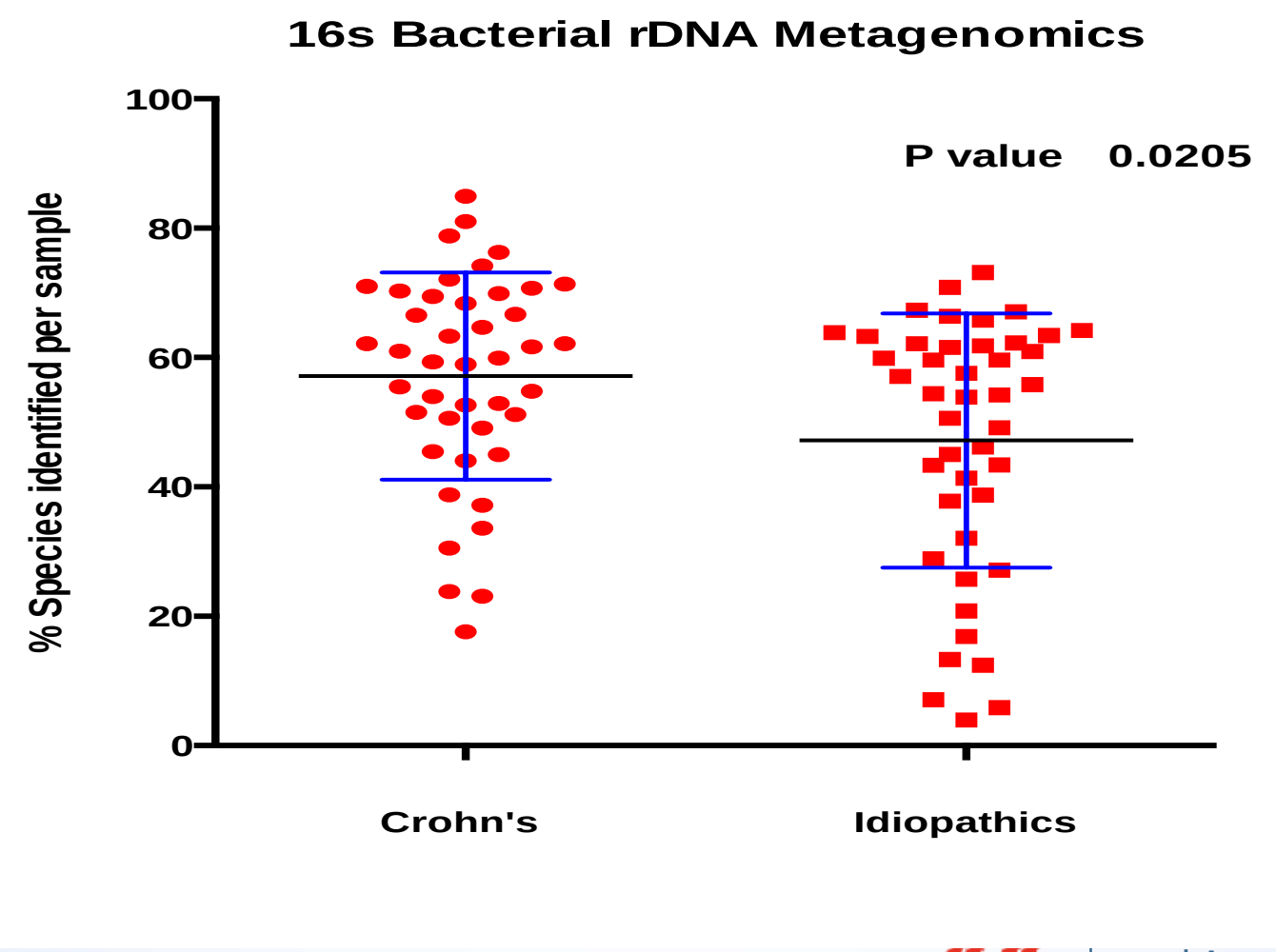
16s Bacterial rDNA Metagenomics



Yassin et al (St Marks), ECCO, ESCP 2015

Summary

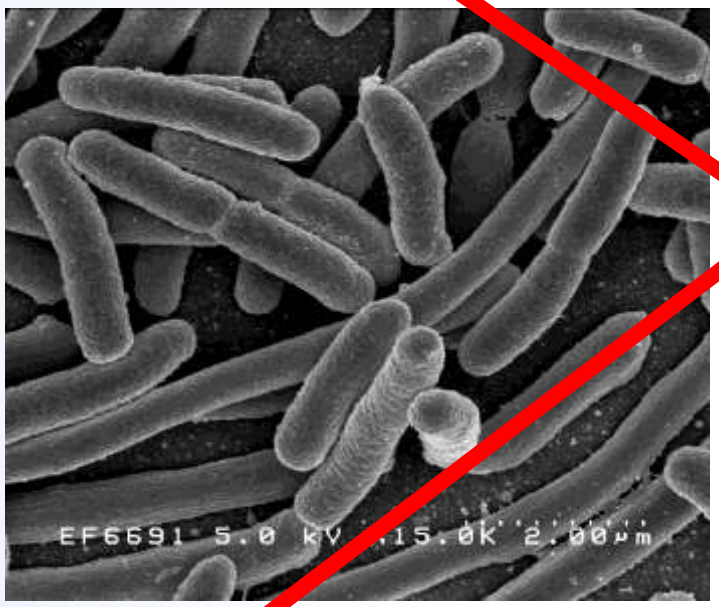
Dysregulated immune response

Crohn’s fistulae have more diverse microbiota

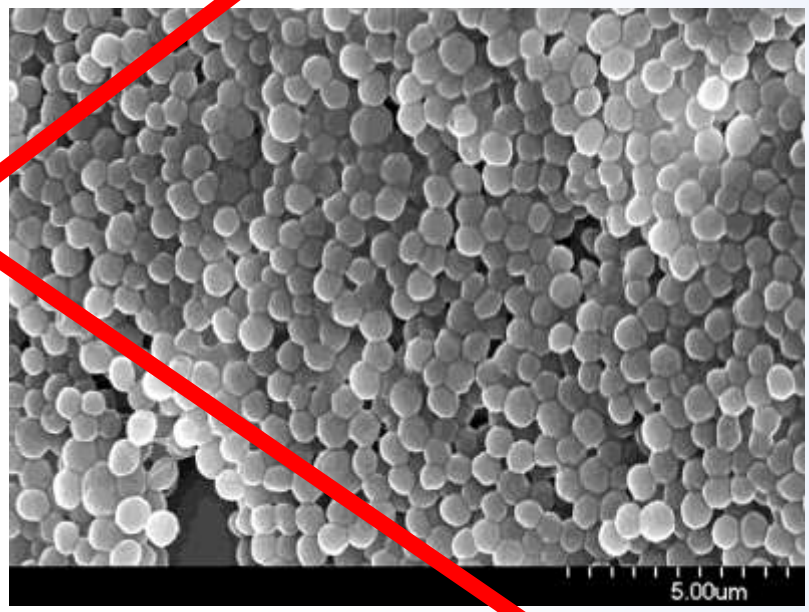
Microbiome – immune system interaction

infection

- idiopathic fistula



- Crohn's related



- enrichment media

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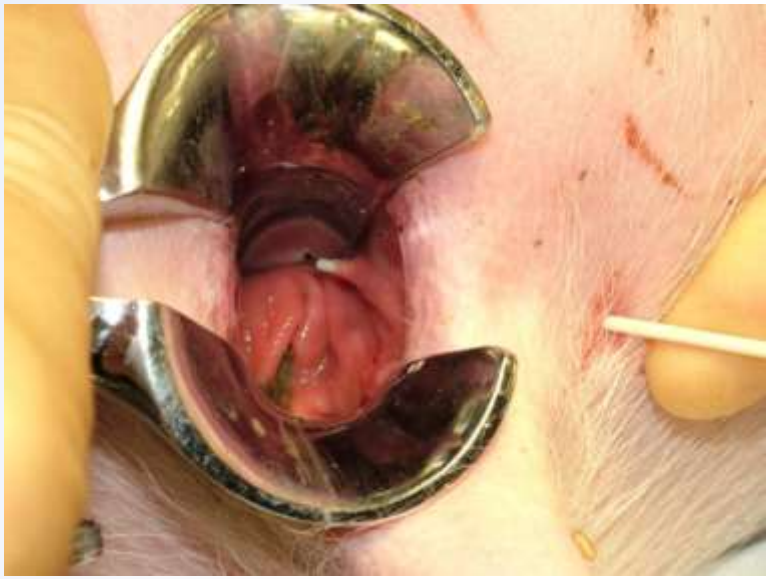
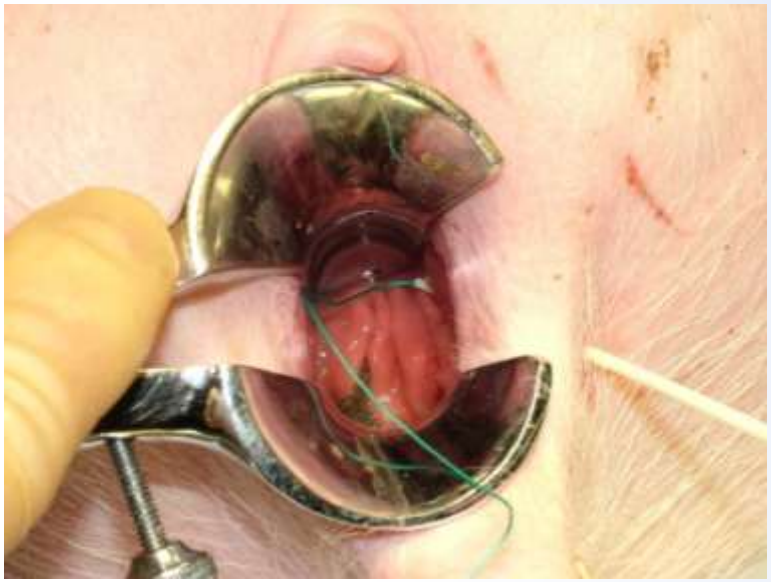
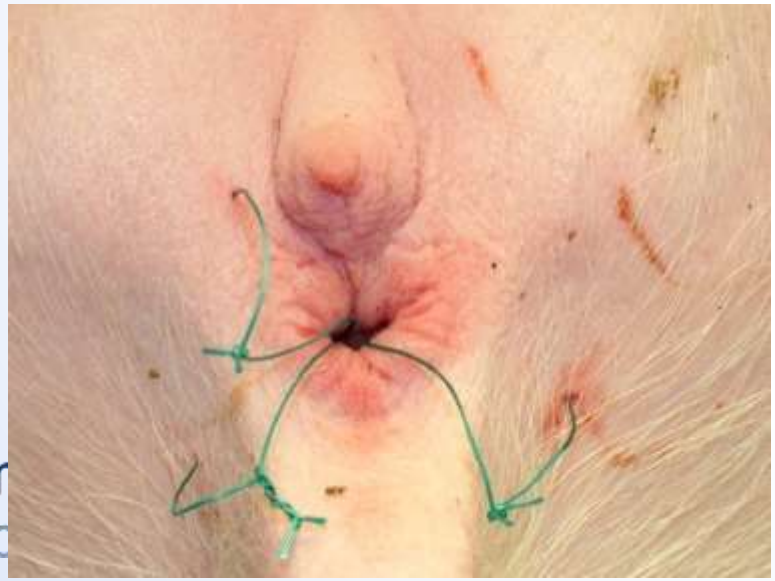
pig model of anal fistula

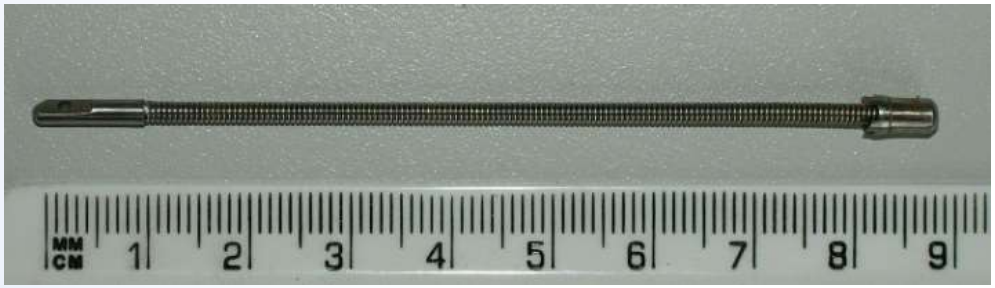


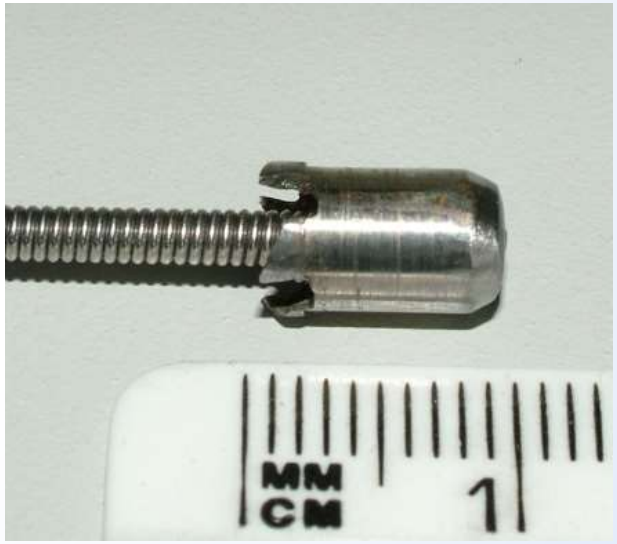




reaming – core out tract

- circumferentially removing granulation tissue and epithelium
- high speed, flexible shaft reamer



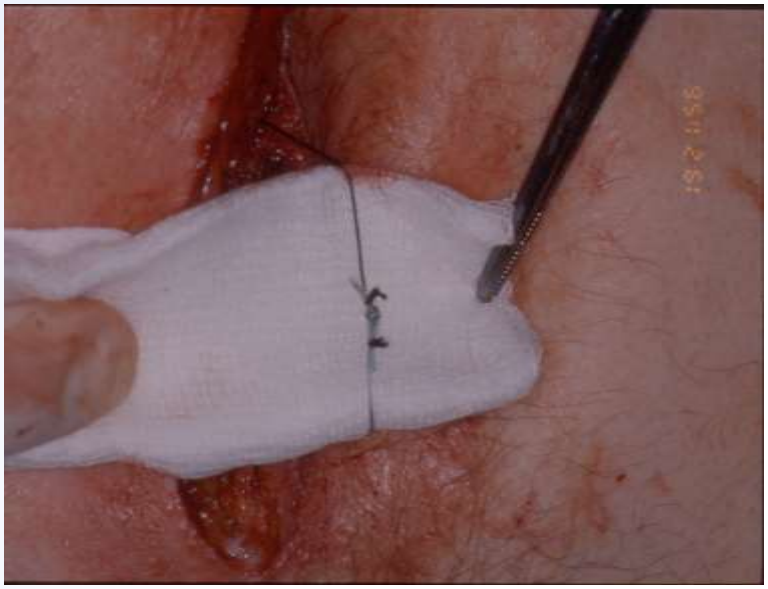


bioglue

- prepared from injectable Permacol™
  - acellular porcine dermal collagen
- centrifugation process
  - produces a thicker consistency
- +/- cultured autologous fibroblasts added

conclusion

- all treated tracks healed
- addition of fibroblasts improved histological appearance
- pilot study in human patients in progress



Laying open and seton

factors influencing continence

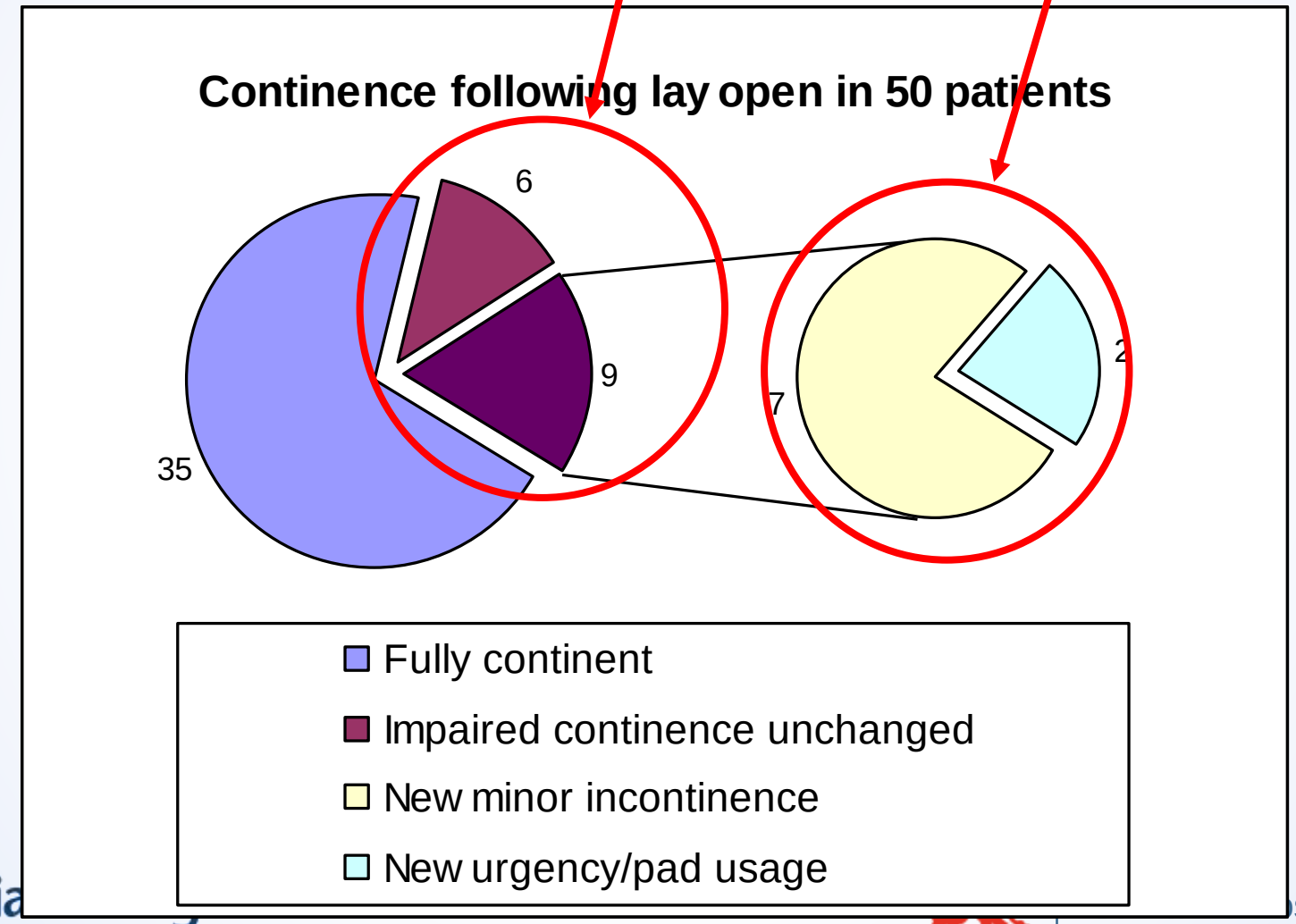
Variable	Category	Continent N (%)	Incontinent N (%)	P-value
Continence at referral	Continent	42 (84%)	8 (16%)	**<0.001**
	Incontinent	3 (27%)	8 (73%)	
Operation type	Lay Open	29 (66%)	15 (34%)	***0.07***
	Seton	18 (90%)	2 (10%)	
Tract anatomy	Intersphincteric	5 (62%)	3 (38%)	***0.08***
	Low TS	14 (93%)	1 (7%)	
	Mid/High TS	21 (64%)	12 (36%)	

Fisher's exact test

outcomes: incontinence

9 new/worse impairment (7 minor)

15 patients (30%) impaired continence at FU (12 minor)



the message

- many high, complex, tertiary referred fistulae can be
  - safely laid open, with
  - low risk of recurrence, and
  - acceptable risk of, mostly minor, further impairment of continence

- type of surgery and continence at referral are associated with healing and final continence

- There is a compromise to laying open
  - CONTINENCE

    Or

  - QUALITY OF LIFE

fistula recurrence but not continence score leads to worse quality of life

- SF36, St Mark's Continence Score
- 146 fistulas, 33 recurrent and 51 loose seton at presentation
  - mean age 45 (18-87), 47 women
- 1 in 5 urgency pre-op; 1 in 3 urgency post-op
- reduced quality of life ($p<0.05$) associated with:
  - fistula; recurrence; secondary extensions; urgency
- no difference in quality of life associated with:
  - continence score; presence of loose seton

Fistulotomy

- There is no doubt that fistulotomy gives the best option for cure
- >95%

- But……
- Everyone worries about incontinence

If we want to change the world we have to understand what we are dealing with

MRI vs. EAUS

MRI

- good assessment near and far
- ‘surgical’ appearance
- good for repeat assessment

- easier to understand

EAUS

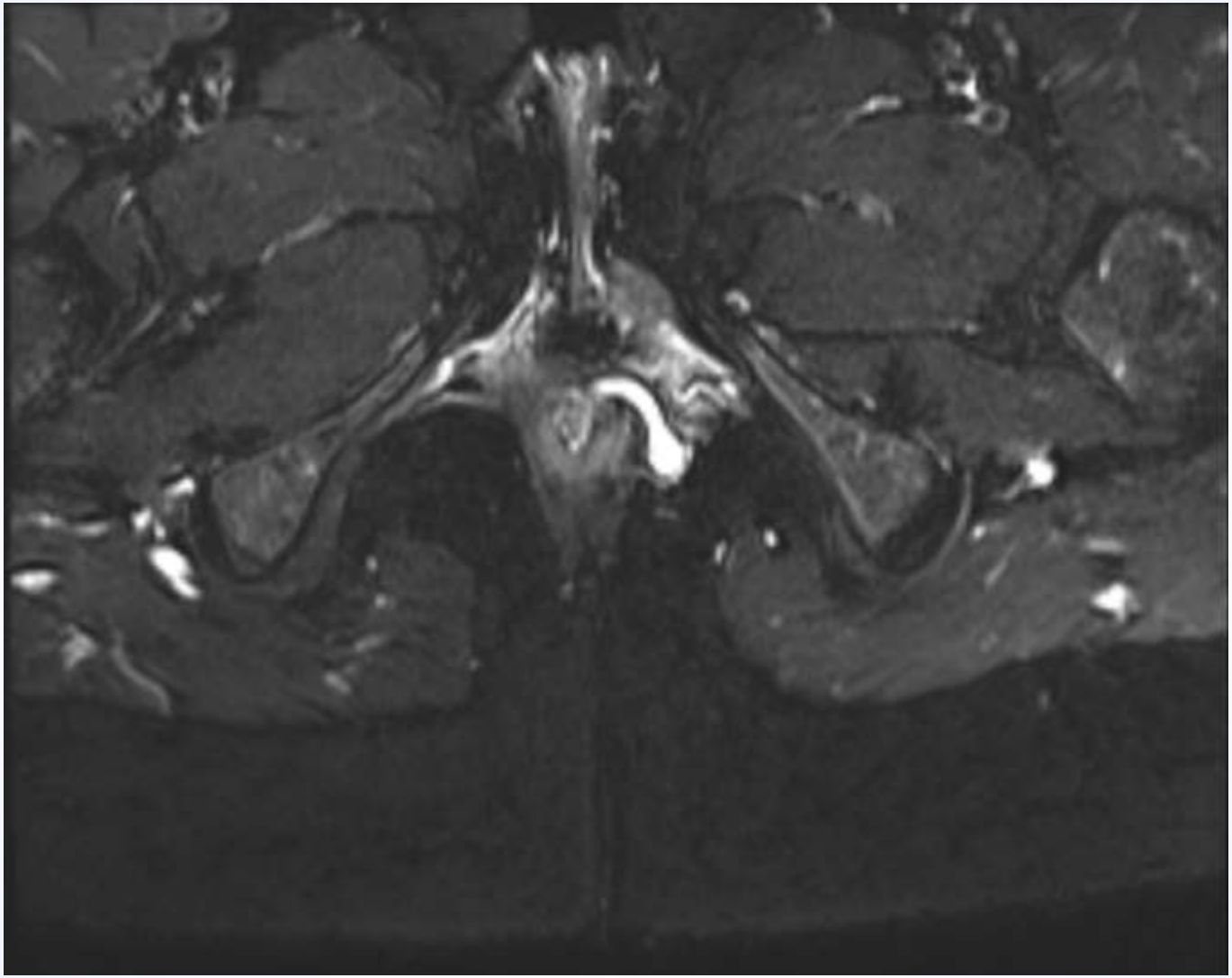
- terrific assessment of the sphincters
- identifies IO

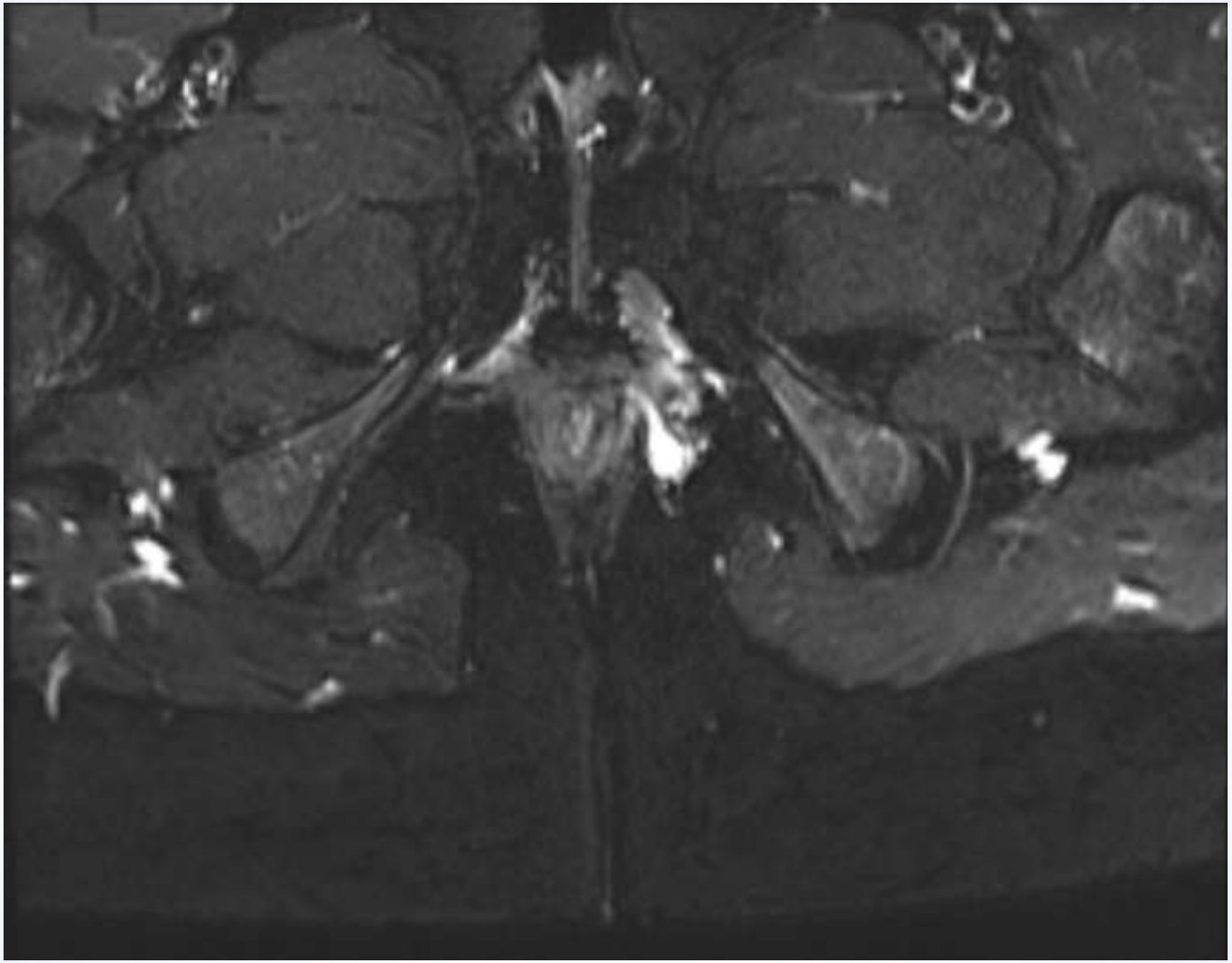
What is the optimal modality for assessment of perianal fistulating Crohn's disease?

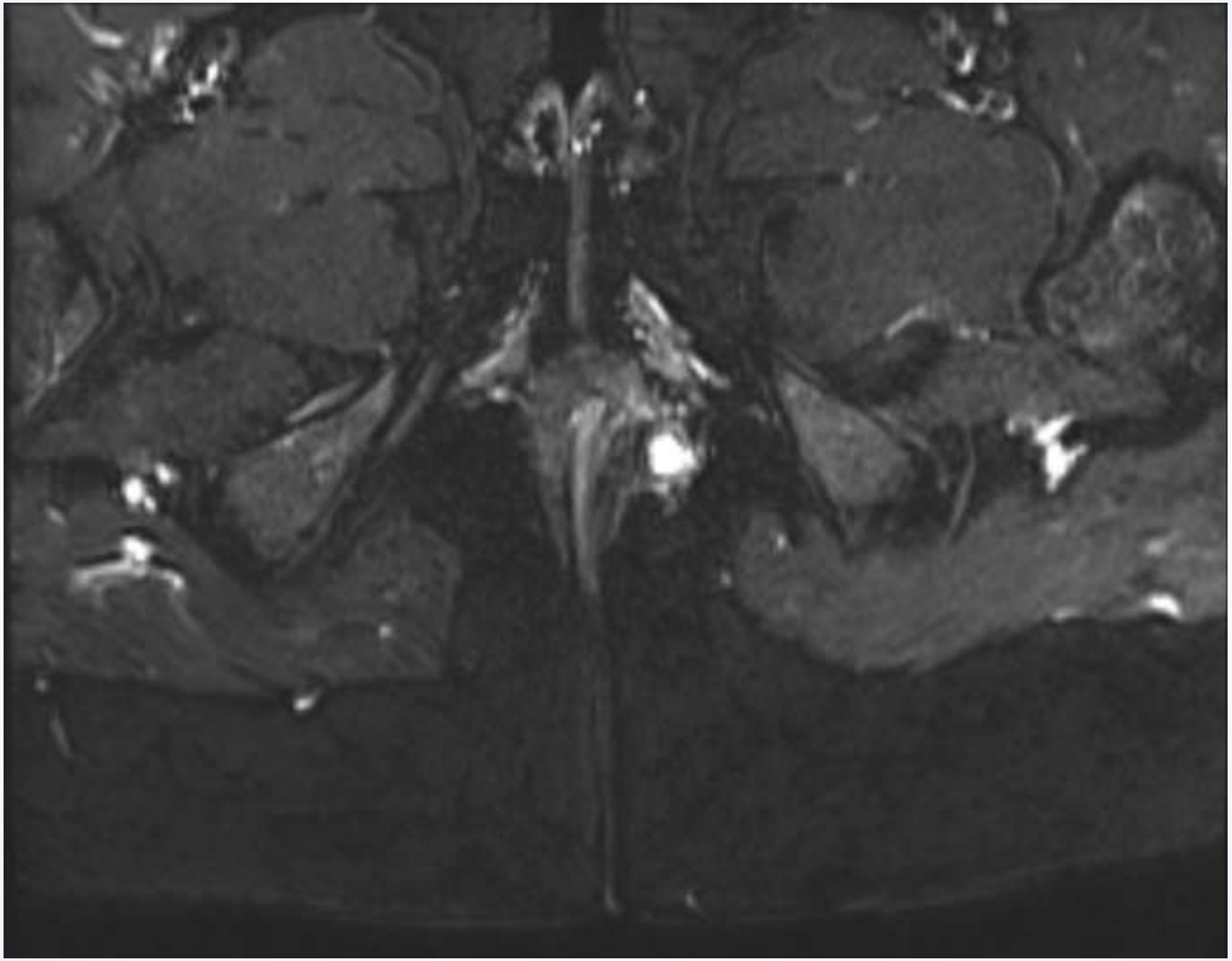
- 34 patients with Crohn's perianal fistulas
- Prospective study comparing accuracy of 3 methods
- Good agreement between all 3 modalities
  anal endosonography 91% accuracy
  MRI 87% accuracy
  accuracy

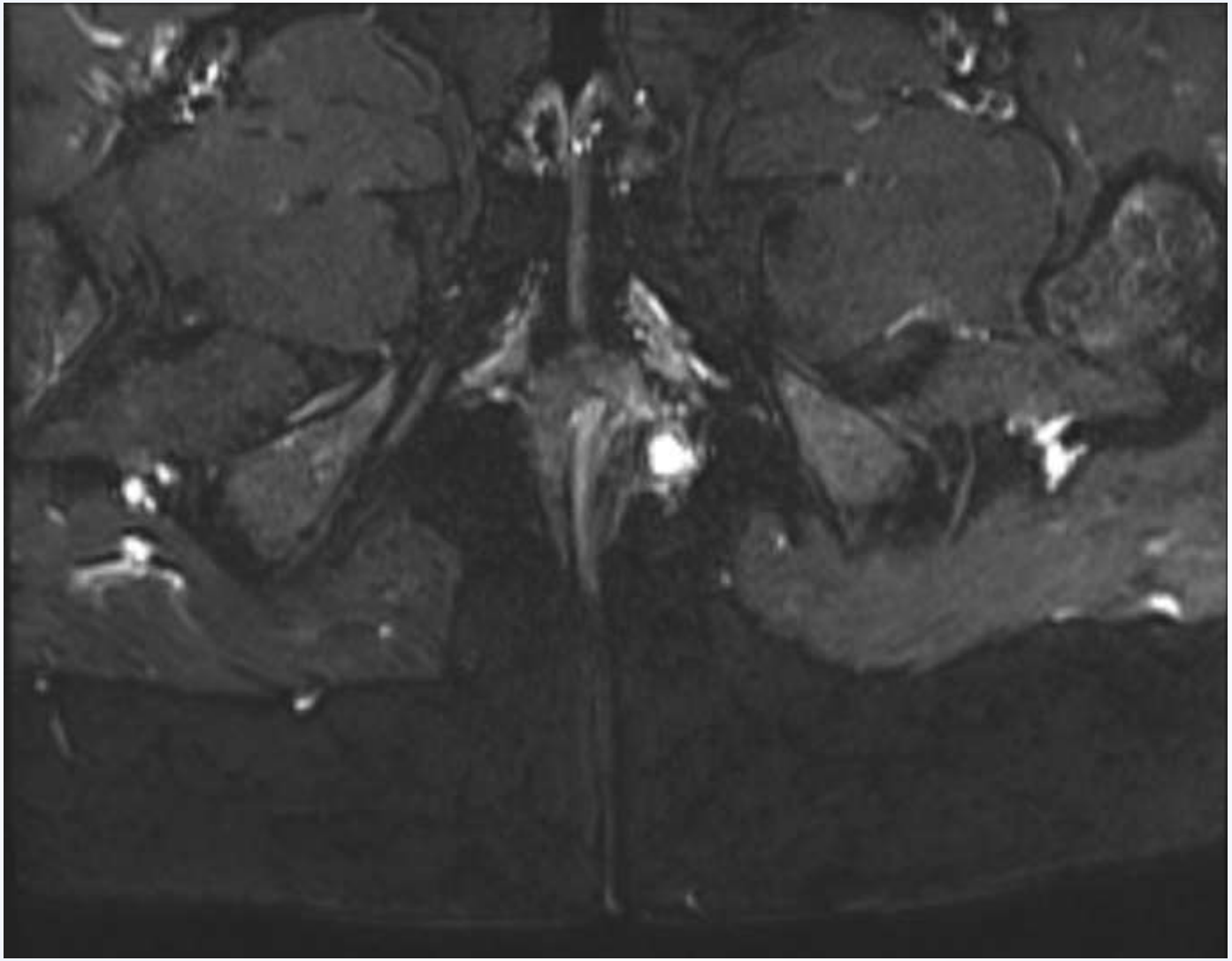
Combination of any 2 methods yielded accuracy of 100%

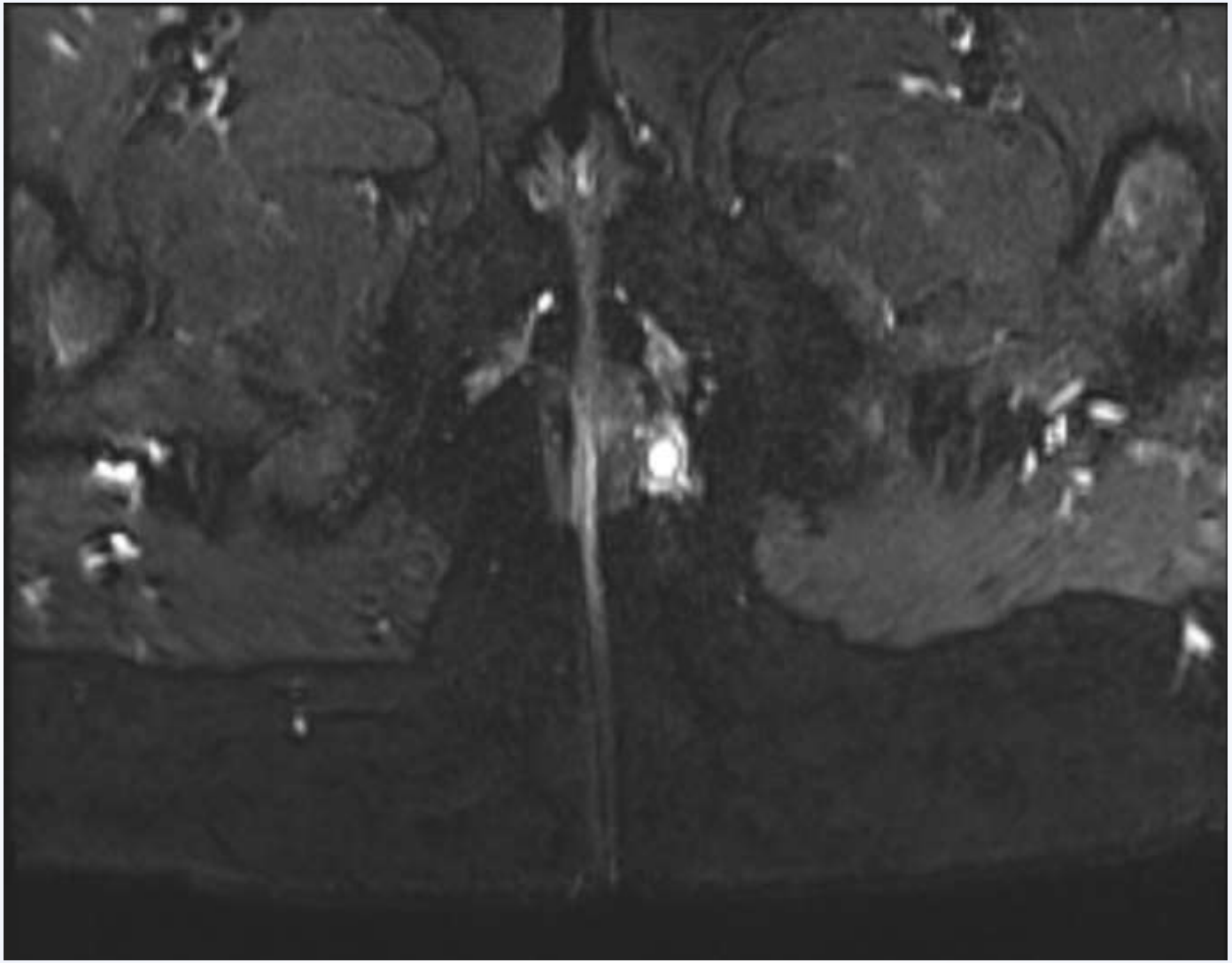
Schwartz et al. Gastroenterology 2001;121:1064-72

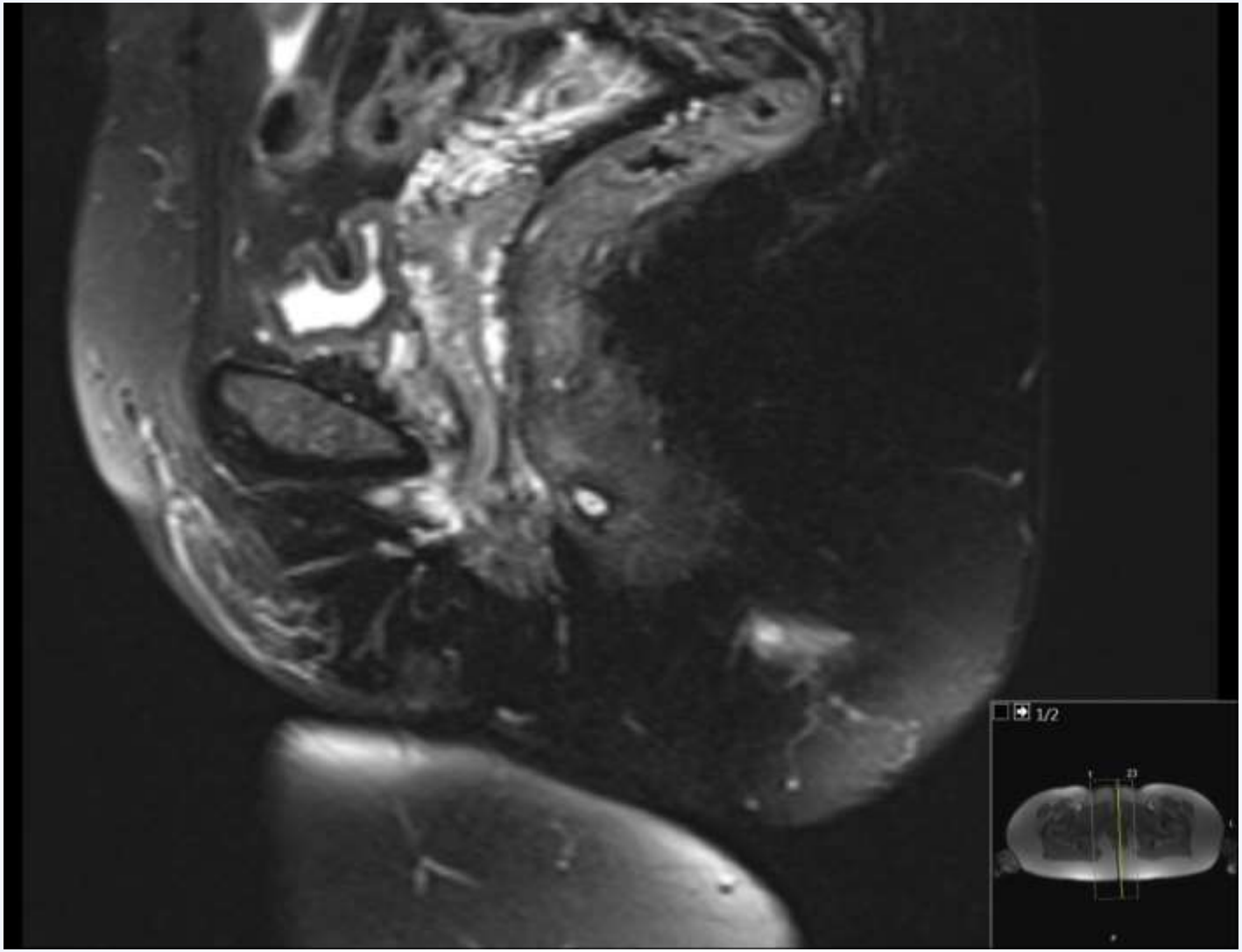








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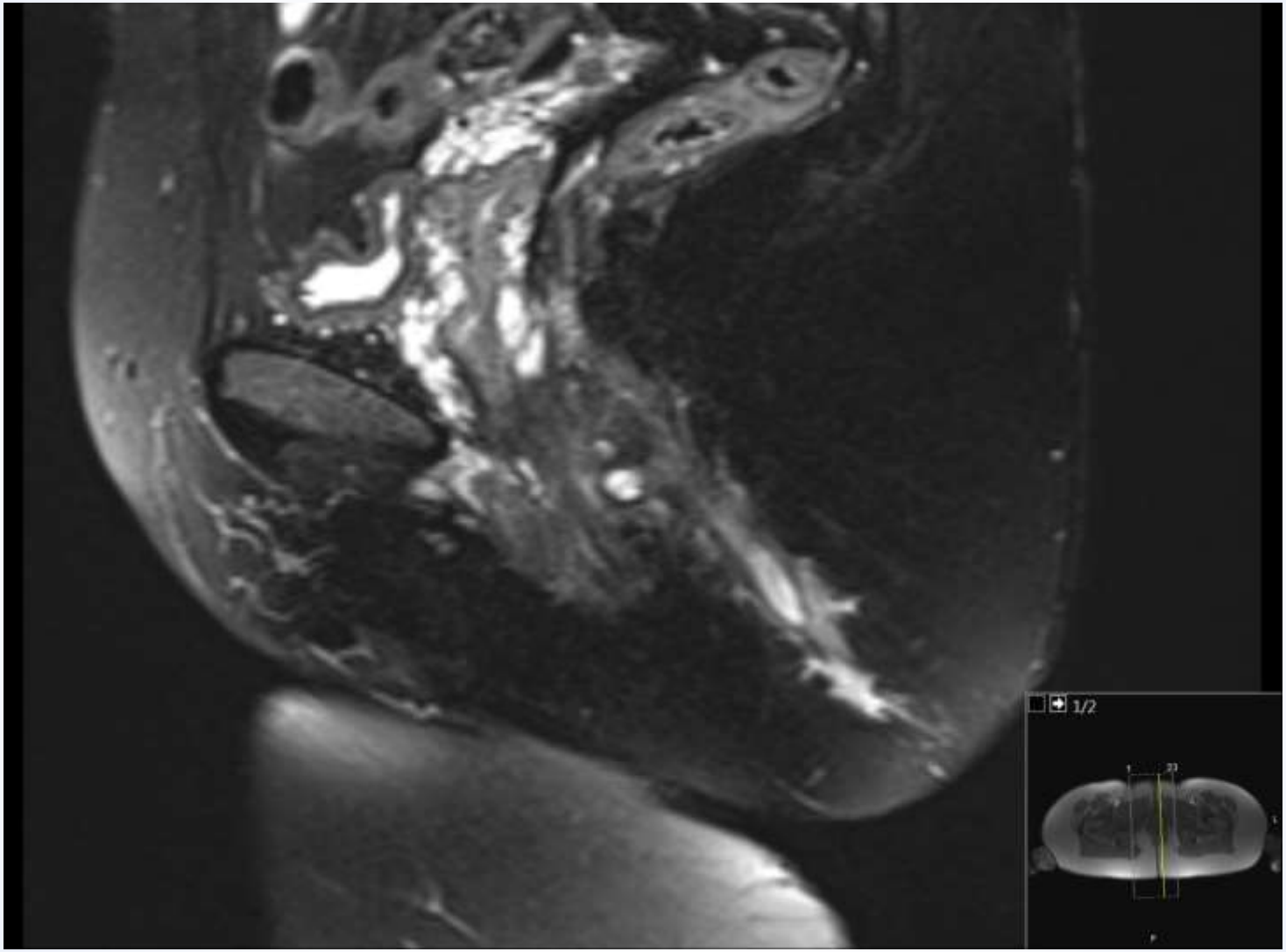
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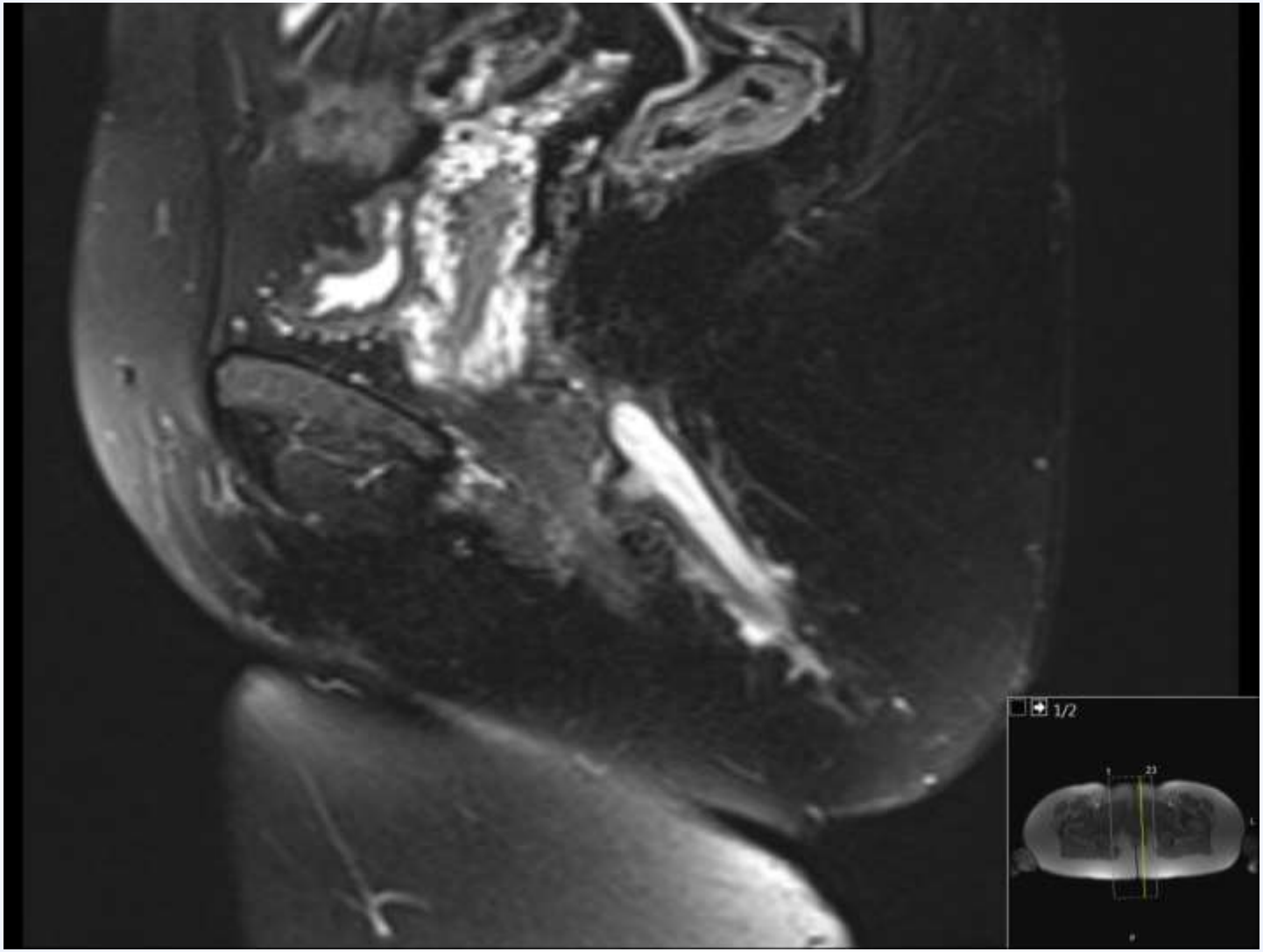
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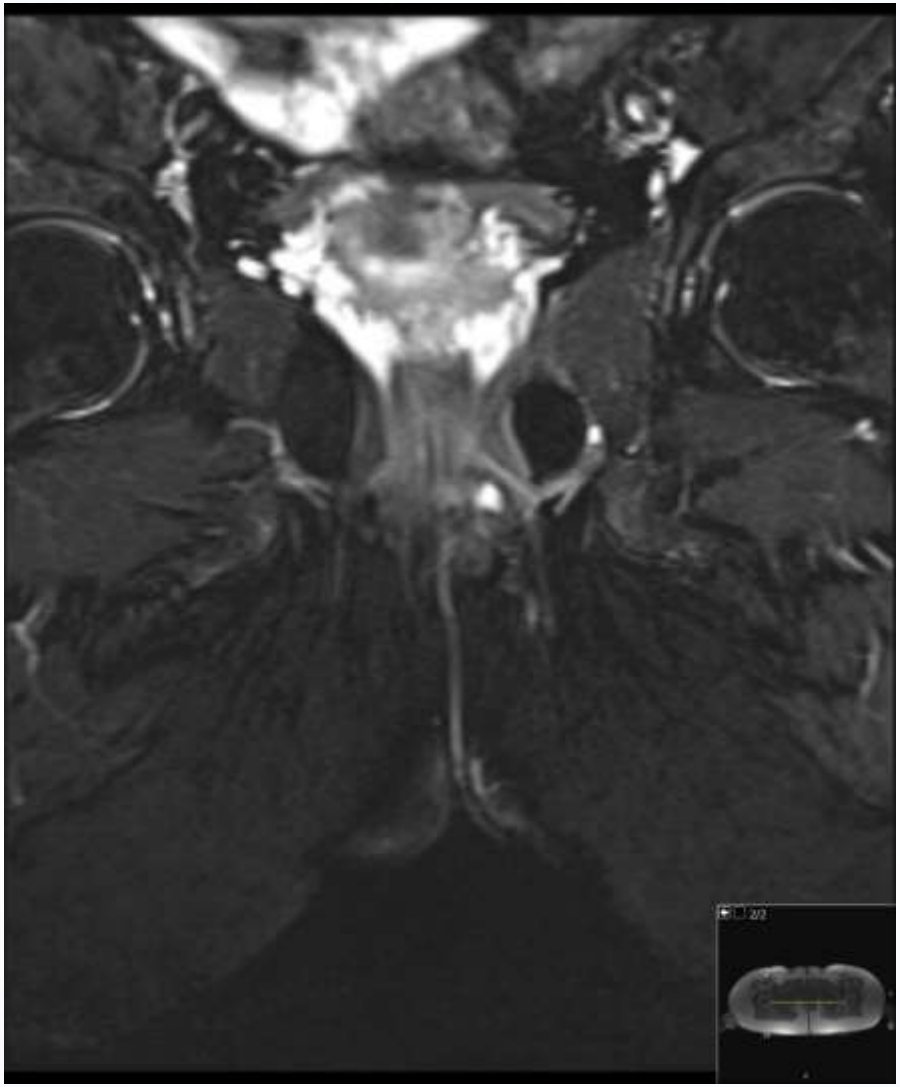

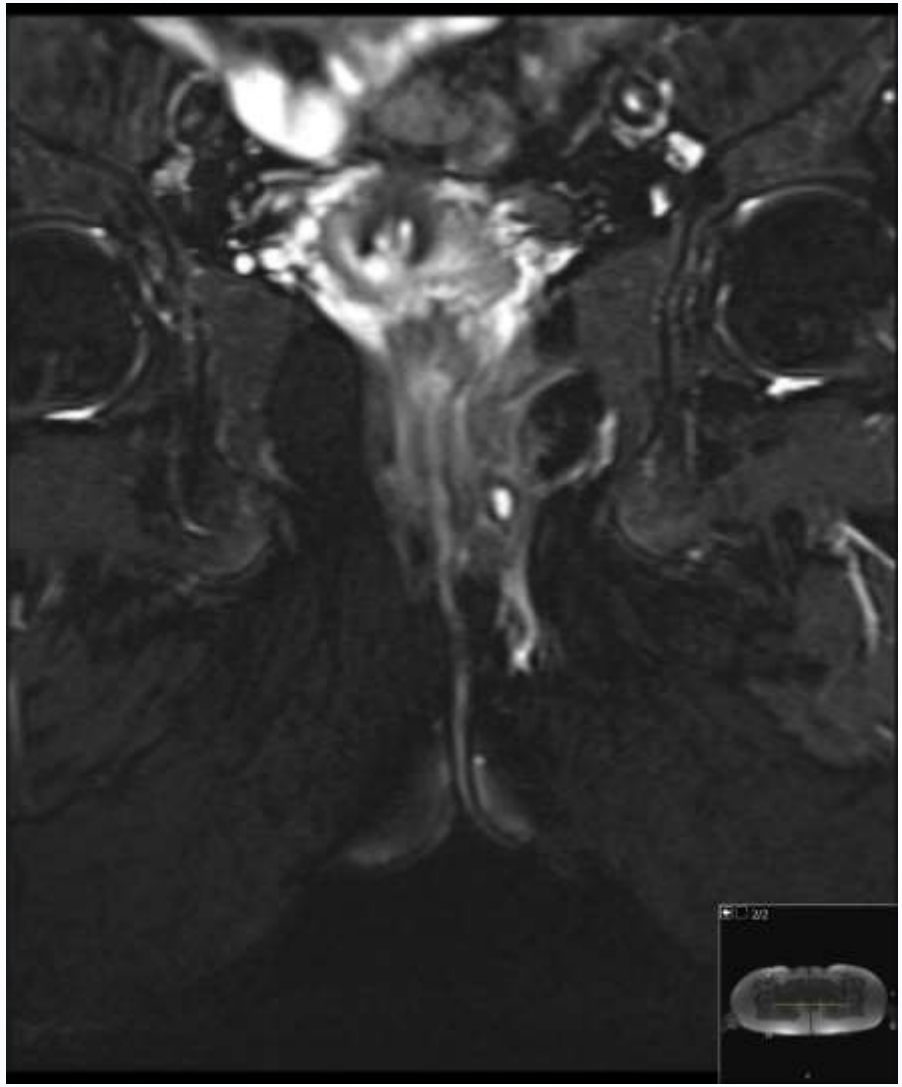

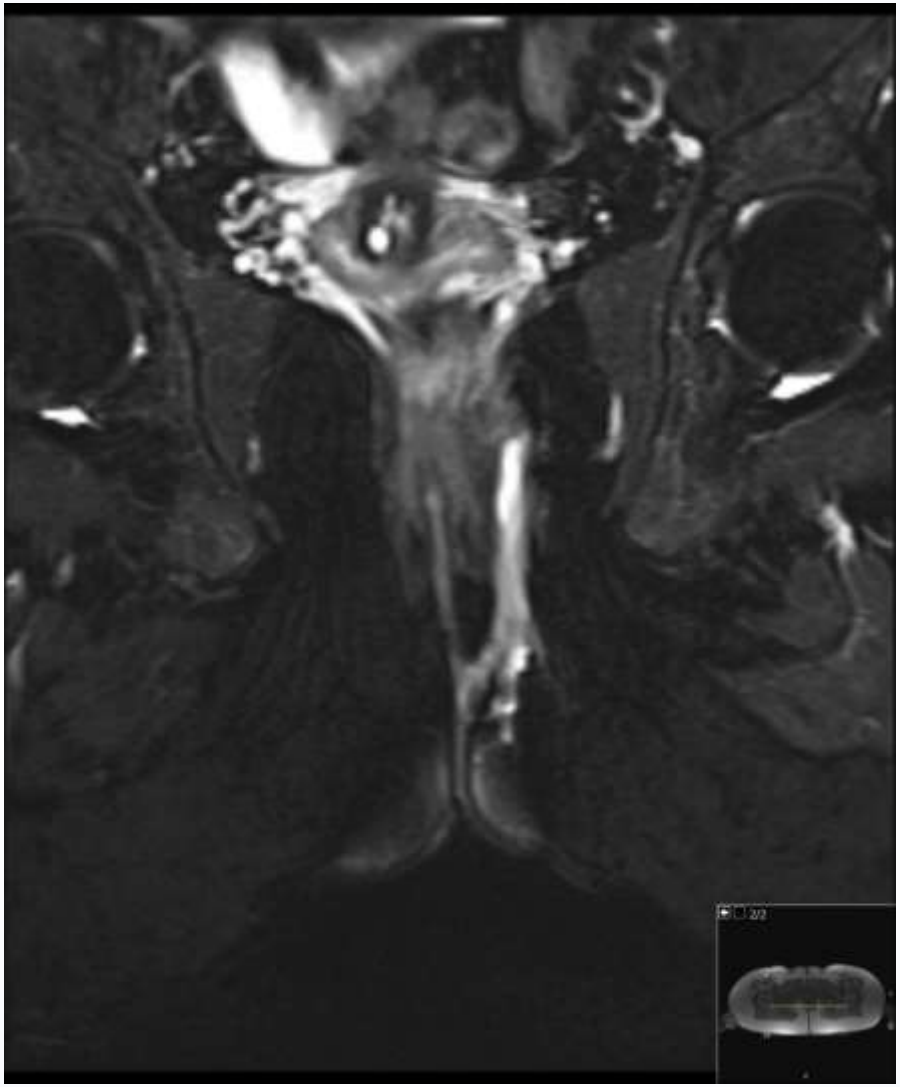

imaging – where we want to be

- improved MRI
  - 3D
  - in theatre access to onlay imaging
- improved EAUS
  - correlation with ARP and clinical outcomes to develop a robust method of determining risk of LO
  - (Andy Williams at GKT is working on this)

3D - "looking at an old problem in a different way"

1. **patient communication**
   informed consent

2. **surgical planning**
   better appreciation of sepsis

3. **medical education**
   better understanding of goals, options and techniques

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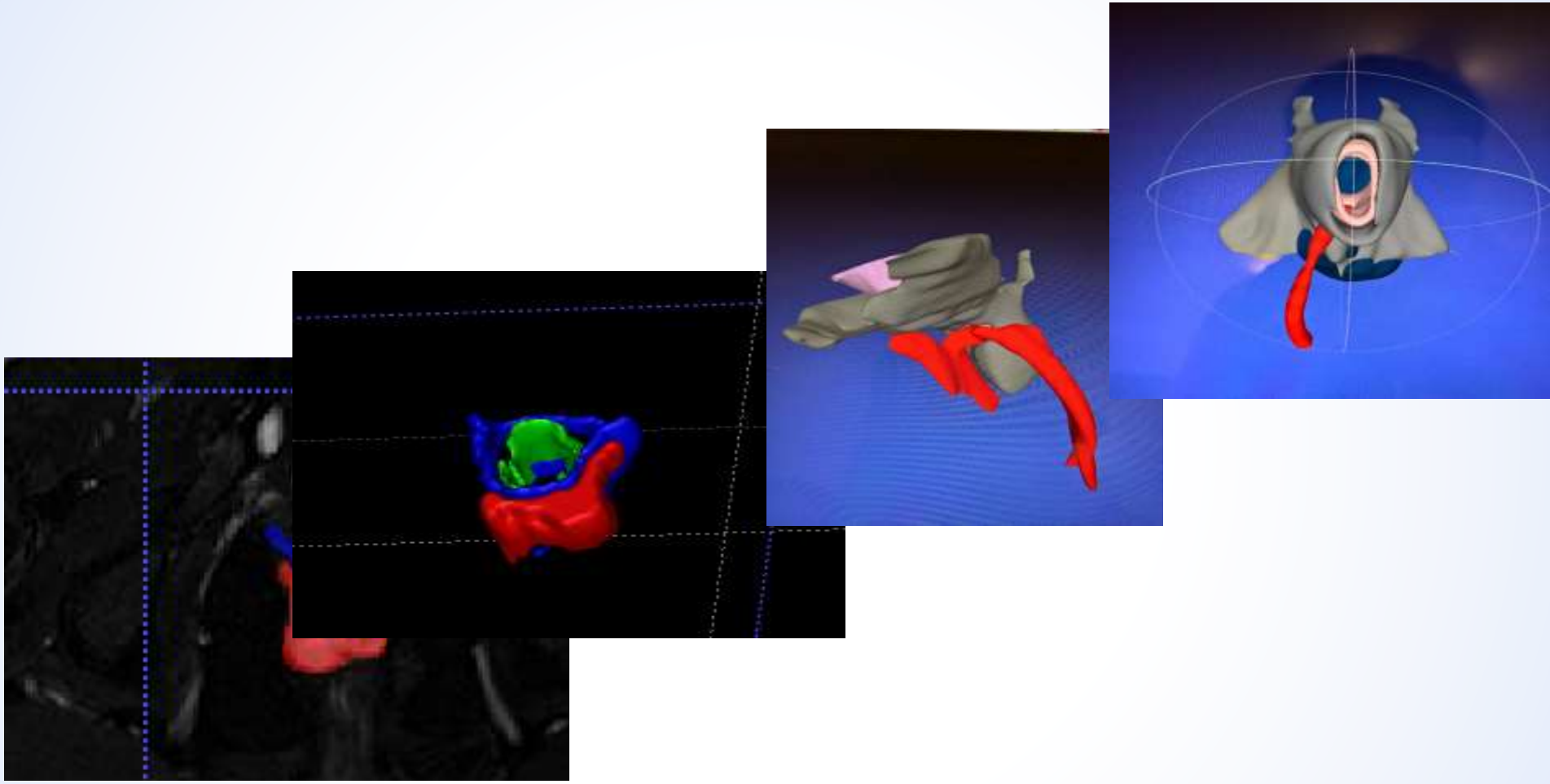

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IS

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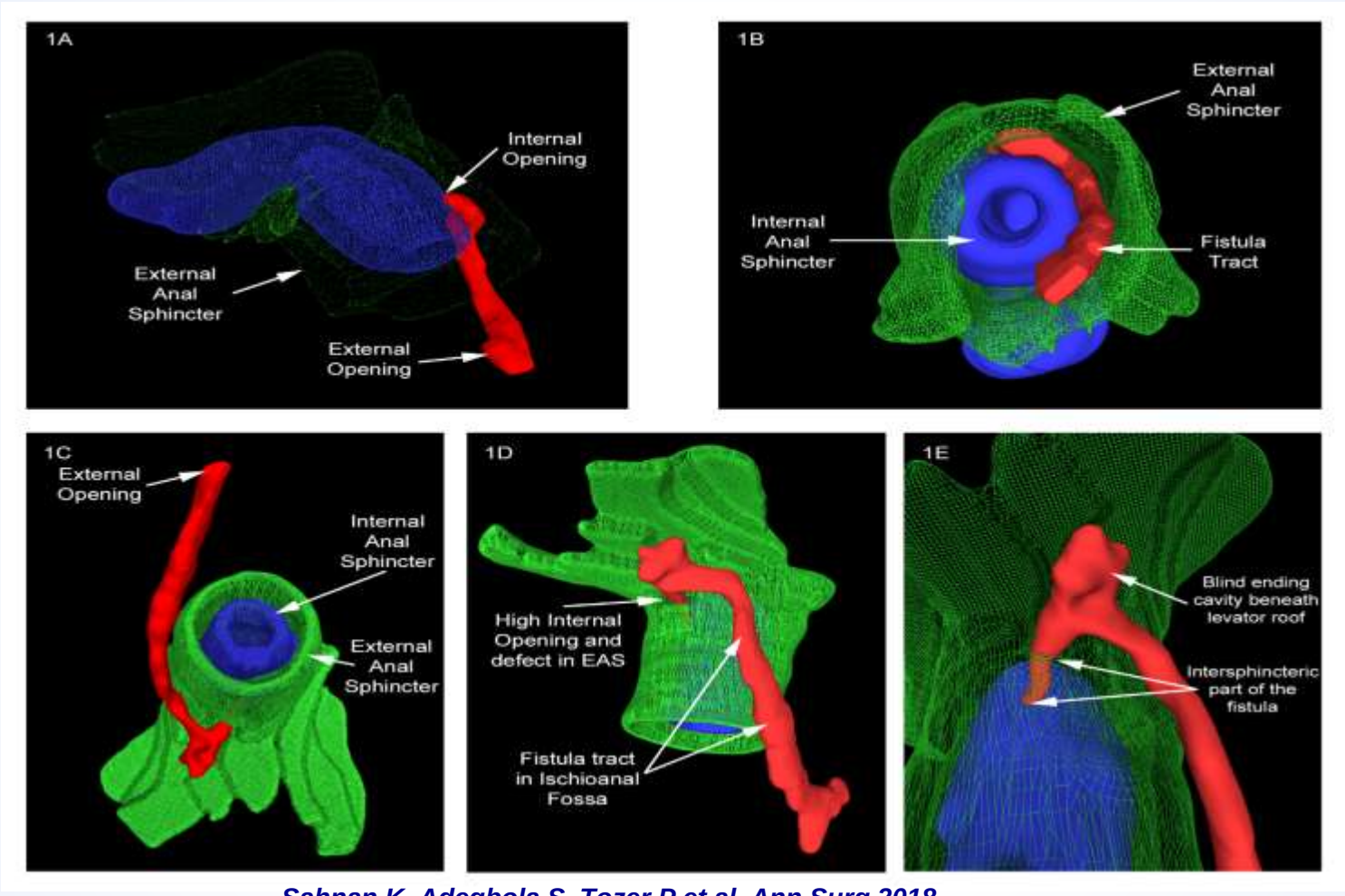
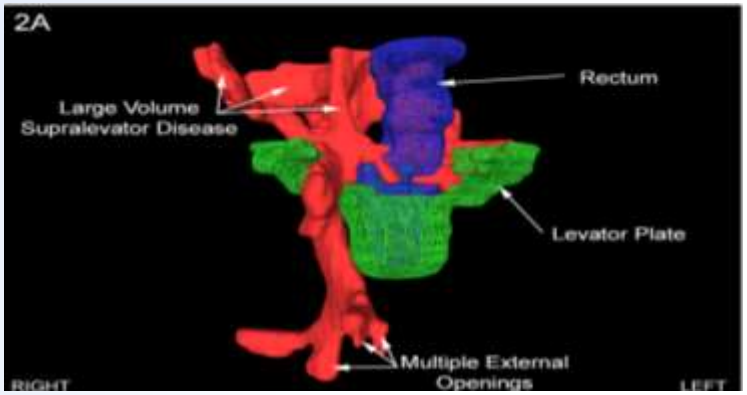
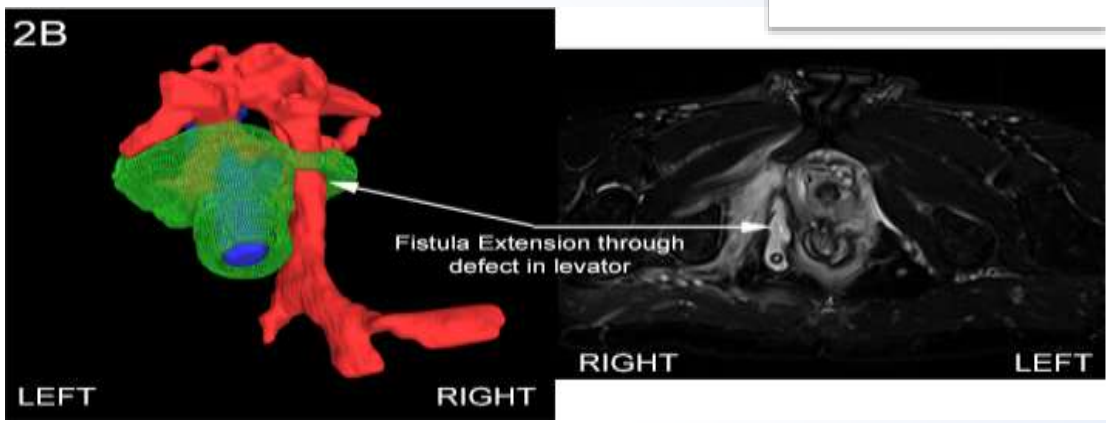
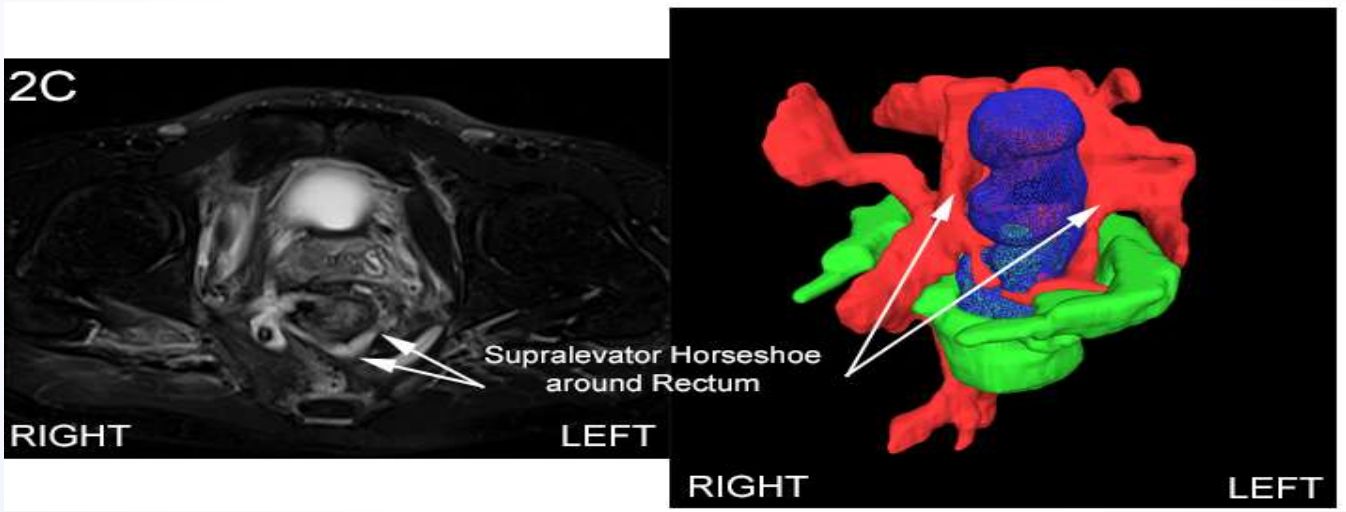


Sahnan K, Adegbola S, Tozer P et al, Ann Surg 2018







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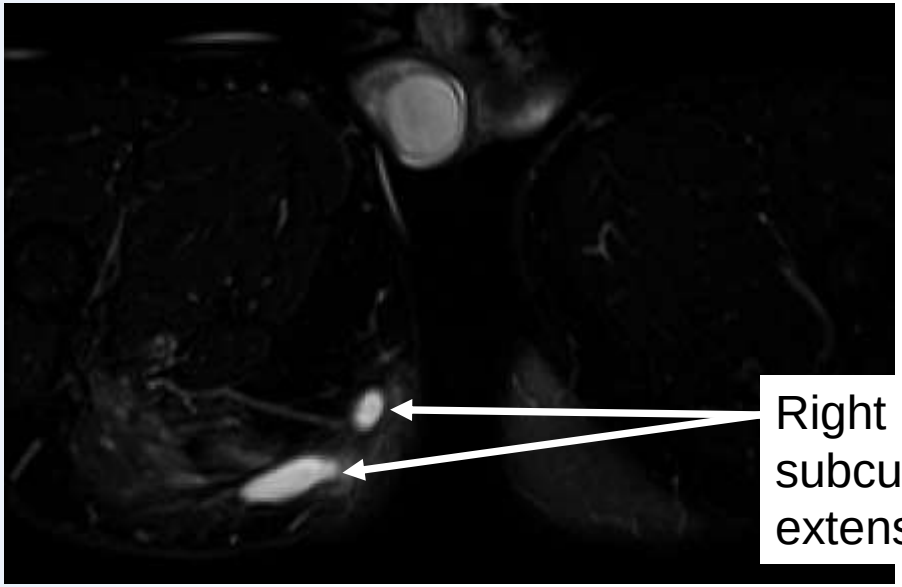
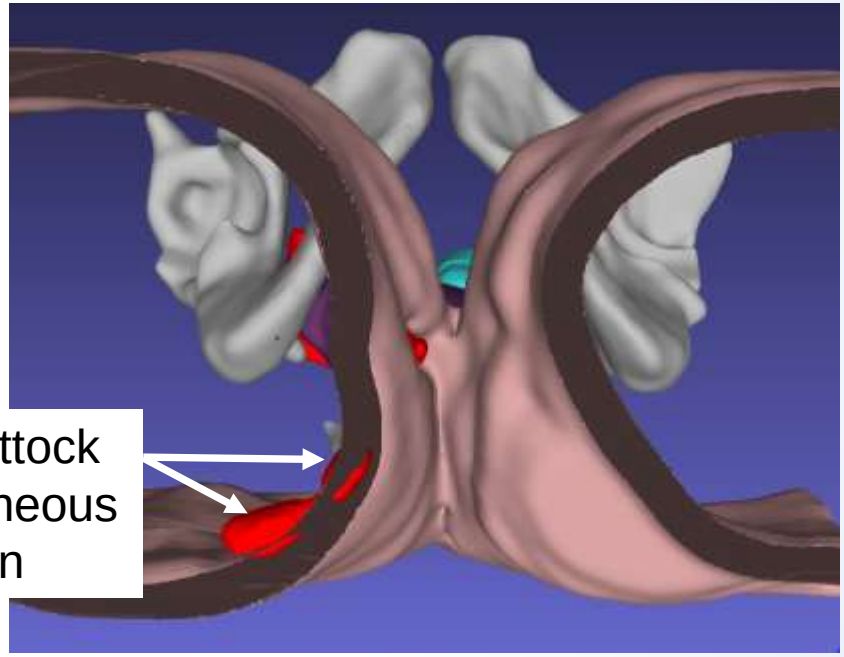
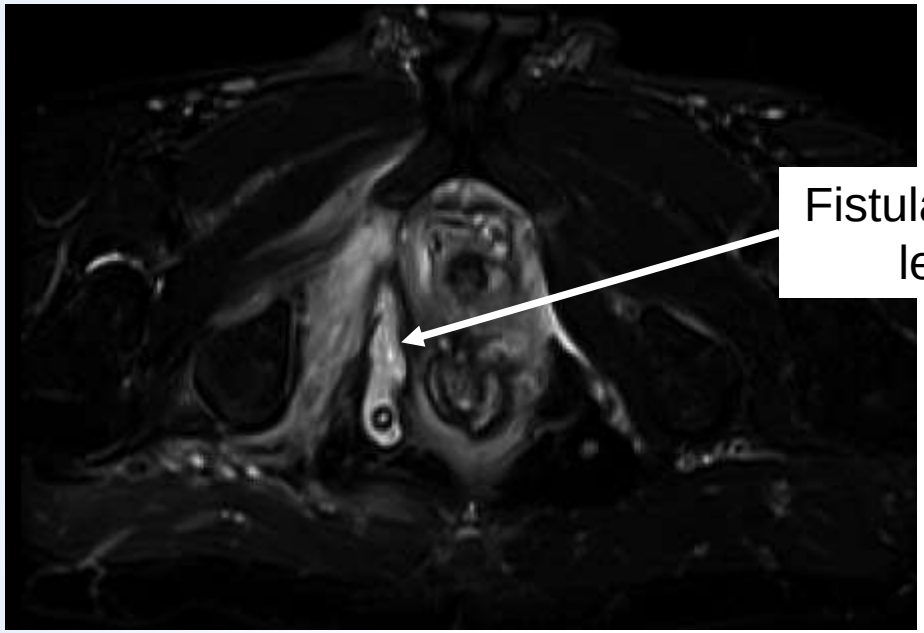
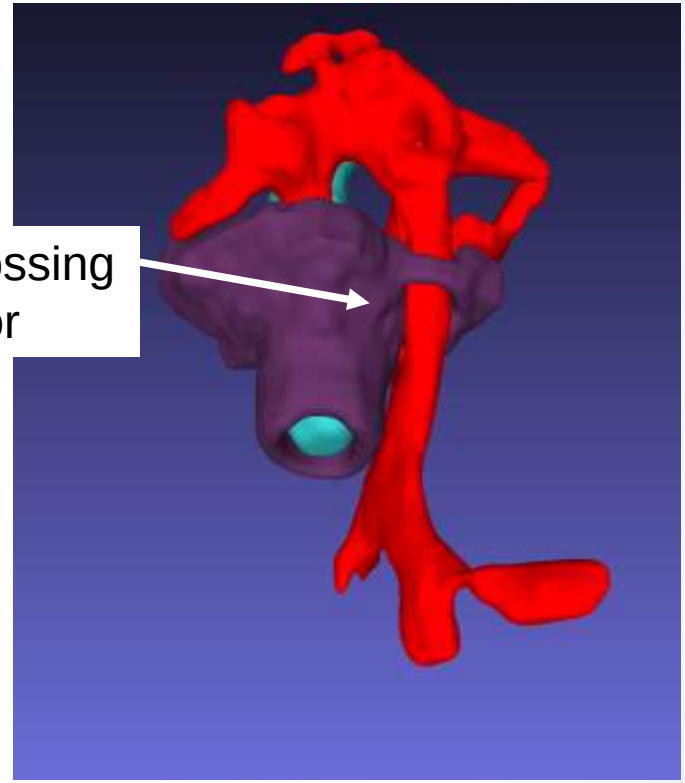


Right buttock subcutaneous extension





Fistula crossing levator



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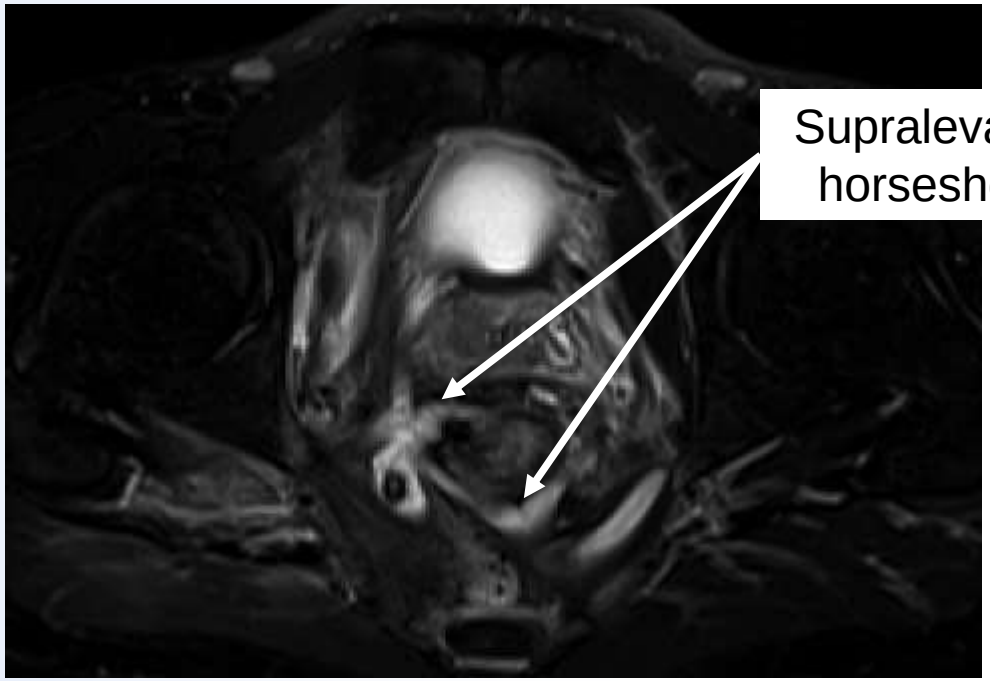
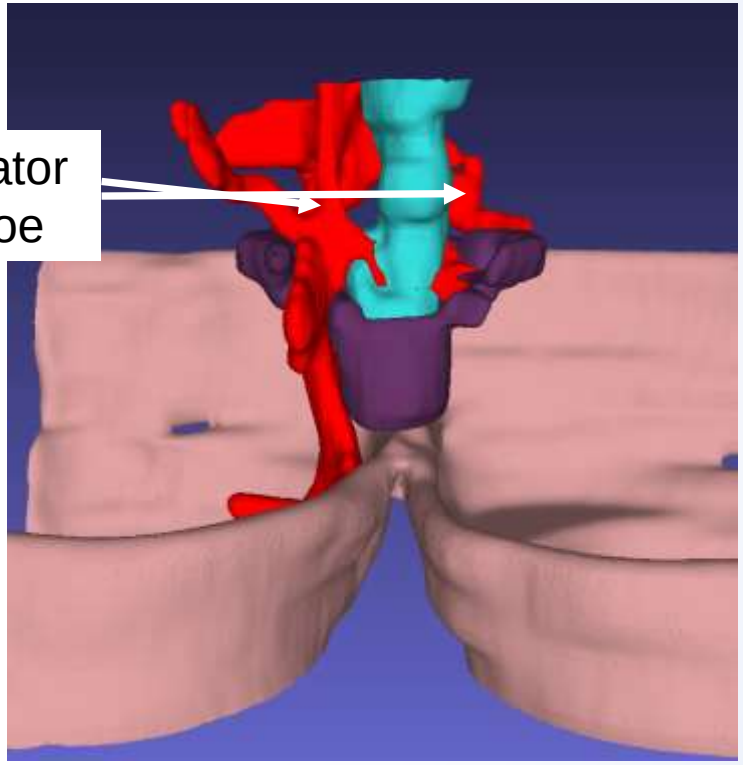
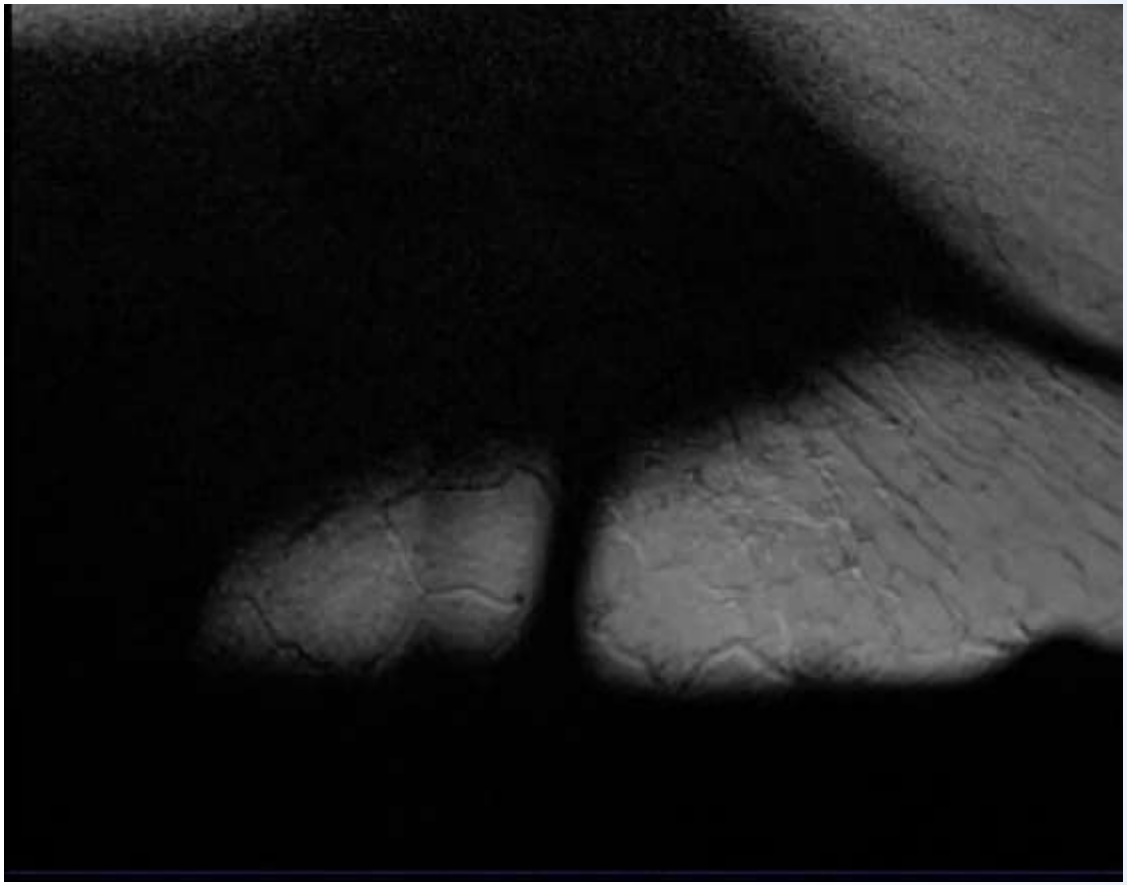
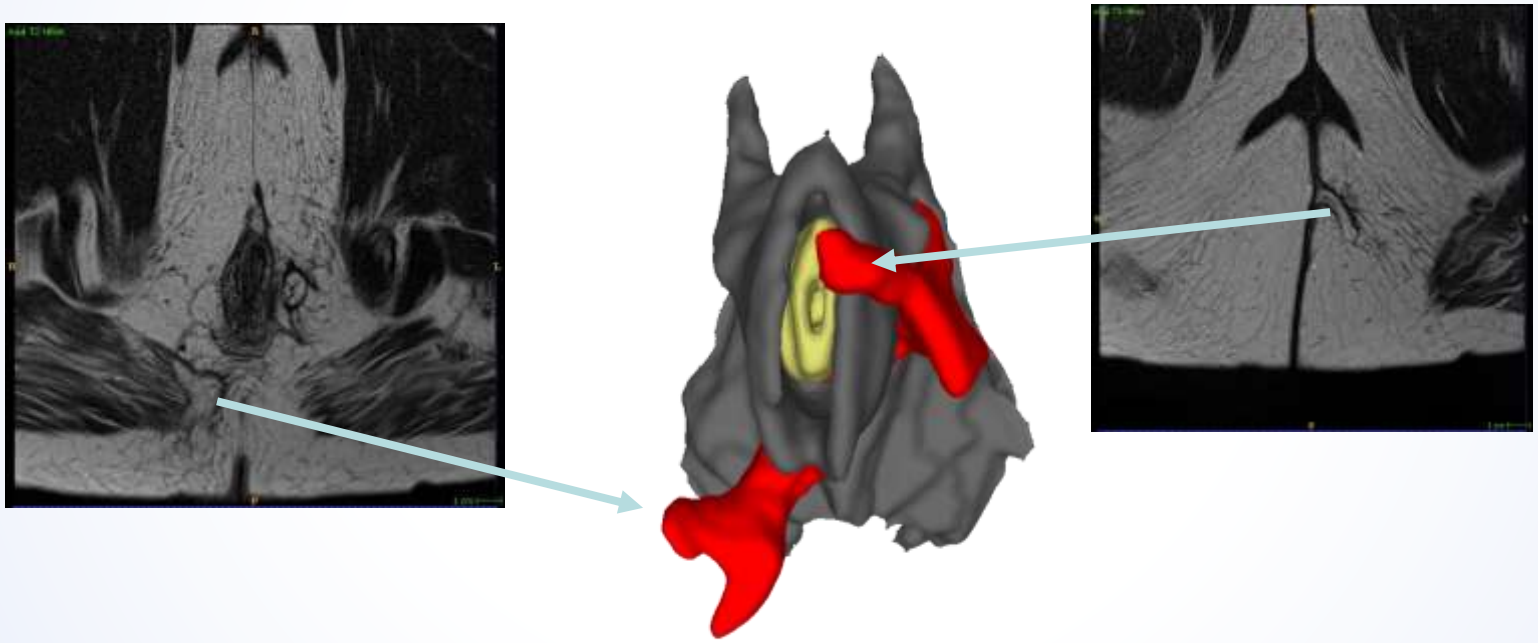

Supralevator
horseshoe



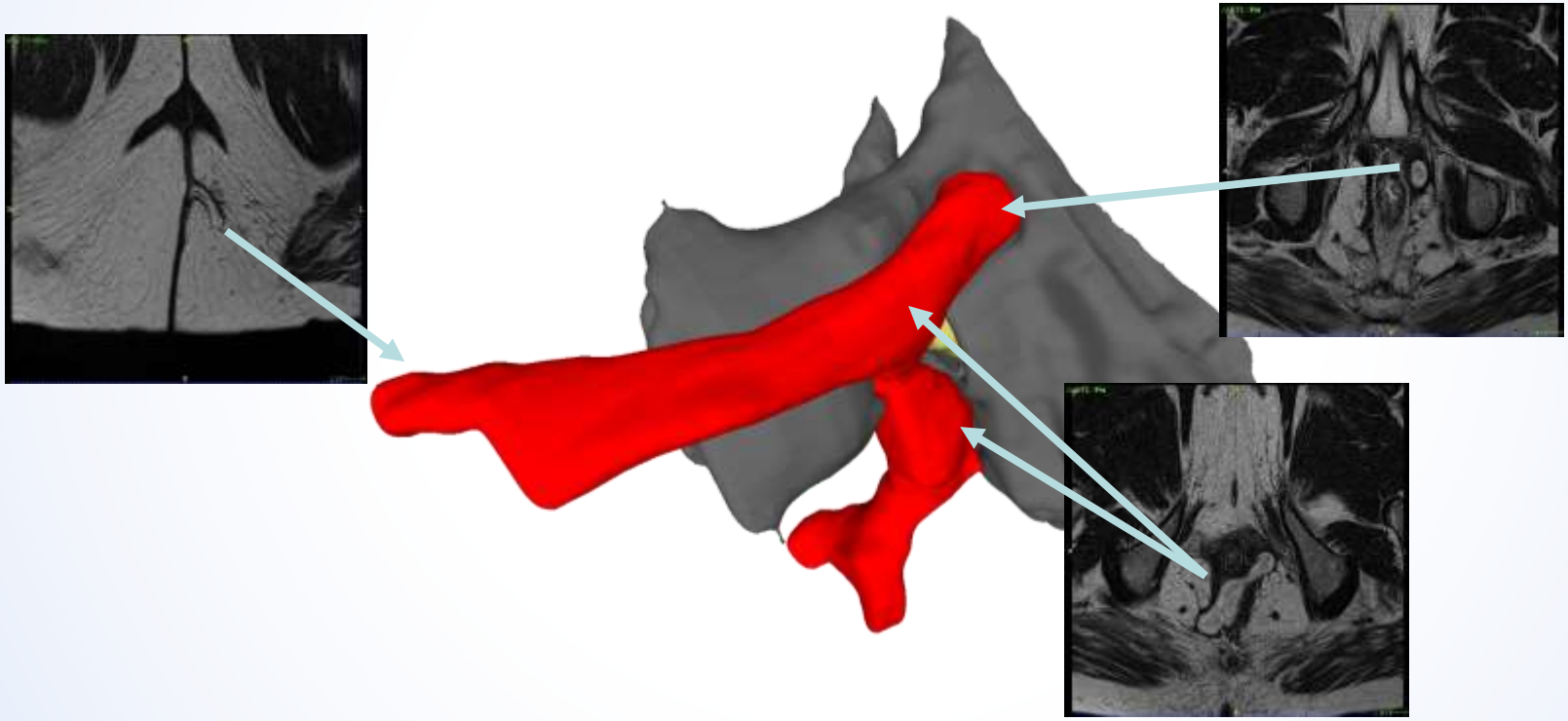
Complex fistula



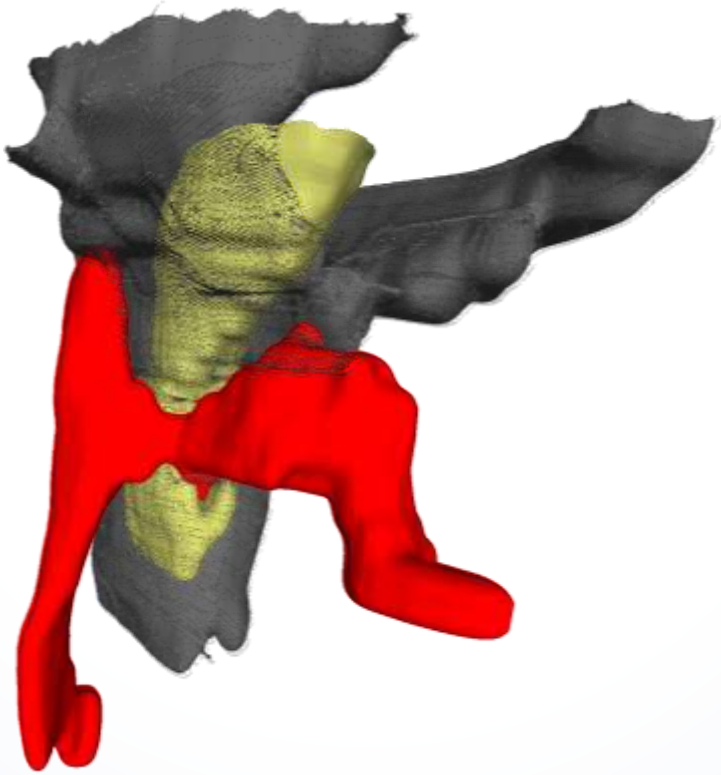
Lithotomy position



View from patient left



Visualisation



Supralevator involvement?

3D printing – PPI (St Marks's IBD patient panel)

Lateral

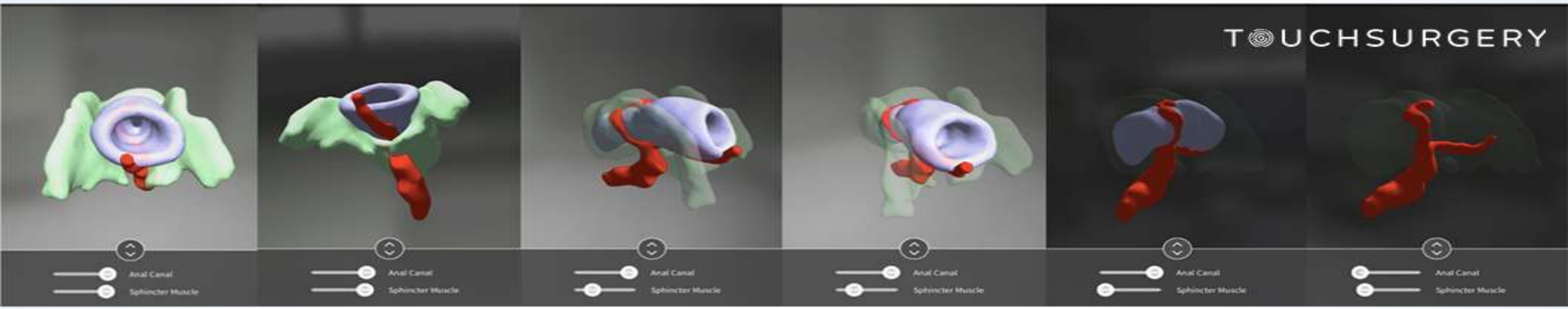
Oblique

Lithotomy

Sahnan K, Adegbola S, Tozer P, **Therap Adv Gastroenterol, 2018**

Send the images to your phone

TOUCHSURGERY



Sahnan K, Adegbola S, Tozer P, Ann Surg 2018

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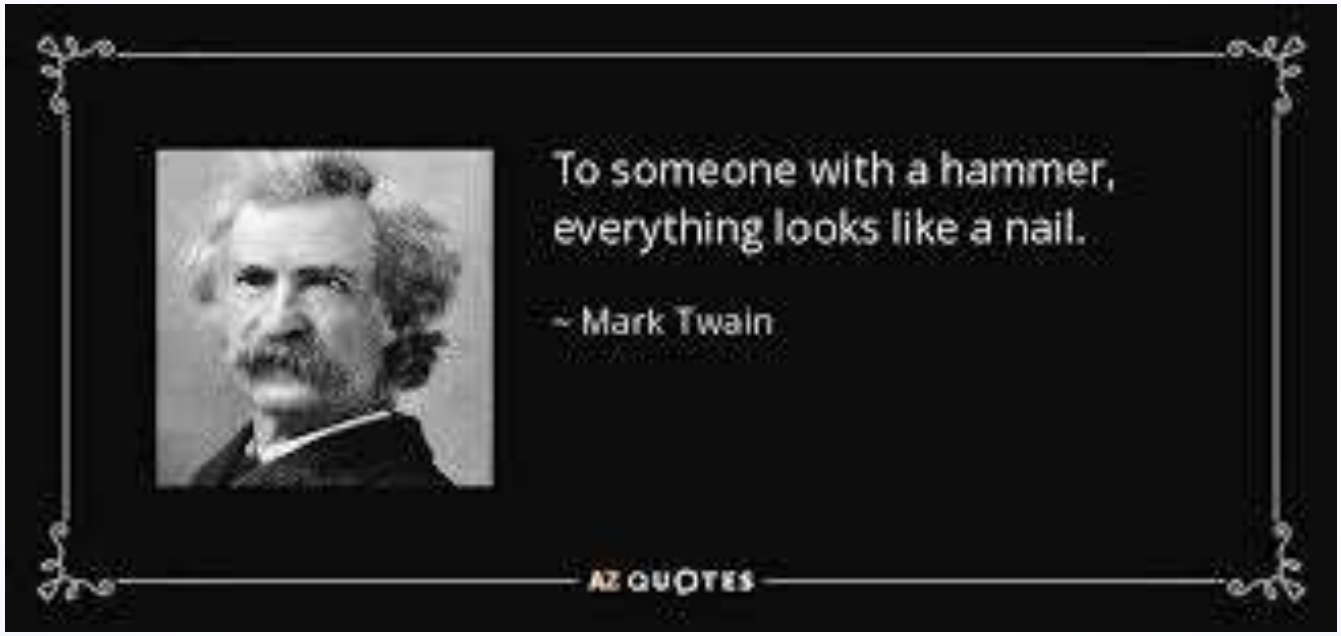
We have to change our concepts on how we think about fistula

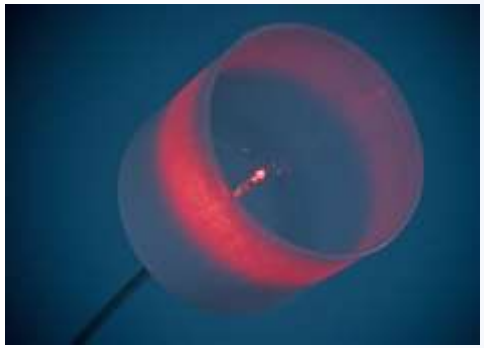


What is the aim

- Cure in most situations

- Setting realistic goals
- consequences of treatment

What do we have in our tool box



- clips (OTSC)
- glue
- stem cells
- plugs
- Laser (FiLaC)
- advancement flap
- immediate sphincter repair
- fistulectomy
- LIFT
- VAAFT
- cutting setons
- fistulotomy

- So if we can’t achieve a cure where do you go from there ?
- The Sphincter Saving Procedures
- But they don’t always work?
- Or work well in the hands of one but not another

or

Lets go back to the toolbox

Do we know to choose the right tool for the right fistula

If we want to choose the right tool – sphincter saving

- WE HAVE TO
- Improve understanding of pathophysiology
- Identify the common ‘fistulotype’
- Understand the precursor lesion

Maybe not quite so much variety

- laying open the track
  - fistulotomy
  - cutting seton
  - LO and repair

excising or obliterating the track

fistulectomy
FiLaC
VAAFT

- disconnecting the track from the gut
  - advancement flap
  - LIFT
  - OTSC

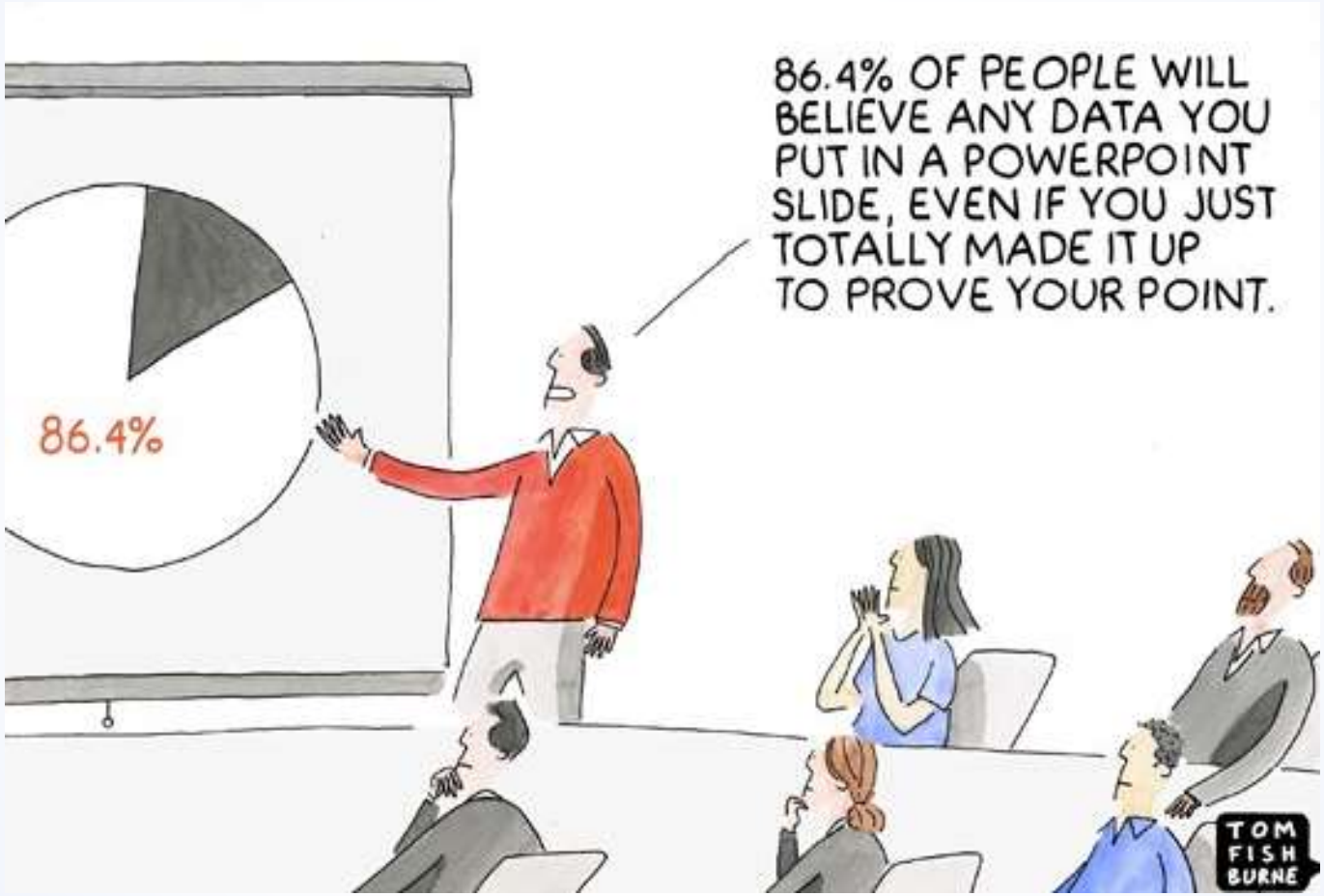
filling the track

glue
plug

correcting the immunopathology

stem cells

How do we unravel the literature to get the best results?



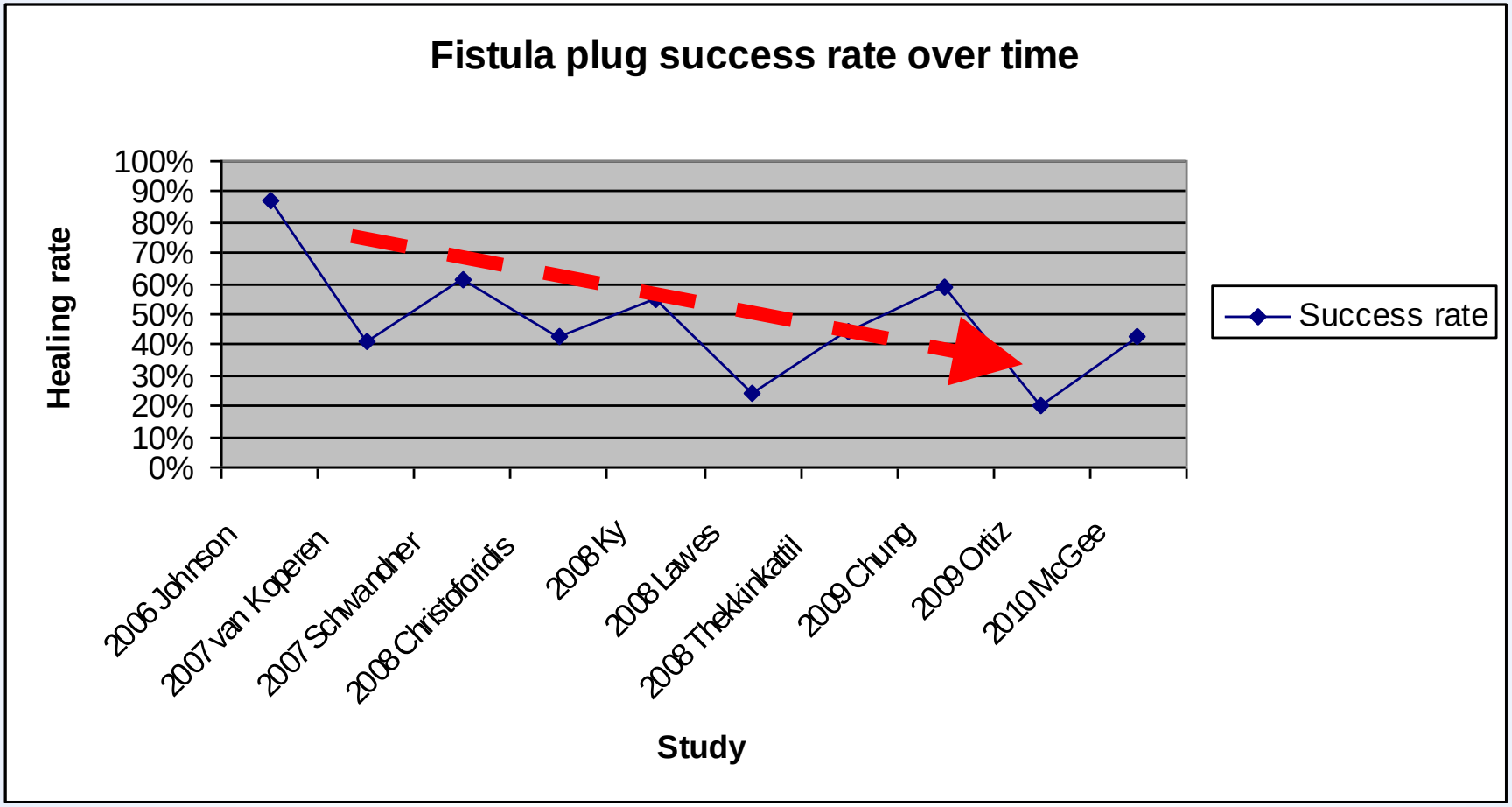
Fistula Glue

- low rate of success
- But is it worth trying?

	Complex only		Simple and complex	
	Healed	Not healed	Healed	Not healed
Abel [12]	6	4		
Sentovich [15]			33	15
Loungnarath [16]	12	27		
Lindsey [19]	9	13		
Cintron [20]			48	31
Zmora [23]	32	28		
Tinay [24]			19	25
Buchanan [25]	3	19		
Venkatesh [26]	18	12		
Patrij [27]			51	18
Zmora [28]	8	16		
Total	88 (42.5%)	119 (57.5%)	151 (63%)	89 (37%)

Fistula Plug

First author	Year	F/U, mo, mean/ median (range)	Successful healing			Plug extrusion (n)
			Overall n (%)	Crohn's n (%)	non-Crohn's n (%)	
Van Koperen[25]	2011	11 (5–27)	9/31 (29)	n/a	9/31 (29)	4
Lupinacci[78]	2010	8.1	7/12 (58)	1/3 (33)	6/9 (67)	3
Chung[79]	2010	3	3/4 (75)	3/4 (75)	n/a	1
McGee[80]	2010	24.5 (7–43)	18/41 (43.9)	n/a	18/41 (43.9)	2
Adamina[81]	2010	7 (1.9–11)	6/12 (50)	n/a	6/12 (50)	n/s
Anyadike[82]	2010	14.2 (2–31.5)	26/36 (72.2)	1/3 (33)	25/33 (73.3)	n/s
Zubaidi[83]	2009	12 (6–18)	19/22 (86)	1/2 (50)	18/20 (86)	2
Schwandner[84]	2009	9	7/9 (77)	7/9 (77)	n/a	0
Schwandner[85]	2009	12	37/60 (62)	n/a	37/60 (62)	2
Ortiz[86]	2009	12	3/15 (20)	n/a	3/15 (20)	3
Wang[87]	2009	9 (3.5–22.3)	10/29 (34)	n/a	10/29 (34)	n/s
Chung[88]	2009	6	19/27 (70.4)	n/a	19/27 (70.4)	5
Christoforidis[89]	2009	14 (6–22)	12/37 (32)	n/a	12/37 (32)	7
Lawes[90]	2008	7.4	4/17 (24)	n/a	4/17 (24)	n/s
Starck[91]	2008	12 (3–17)	26/41 (63)	7/9 (78)	19/32 (59)	n/s
Garg[92]	2008	9.4 (6.2–17.5)	15/21 (71.4)	n/a	15/21 (71.4)	5
El-Gazzaz[93]	2008	7.1 (1.4–22)	8/30 (26.7)	2/11 (18)	6/19 (31.6)	n/s
Echenique[94]	2008	10	14/23 (60)	n/a	14/23 (60)	1
Van Koperen[95]	2007	7 (3–9)	7/17 (41)	1/1 (100)	6/16 (37.5)	7
Champagne[22]	2006	12 (6–24)	38/46 (83)	n/a	38/46 (83)	4


Fistula plug success rate over time
Healing rate
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2006 Johnson
2007 van Koperen
2007 Schwandner
2008 Christodoridis
2008 Ky
2008 Lawes
2008 Thekkinkattil
2009 Chung
2009 Ortiz
2010 McGee
Study
Success rate

FiLAC

Study	Median duration of follow-up mths (range)	Numbers	Operation time (mins)	Success
Giamundo et al. (2015)	30 (6-46)	45	20 (6-35)	32 (71%)
Ozurk et al. (2014)	12 (2 – 18)	50	-	41 (82%)
Wilhelm (2014)	7.4 (2-11)	11	-	9 (82%)
Wilhelm 2017	25.4 (6-60)	117	-	75 (64%)
Overall		223		

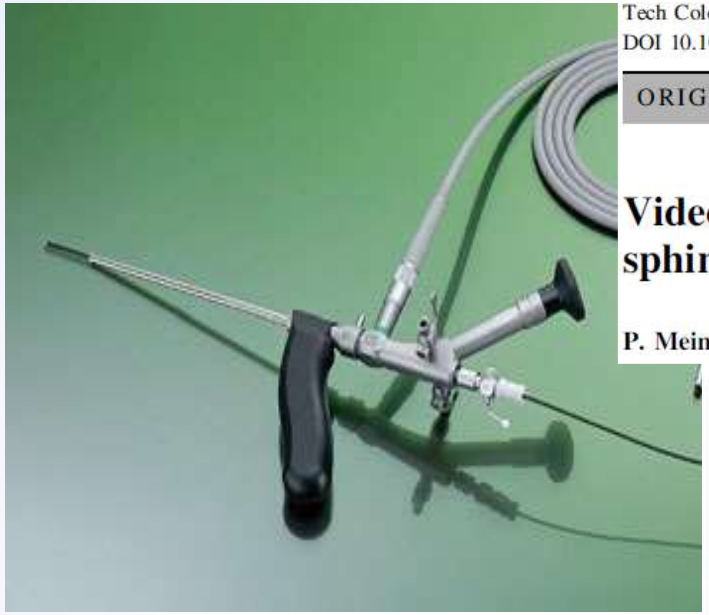
- Wilhelm closed the IO (usually)
- wider tracts probably fail more often
- similar success in (small n) Crohn's

complications

- recurrence
- recurrence
- recurrence (via abscess)

- pain, bleeding

- little or no incontinence reported



Tech Coloproctol (2011) 15:417–422
DOI 10.1007/s10151-011-0769-2

ORIGINAL ARTICLE

Video-assisted anal fistula treatment (VAAFT): a novel sphincter-saving procedure for treating complex anal fistulas

P. Meinero · L. Mori

good for assessing complex, branching tracts

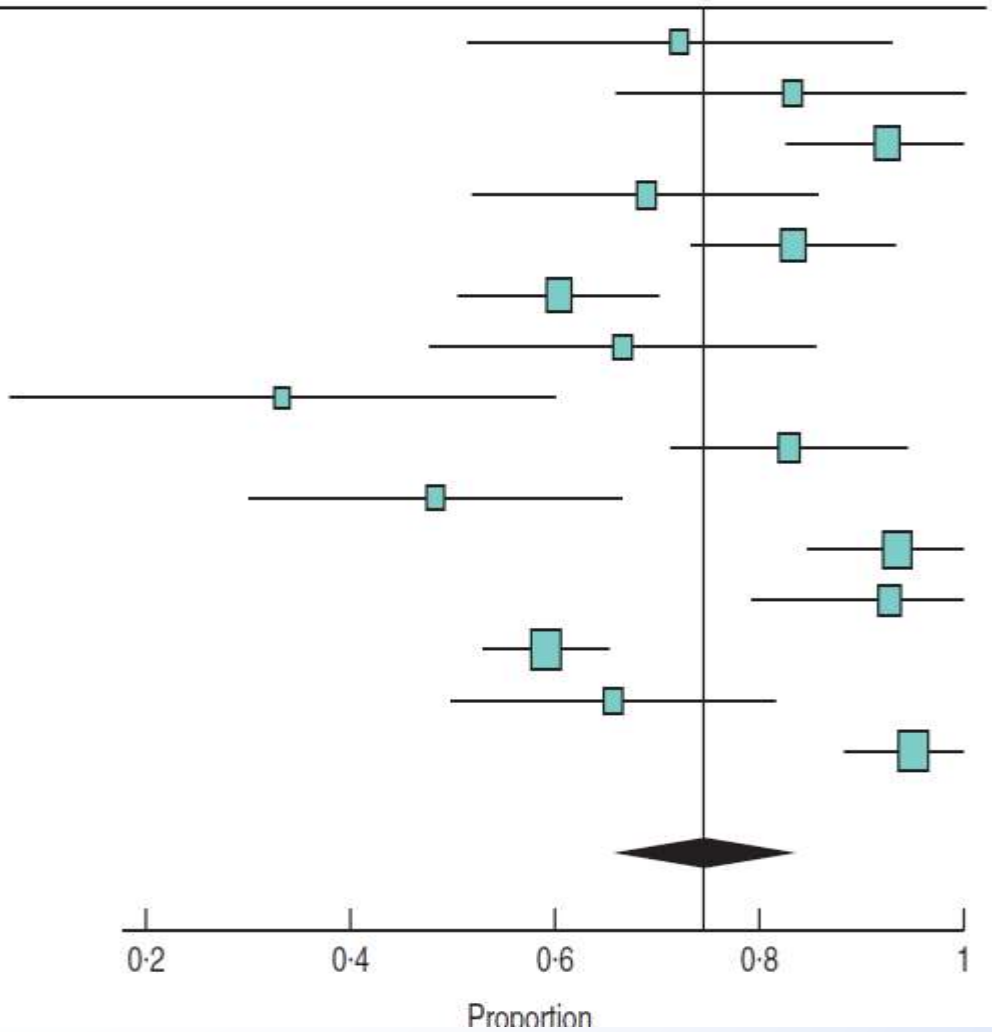
Meniero performs advancement flap

Study	Median duration of follow-up in mths (range)	Numbers	Operation time (mins)	Success (healing)
Schwandner 2012 (Ger)	8.5 (6-9)	10	22* (18-42)	9 (81%)
Kochhar et al. 2014 (Ind)	6	82	45 (30-90)	69 (84%)
Meinero et al. 2014 (Ita)	15 (6-69)	203	90 (60-120)	74%**
Mendes et al. 2014 (Bra)	5*	8	31.7 (18-45)	7(88%)
Walega et al. 2014 (Pol)	10*	18	67 (45 -135)	12(67%)
Grolich et al. 2014 (Cze)	4 (<1-30)	30	NS	N/A
Zarin et al. 2015	6	40	NS	40 (100%)***
Chowbey et al. 2015	NS	416	50 (22 – 94)	99 (73.8%?)
Overall		807		

Reference	Country	N	Age	F/U	CD	Time	Success
OTSC							
Prosst	Germany	96	50(20-80)	6	NS	32(17-66)	72(79%)
Menningen	Germany	10	41(26-69)	7(5-17)	4	41 (24-64)	7 (70%)
Gautier	France	10	43(24-86)	5(1-13)	4	25(15-35)	2 (20%)
Total		116			10		

- Advancement flaps

Reference	Estimate	Event rate
Van der Hagen *et al.*[18]	0·722 (0·515, 0·929)	13 of 18
Ellis and Clark[20]	0·833 (0·661, 1·000)	15 of 18
Perez *et al.*[21]	0·926 (0·827, 1·000)	25 of 27
Ellis and Clark[22]	0·690 (0·521, 0·858)	20 of 29
Van Koperen *et al.*[23]	0·833 (0·734, 0·933)	45 of 54
Chung *et al.*[24]	0·604 (0·506, 0·702)	58 of 96
Wang *et al.*[25]	0·667 (0·478, 0·855)	16 of 24
Adamina *et al.*[28]	0·333 (0·067, 0·600)	4 of 12
Jarrar and Church[30]	0·829 (0·714, 0·944)	34 of 41
Van Koperen *et al.*[32]	0·483 (0·301, 0·665)	14 of 29
Tan *et al.*[35]	0·935 (0·849, 1·000)	29 of 31
Mushaya *et al.*[8]	0·929 (0·794, 1·000)	13 of 14
Van Onkelen *et al.*[40]	0·591 (0·531, 0·652)	149 of 252
Madbouly *et al.*[9]	0·657 (0·500, 0·814)	23 of 35
Uribe *et al.*[42]	0·951 (0·885, 1·000)	39 of 41
Overall: $I^2 = 89\%$, $P < 0·001$	0·476 (0·656, 0·837)	497 of 721

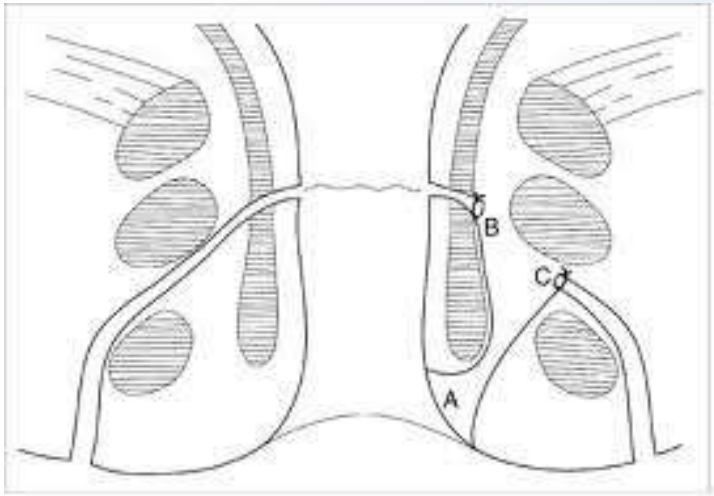


Imperial College London

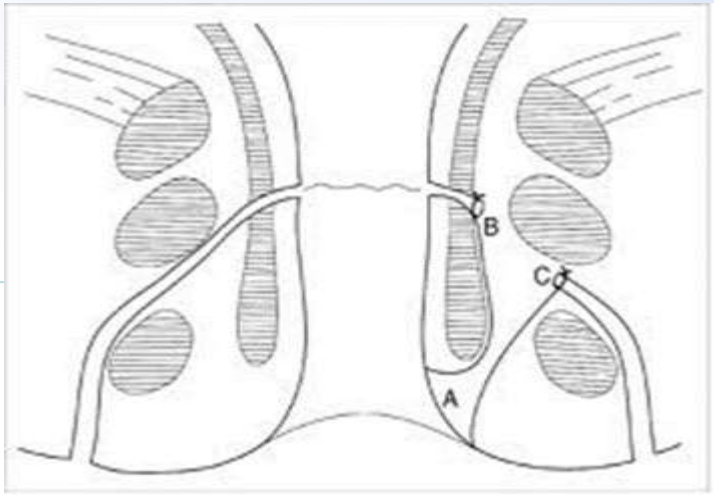
Stellingwerf et al BJS Open 2019

St Mark's Hospital and Academic Institute

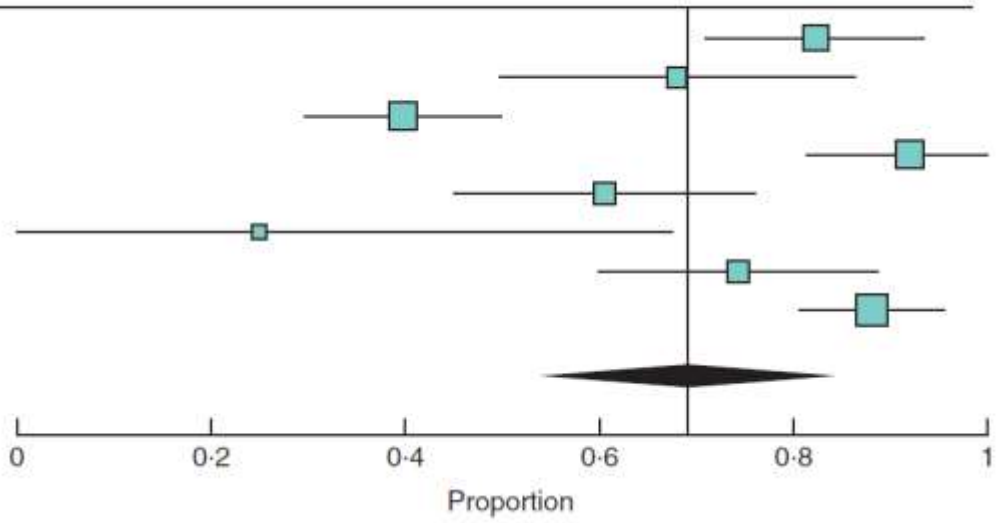
LIFT Procedure



Average healing approximately 70%



Reference	Estimate	Event rate
Shanwani *et al.*[27]	0·822 (0·711, 0·934)	37 of 45
Ooi *et al.*[33]	0·680 (0·497, 0·863)	17 of 25
Wallin *et al.*[34]	0·398 (0·298, 0·497)	37 of 93
Mushaya *et al.*[8]	0·920 (0·814, 1·000)	23 of 25
Liu *et al.*[37]	0·605 (0·450, 0·761)	23 of 38
Lehmann and Graf[38]	0·250 (0·000, 0.674)	1 of 4
Madbouly *et al.*[9]	0·743 (0·598, 0·888)	26 of 35
Schulze and Ho[43]	0·880 (0·806, 0·954)	66 of 75
Overall: $I^2 = 91\%$, $P < 0{\cdot}001$	0·691 (0·539, 0·843)	230 of 340



LIFT

Would Bio LIFT add value in difficult cases?

Imperial College London

St Mark's Hospital and Academic Institute

Stem Cells

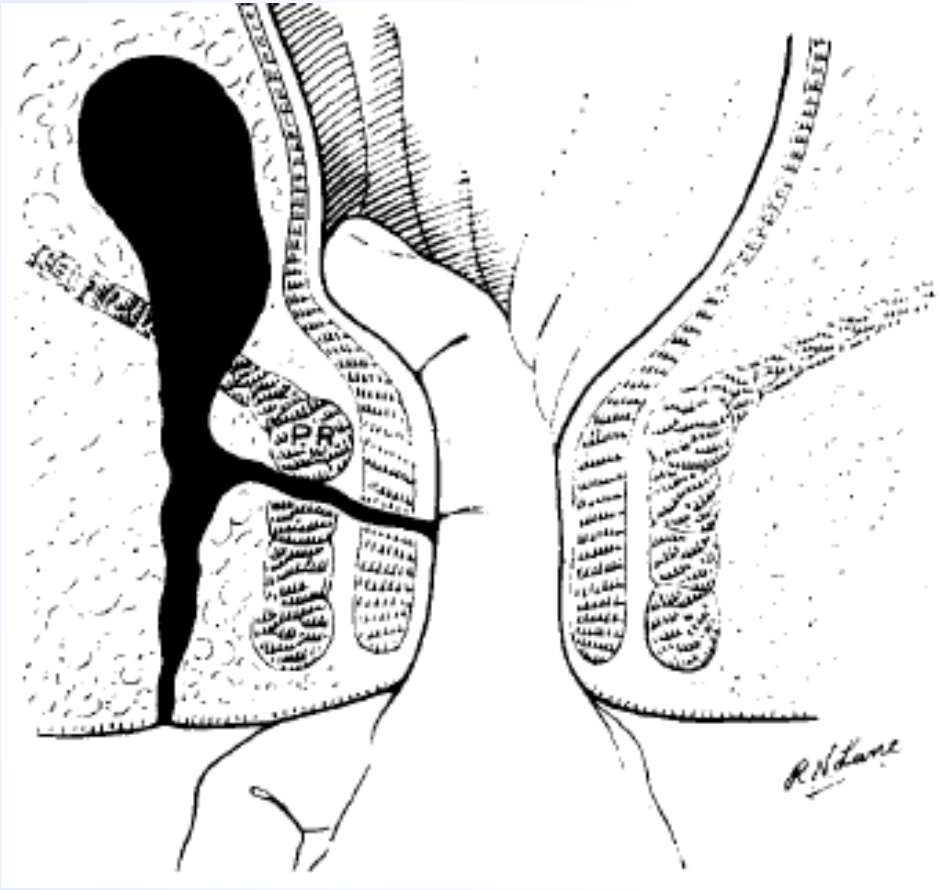
Ref.	Procedure	No. of patients treated	Healed (*n*)	Follow-up (mo)	Recurrence (*n*)	SAE (*n*)
García-Olmo *et al*[11]	Closure of IO. Injection in site, without fibrin glue	1	1	3	0	0
García-Olmo *et al*[12]	Cells resuspended in fibrin glue. Injection in site	9	6	12	Not specified	0
García-Olmo *et al*[13]	Closure of IO. Injection in site	Fibrin glue: 25 Fibrin glue + eASC: 24	Fibrin glue: 3 Fibrin glue + eASC: 17	12	Fibrin glue: 0 Fibrin glue + eASC: 2	4 (1 related to fibrin glue, others unrelated)
García-Olmo *et al*[22]	Closure of IO. Injection in site, without fibrin glue	1	1	36	1	0
Ciccocioppo *et al*[25]	Four injections in site	10	7	12	0	0
Cho *et al*[24]	Closure of IO and fibrin glue. Injection in site	9	3	15	0	0
Herreros *et al*[14]	Closure of IO. Injection in site	eASC: 64 Fibrin glue + eASC: 60 Fibrin glue: 59	eASC: 27 Fibrin glue + eASC: 24 Fibrin glue: 23	6	eASC: 0 Fibrin glue + eASC: 4 Fibrin glue: 0	4 unrelated to study treatment
Herreros *et al*[14]	Closure of IO. Injection in site	Not specified	eASC: 57% Fibrin glue+ eASC: 52.4% Fibrin glue: 37.3%	12	Not specified	1 unrelated to study treatment
Guadalajara *et al*[23]	Closure of IO. Injection in site	Fibrin glue: 13 Fibrin glue + eASC: 21	Fibrin glue: 3 Fibrin glue + eASC: 10	38	Fibrin glue: 1 Fibrin glue + eASC: 5	0
de la Portilla *et al*[17]	Closure of IO. Injection in site, without fibrin glue	24	9	4	Not specified	2 unrelated to study treatment
Lee *et al*[20]	Injection in site and fibrin glue	43	27	12	4	0

surgery – where we want to be

- the holy grail!! – does it exist or really should it exist
- MIS for extensions
- augmentation to improve outcomes for SPPs

Factors to consider when treating a fistula

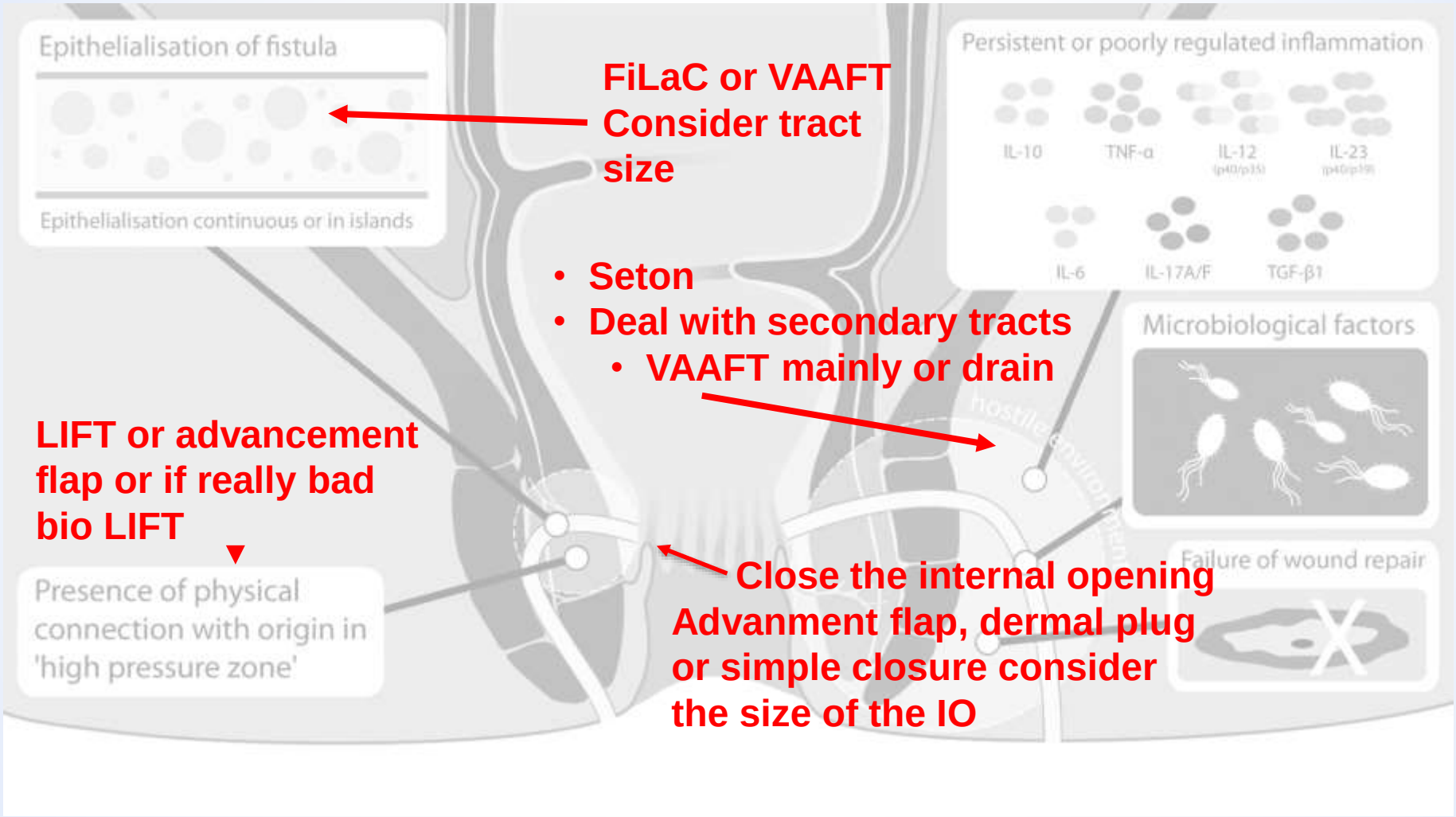
- Intersphincteric or Transphincteric
- How many tracts
- Size of the internal opening
- Degree of muscle damage from repeated sepsis
- some clues that may help you
- Is there faeces or air coming from the E/O
- probably big internal opening
- Amount of discharge
- maybe undrained collections



drain adequately from below?
place a seton
hope for improvement

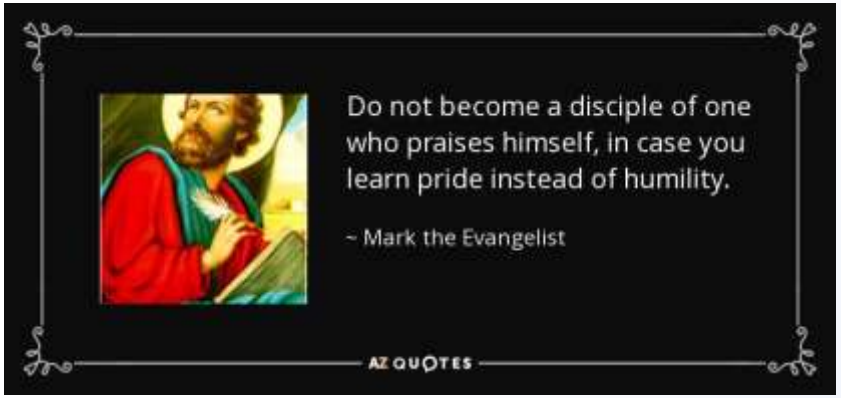
can we shrink the cavity without making a big hole?

dVAAFT


Epithelialisation of fistula
Epithelialisation continuous or in islands
FiLaC or VAAFT
Consider tract size
Persistent or poorly regulated inflammation
IL-10
TNF-α
IL-12
IL-23
IL-6
IL-17A/F
TGF-β1
Microbiological factors
Seton
Deal with secondary tracts
VAAFT mainly or drain
LIFT or advancement flap or if really bad bio LIFT
Presence of physical connection with origin in 'high pressure zone'
Close the internal opening
Advanment flap, dermal plug or simple closure consider the size of the IO
Failure of wound repair

One size does not fit all
Tailor the approach to the patient

Do not be a fistula evangelist



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