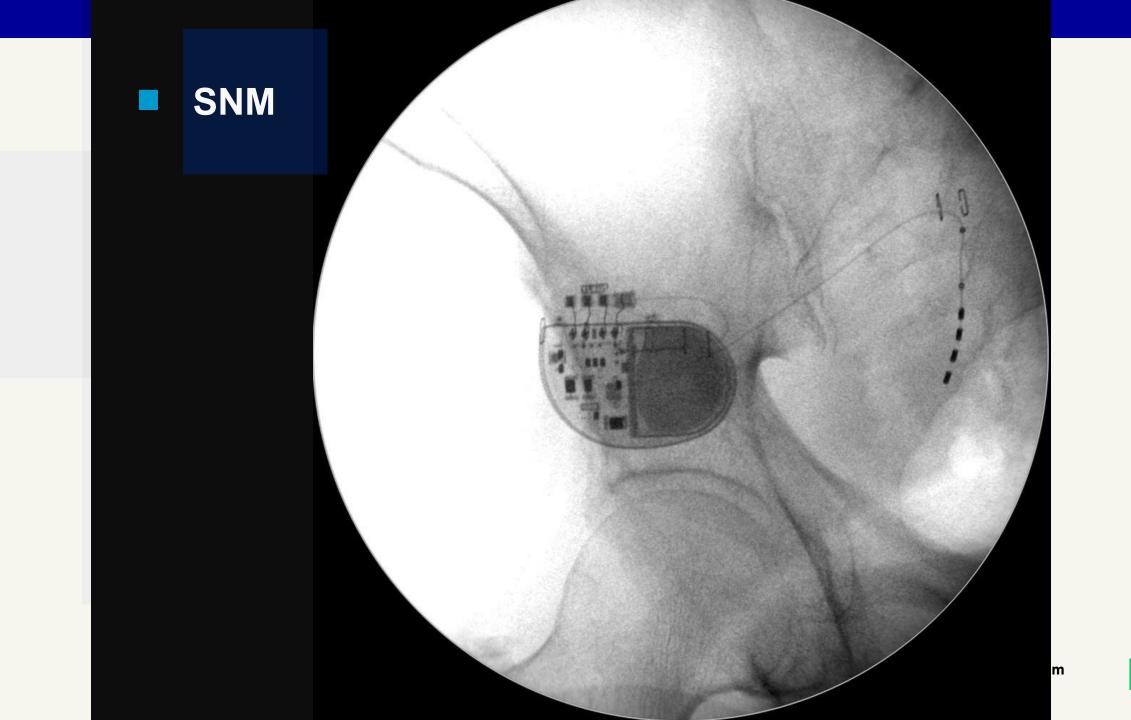
Sacral neuromodulation for fecal incontinence: Long term outcomes

K. E. Matzel

Department of Surgery, University Erlangen, Germany

21. Annual Conference of EGCRS, Cairo 28.08.2019







First implant for FI June 24, 1994

PM-Approval FDA March 14, 2011

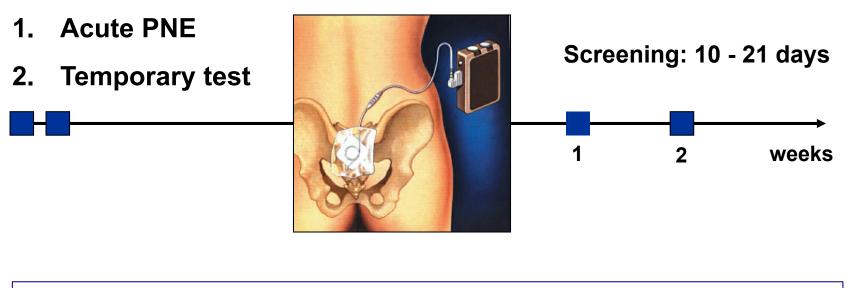
Evidence: Long Term Outcome

- Function
- QoL

Challenges with longterm therapy



SNM: Selection



Success:50% Improvement:Number of ICDays with IC

Success: 70%-80% Improvement



SNM: Outcome Measures

- Frequency of FI (n, days w/ FI)
- FI Score
- Urgency
- QoL

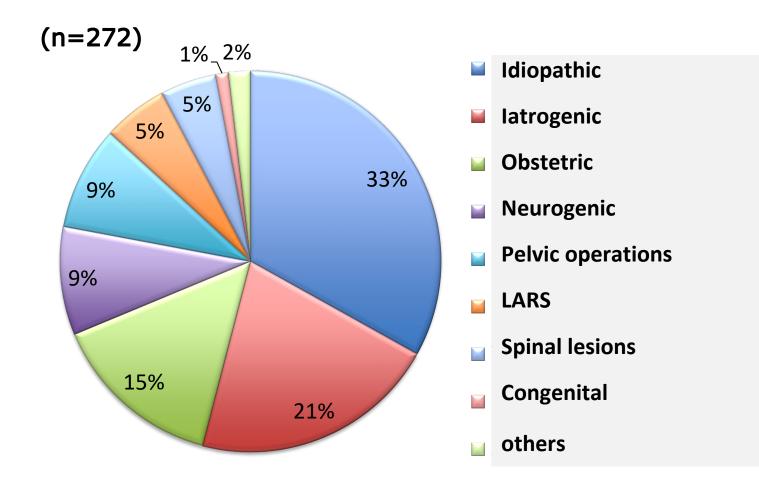


SNM: Outcome Measures

- Frequency of FI (n, days w/ FI)
- FI Score
- Urgency
- QoL
- Classification of success
 - 50% during the test
 - 50% with permanent implant
- PP vs ITT



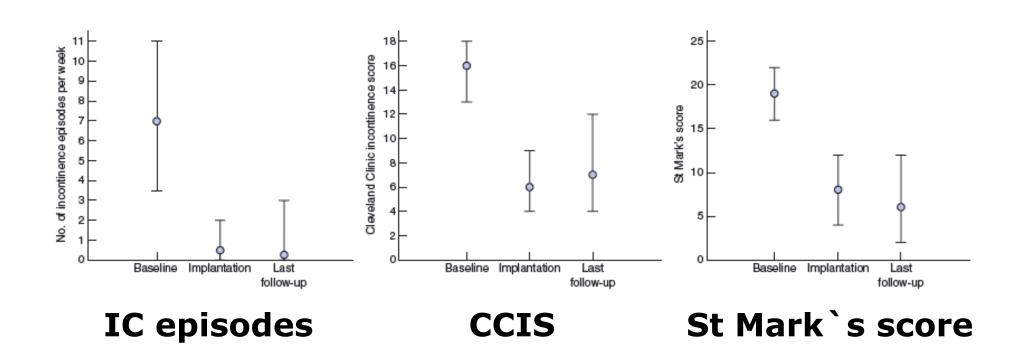
SNM: Long Term 84 m





Altomare et al, Br J Surg. 2015;102:407-15

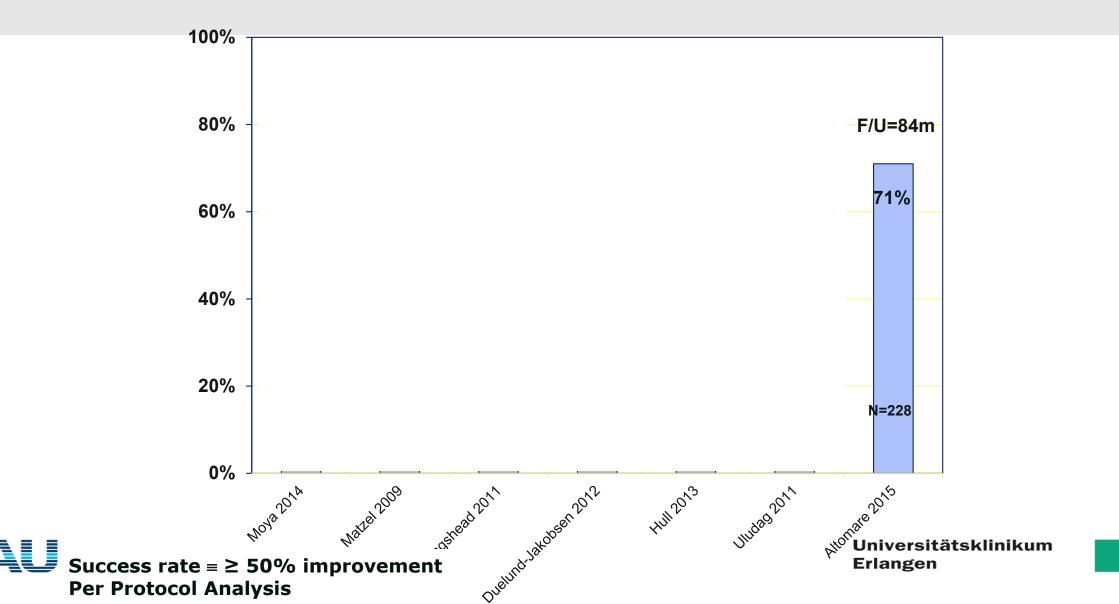
SNM: Long Term 84 m



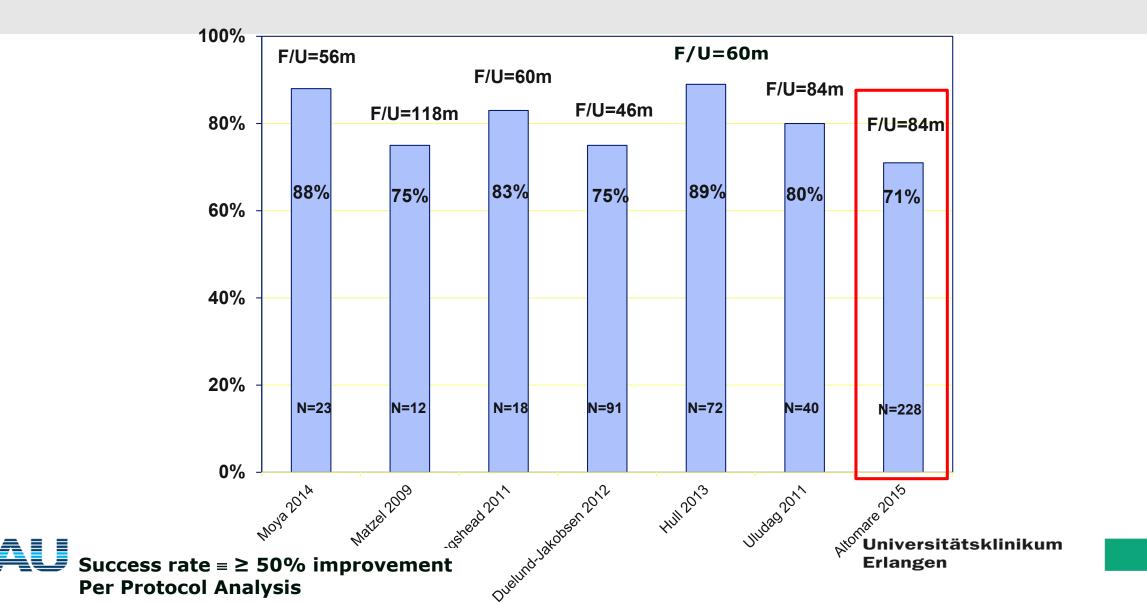


Altomare et al, Br J Surg. 2015;102:407-15

Long Term 46-118 m: 50% improvement



Long Term 46-118 m: 50% improvement



Original article

Long-term outcomes of sacral nerve stimulation for faecal incontinence

D. F. Altomare¹, S. Giuratrabocchetta¹, C. H. Knowles², A. Muñoz Duyos³, J. Robert-Yap⁴ and K. E. Matzel⁵ on behalf of the European SNS Outcome Study Group*

		No. of	patients	PP (%)
Reference	Follow-up (months)*	Baseline	Follow-up	≥ 50% improvement	Full continence
Maeda et al. ¹⁵	60	141	101	55.6	ñ.c.
George et al. ¹⁶	114	23	19	n.a.	52
Moya et al. ¹⁷	56	52	50	96	n.c.
Matzel et al. ¹⁸	118	12	9	78	44
Lim <i>et al.</i> ¹⁹	51	53	41	n.c.	n.c.
Hollingshead et al.20	60†	86	18	21	n.a.
Vallet et al.21	44‡	32	23	72	4
Duelund-Jakobsen et a	84		91	>50%:	710/
Altomare et al. ³¹			52		
Hull et al. ³²	mont	hs	77	100%	:50%
Uludağ et al. ²³	0-	00	36		
Present study	84	407	228	71.3	50.0
Summary median (range)	85 (44–118)	55 (12–407)	36.5 (9–228)	78 (21–96)	36 (4–52)



BJS 2015, 102, 407-15

Original article

Long-term outcomes of sacral nerve stimulation for faecal incontinence

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Altomare et al. ³¹			52		
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Uludağ et al. ²³	U-1	50	36		
Present study	84	407	228	71.3	50.0
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BJS 2015, 102, 407-15

SNM: Long Term Results: FI episodes short vs. medium vs. long

		Permanent implants			Faecal incontinence episodes				
Reference	Median follow-up (months)	No. at baseline	No. at follow-up	% at follow-up	No. at. baseline*	No. at follow-up*	Difference	Р	
Summary* Short term Medium term Long term	12 (1–12) 24 (15–36) 51 (44–118)		27 (8–106) 16 (5–86) 13 (2–147)	88 (39–100) 64 (12–100) 70 (6–100)	8 (1–16) 8 (1–26) 8 (1–12)	1 (0–5) 1 (0–4) 1 (0–2)	7 (1 to13) 7 (1 to25) 7 (1 to12)		
	short (1	2m):		8 (1-1	5) 🔿	1 (0-	5)		
	medium	(24 m):	8 (1-2	5) 🔿	1 (0-	4)		
	long (51	m):		8 (1-12	2) 🔿	1 (0-	2)		



SNM: Results: CCIS

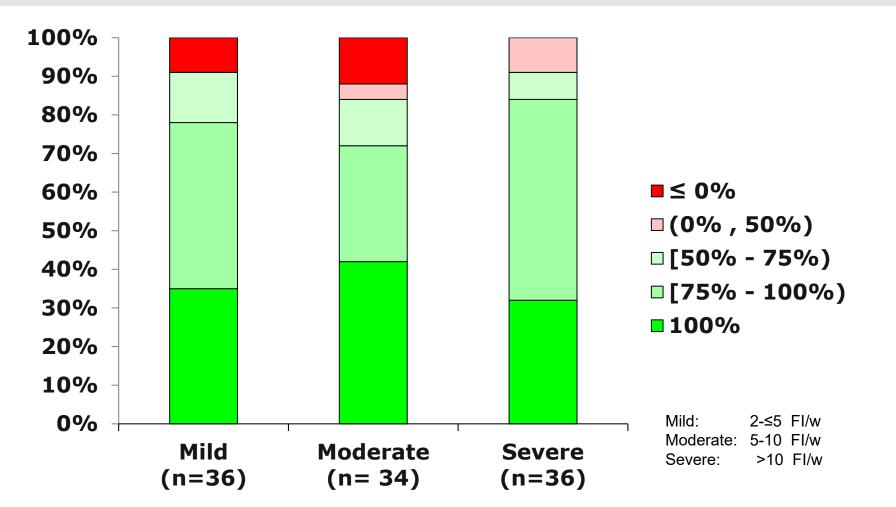
short vs. medium vs. long

			Permanent imp	plants				
Reference	Median follow-up (months)	No. at baseline	No. at follow-up	% at follow-up	Baseline score*	Follow-up score*	Score difference	
Summary*			~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	100.005.100				
Short term Medium term	6 (1-12) 24 (13-36)		29 (11–130) 41 (10–126)	100 (65–100) 100 (27–100)	15 (12–16) 15 (14–18)	6 (1–10) 8 (3–12)	-9 (-3 to -15) -7 (-3 to -14)	
Long term	50 (37–118)		23 (9–87)	75 (8–100)	15 (12-20)	7 (5–10)	-8 (-4 to -13)	
		•				C (4	10)	

short (6m):	15 (12-16) 🔿 6 (1-10)
medium (24m):	15 (14-18) 눡 8 (3-12)
long (50m):	15 (12-20) 💛 7 (5-10)



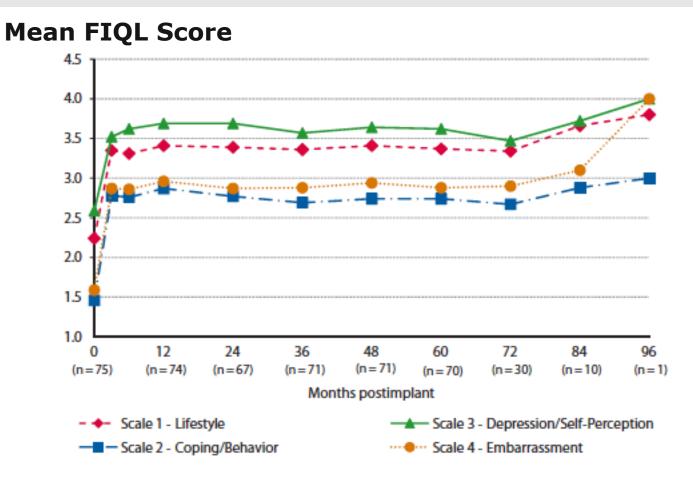
SNM IC: Efficacy after 5y





Mellgren A et al, Dis Col Rectum, 56 (5),43, 2013

SNM North American Multicenter Trial: 5 y



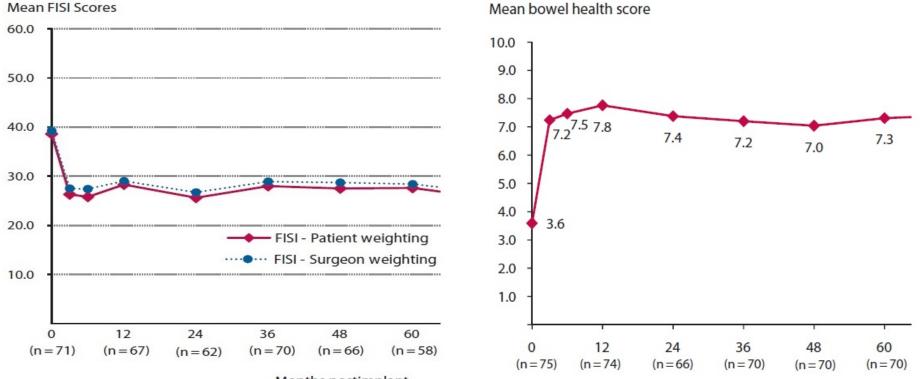


Hull et al, Dis Col Rectum, 56, 234-45, 2013



Mean FISI Score

Mean Bowel Health Score



Months postimplant



Hull T et al. Dis Colon Rectum. 2013;56:234-245 Mellgren A et al. Dis Colon Rectum. 2011;54:1065-1075

Study or sub-category	N	SNS Mean (SD)	N Na:	Conserv Therapy Mean (SD)	WWD (random) 95% Cl	Weight	WHD (random) 95% Cl
01 Physical functioning							
Hetzer	30	85.00(22.50)	37	55.00(25.00)		14.31	30.00 [18.61, 41.39]
Jamett 2005b Kenefick 2002b	15	92.50(1.25)	2	87.50(3.75)	-	18.65	5.00 [-0.48, 10.48]
Referics 20020	15	89 00(5 00)	15	69 40(23 25)	- Media	6.55	15.00 [-10.14, 40.14] 19.60 [-1.67, 40.87]
Hatzel 2004	29	1 0 25.201		64. 0 (8. 60)		18.10	.40 [-5.60, 20.40]
Ratto				47.0.7.0		1002	
Valsey			2	71 00 0.		0 19	
Subtotal (95% CI)	B		02			1 00 00	1 . 16 .
Test for heterogeneity: Ch = 16.1	53, df = 6 ()	P = 0.01), P = 67 /%					
Test for overall effect: Z = 5.09 (8	P < 0.00001	0	_	. .			
			Tan o	tal Int	J Colorect 2011		
02 Social functioning				L all IIIL			
Hetzer	30	75.00(21.75)	37	63.00(23.50)		18.76	12.00 [1.14, 22.86]
Jarrett 2005b	2	68.50(3.25)	2	44.00(9.50)		15.87	24.50 [10.58, 38.42]
Kenefick 2002b	1.5	75.00(30.00)	15	37.00(31.00)		10.08	38.00 [16.17, 59.83]
Malouf	5	67.20(22.00)	5	47.40(25.00)		6.79	19.80 [-9.39, 48.99]
Matzel 2004	29	81.90(27.50)	37	61.10(33.60)		15.14	20.80 [6.06, 35.54]
Ratio	4	59.50(4.25)	4	48.25(2.75)	-	24.18	11.25 [6.29, 16.21]
Vaisey	2	87.50(6.25)	2	43.50(15.75)		9.19	44.00 [20.52, 67.48]
Subtotal (95% CI)	87		102		•	100.00	20.91 [12.52, 29.29]
Test for heterogeneity: ChP = 15. Test for overall effect: Z = 4.89 (8	10, df = 6 () P < 0.00001	P = 0.02), P = 60.3%					
3 Role physical							
Hetzer Jamett 2005b	-30	75.00(25.00)	37	50.00(25.00)		18.98	25.00 [12.96, 37.04]
Jamen 20055 Kenefick 2002b	2	100.00(0.25) 75.00(49.00)	2	62.50(6.25)		22.52	37.50 [28.83, 46.17] 75.00 [44.23, 105.77]
Kenefick 2002b	15	75.00(49.00)	15	60.00(36.00)		+ 6.76 6.68	75.00 [44.23, 105.77] 35.00 [4.01, 65.99]
Malout Matzel 2004	29	75.00(25.00) 54.30(43.30)	37	40.00(25.00)		6.68	35.00 [4.01, 65.99] 9.70 [-11.61, 31.01]
Ratto	29	54.30(43.30) 63.00(5.50)	37	44.60(44.50) 45.25(2.50)		11.18	
Vaisev	2	100.00(0.25)	2	37.50(18.75)		8.64	17.75 [11.03, 23.67] 62.50 [36.51, 88.49]
Valsey Jubiotal (95% Cib	87	100.00(0.28)	102	37.80(18.75)		100.00	33.82 [20.95, 46.70]
Fest for heterogeneity: ChP = 34.1		P = 0.000015 E = 03 404			-	100.00	33.82 [20.95, 46.70]
rest for overall effect: Z = 5.15 ()	P < 0.00001)					
4 Role emotional							
Hetzer	30	78.00(20.50)	37	74.00(24.75)		27.53	4.00 [-6.84, 14.84]
Jamett 2005b	2	100.00(0.25)	1	100.00(0.00)			Not estimable
Kenefick 2002b	15	33.00(49.00)	15	0.00(41.00)		8.52	33.00 10.67, 65.331
Halouf	5	43.20(25.00)	3	11.00(8.25)		13.22	32.20 [8.38, 56.02]
Hatzel 2004	29	77.90(37.90)	37	56.00(43.60)		16.68	21.10 [1.41, 40.79]
Ratio	4	61.75(5.75)	4	41.25(2.50)	-	34.05	20.50 [14.36, 26.64]
Valsey	2	83.00(8.50)	1	33.00(0.00)			Not estimable
Subtotal (95% CI) Test for heterogeneity: ChP = 9.3 Test for overall effect: Z = 3.55 ()	87 3, df = 4 (P P = 0.0004)	= 0.05), P = 57.1%	58		-	100.00	18.48 [8.28, 28.68]
05 Mental beath							
Hetzer	30	73.00(15.00)	37	60.00(23.75)		15.97	13.00 [3.65, 22.35]
Jamett 2005b	2	27.50(7.25)	2	54.00(9.00)		11.10	23.50 [7.48, 39.52]
Kenefick 2002b	15	60.00(26.00)	15	36.00(27.00)		3.36	24.00 [5.03, 42.97]
Halouf	5	67.20(10.00)	5	57.00(11.00)		13.16	10.20 [-2.83, 23.23]
Hatzel 2004	29	70.10(22.00)	37	62.60(24.30)		14.37	7.50 [-3.91, 10.91]
Ratto	4	58,75(6,25)	4	42.50(1.25)	-	18.26	16.25 [10.00, 22.50]
Valacy	2	80.00(4.00)	2	70.00(3.00)	-#-	17.78	10.00 [3.07, 16.93]
Subtotal (95% Ci)	87		102		•	1.00.00	13.43 [9.85, 17.01]
Test for heterogeneity: ChP = 5.7 Test for overall effect: Z = 7.36 (i	2, df = 6 (P P < 0.00001	= 0.46), F = 0%					
16 Vitality							
Hetzer	30	66.00(18.75)	37	63.00(23.50)	-	17.72	3.00 [-7.12, 13.12]
Jamett 2005b	2	73.00(3.50)	2	55.00(7.50)		16.52	18.00 [6.53, 29.47]
Kenefick 2002b	15	35.00(28.00)	15	25.00(24.00)		10.98	10.00 [-8.66, 28.66]
Halouf	5	43.00(18.75)	5	34.00(15.00)		9.58	9.00 [-12.05, 30.05]
Matzel 2004	29	57.50(28.40)	37	48.80(29.00)		14.42	8.70 [-5.23, 22.63]
Ratto	4	47.25(5.25)	4	39.75(3.25)	-	21.20	7.50 [1.45, 13.55]
Valsey	2	75.00(2.50)	2	40.00(15.00)		9.57	35.00 [13.92, 56.08]
Subtotal (95% CI)	87		102		•	100.00	35.00 [13.92, 56.08] 10.77 [4.66, 16.07]
Test for heterogeneity: ChP = 9.76 Test for overall effect Z = 3.46 (i	6, df = 6 (P	= 0.14), P = 38.5%			-		
07 Bodily pain							
Hetzer	30	68.00(20.00)	37	58.00(22.50)		18.38	10.00 [-0.19, 20.19]
Jamett 2005b	2	80.50(9.75)	2	81.00(9.50)		11.30	-0.50 [-19.37, 18.37]
Kenefick 2002b	15	40.00(30.00)	15	50.00(26.00)		10.53	-10.00 [-30.09, 10.09]
Halouf	5	61.40(22.00)	5	37.20(15.50)		8.65	24.20 [0.61, 47.79]
Matzel 2004	29	55.80(30.10)	37	65.40(30.40)		14.37	-9.60 [-24.30, 5.10]
Ratto	4	53.75(2.75)	4	49.00(2.75)	-	23.62	4.75 [0.94, 8.56]
Valsey	2	92.00(4.00)	2	52.00(11.00)		13.16	40.00 [23.78, 56.22]
subtotal (95% CI)	87		102		•	100.00	7.99 [-2.32, 18.30]
est for heterogeneity: ChP = 27.1 est for overall effect Z = 1.52 (i	38, df = 6 ()	P = 0.0001), P = 78.1%			-		
8 General heath							
Hetzer	30	60.00(21.25)	37	50.00(25.00)		14.84	10 00 1-1 08 21 001
Jamett 2005b	30	83.00(2.50)	37	45.00(25.00)		19.39	10.00 [-1.08, 21.08]
Jamett 20055 Kenefick 2002b	15	83.00(2.50)	15	45.00(2.50)	-	19.39	38.00 [33.10, 42.90]
	15	40.00(31.00) 50.60(19.25)	15	37.00(27.00) 50.40(21.50)		6.66	3.00 [-17.80, 23.80] 0.20 [-25.10, 25.50]
	29	62,80(30,80)	37	54.60(29.00)		12.22	8.20 [-6.39, 22.79]
Malouf				33.50(1.75)	-	18.92	10 50 112 04 24 151
Malouf Matzel 2004							
Malouf Matzel 2004 Ratto	4	52.00(5.50)	4		-		10 00 10 14 17 051
Malouf Matzel 2004 Ratto Voisey	2	52.00(5.50) 92.00(0.25)	2	79.00(3.50)	+	19.41	13.00 [8.14, 17.86]
Malouf Matzel 2004 Ratto	2 87	92.00(0.25)	102		÷		18.50 [12.84, 24.16] 13.00 [8.14, 17.86] 14.92 [4.10, 25.74]

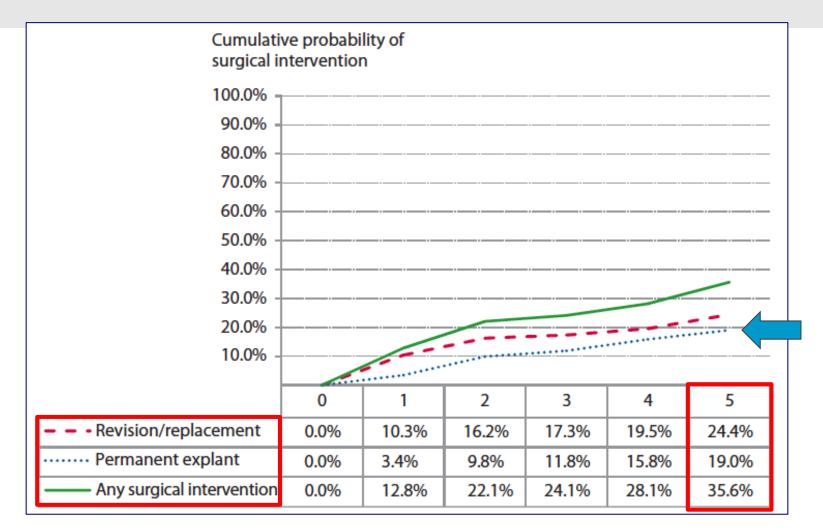
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n



^{-100 -50 0 50 100} Feynura Censery By Feynura SNS

SNM: Device Retention Rate 5 y: 81%

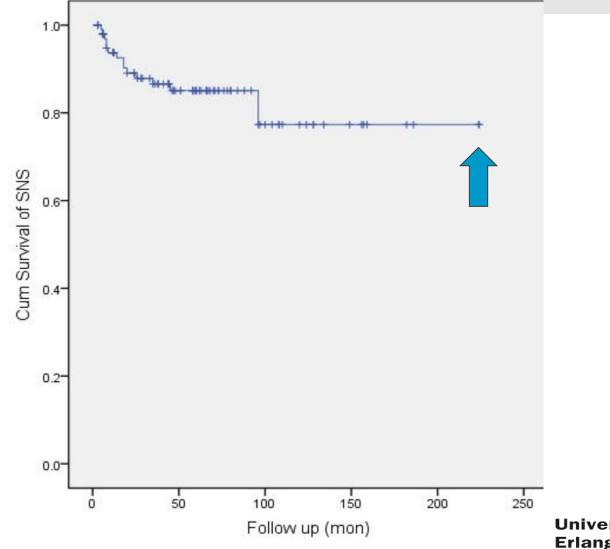




Universitätsklinikum Erlangen

Hull et al. Dis Colon Rectum 56, 234-45, 2013

SNM:18 y: Device Retention Rate: 78%





SNM for Fecal Incontinence

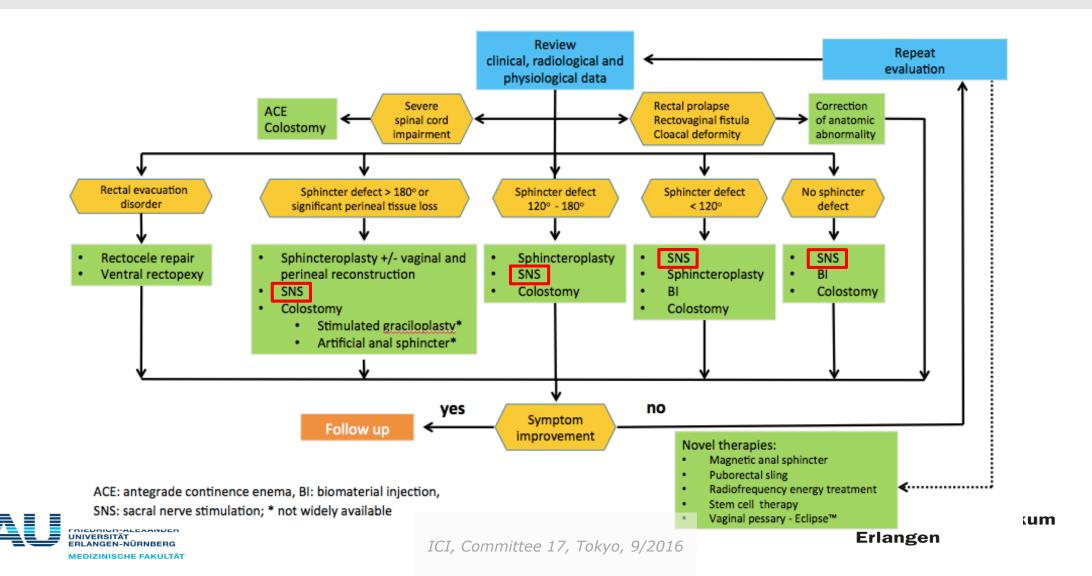
Efficacy: mostly immediately, IC & Qol improved (LE3)

- Incontinence scores & incontinence episodes/week are significantly decreased (LE2)
- SNS can be primary treatment for patients with sphincter defects (LE3)
- RCTs: QoL (SF-12, ASCRS, FIQL, EQ-4D) improved (LE2)
- The mechanism of action is most likely multifactorial and dependent on the underlying condition (LE4)

Cost Benefit (LE3)



Surgery for FI Algorithm





Battery longevity: replacement

Function after replacement for battery depletion

Loss of efficacy



Battery Longevity

	Battery life (years)	Publication year
Medtronic estimate (1)	Ø4.4 yr	2012
Author's opinion (2)	5-7 yr	2018
Author's opinion (3)	5-7 yr	2017
Real-life data (4)	≈ 6 yr (5-7)*≆	2019
Real-life data (5)	≥ 5 yr* ^γ	2016
Real-life data (6)	5.3 yr (<2V)* _Ÿ	2016
Real-life data (7)	6.3 yr*	2014

* explicitly referred to Interstim II; ^v median values



[1] cited in Cameron AP et al. Neurourol Urodyn. 2013;32:238-41; [2] Tahseen S. Int Urogynecol J. 2018;29:1081-1091;[3] Fontaine CL et al. Urol Ann 9:249-252; [4] Widmann B et al. J Neurogastroenterol Motil. 2019;25:159-170; [5] Duchalais et al. Int J Colorectal Dis. 2016;31:439-44;
[6] Siegel S et al. Female Pelvic Med Reconstr Surg. 2018;24(4):267-271; [17 Cui Zhe https://pdfs.semanticscholar.org/ef17/aa6b02290ced3ac8599de48b6205e735b0df.pdf

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How to Improve Battery Life?

- N: 27: battery exchange without lead revision at the time of battery depletion
- median battery life:
 - Amplitude ≤ 2V (n=15): 64 months
 - Amplitude > 2V (n=12): 38 months

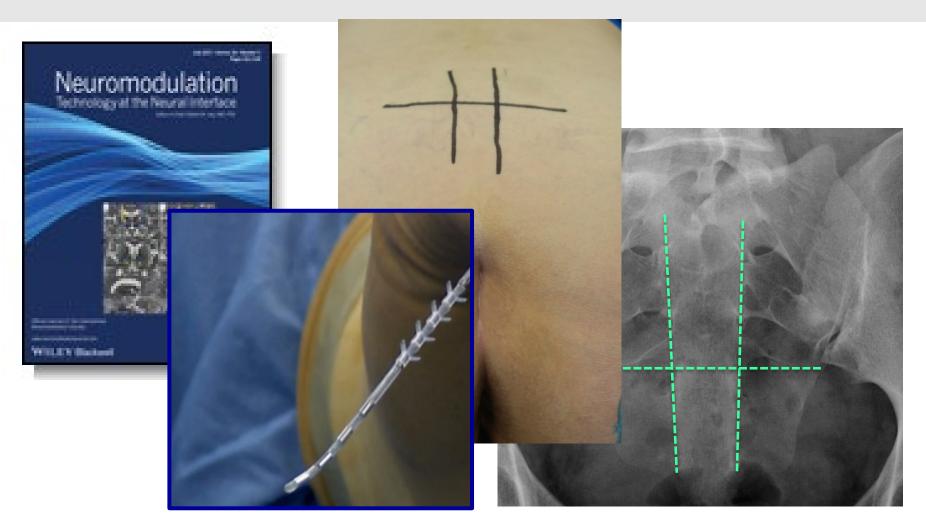


How to Improve Battery Life?

- N: 27: battery exchange without lead revision at the time of battery depletion
- median battery life:
 - Amplitude ≤ 2V (n=15): 64 months
 - Amplitude > 2V (n=12): 38 months
- optimized lead placement
- programming using extended duration cycling (e.g. 10 min ON; 10 min OFF)



Standardised Electrode Placement Technique





Matzel KE, et al Neuromodulation. 2017;20:816-824

Current Mean Amplitudes Historical Data vs. Standarisied Technique

2011

- Traditional implantation technique
- ≈2.1V @12months

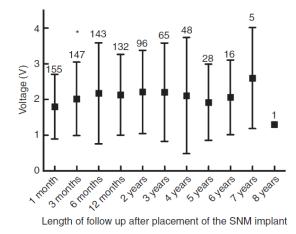


Figure I Mean voltage of the sacral nerve modulation (SNM)

Govaert B et al Colorectal Dis. 2011;13:78-81



2018

 Optimized lead placement with 3889 tined lead and curved stylet

1.0V @12month

Duelund-Jakobsen J et al. Colorectal Dis. 2018; 20:0152-0157.

Long-term Outcome after IPG exchange

- N: 143: N: 39: Replacement: (F: N=37)
- Med. follow-up before replacement: 115 months
- Med. follow-up after replacement: 29 months
- 82% (32/39): satisfaction similar as before IPG replacement
- 18% (7/39): reduced satisfaction, similar as before IPG replacement
- **Satisfied patients were younger** (65 years vs. 76 years)



Long-term Outcome after IPG exchange

- N: 143: N: 39: Replacement: (F: N=37)
- Med. follow-up before replacement: 115 months
- Med. follow-up after replacement: 29 months

Variable	Group A (N=32)	Group B (N=7)
PRO (0-10)	7.6 ± 1.6	5.5 ± 0.9
∆CCF-FI	-0.63	+1.86
∆FIQL	+0.27	-0.46

PRO: patient-reported outcome (0-10 with 10 reflecting the best clinical outcome/satisfaction); CCF-FI: Cleveland Clinic Fecal Incontinence Score; FIQL: Fecal Incontinence Quality of Life score



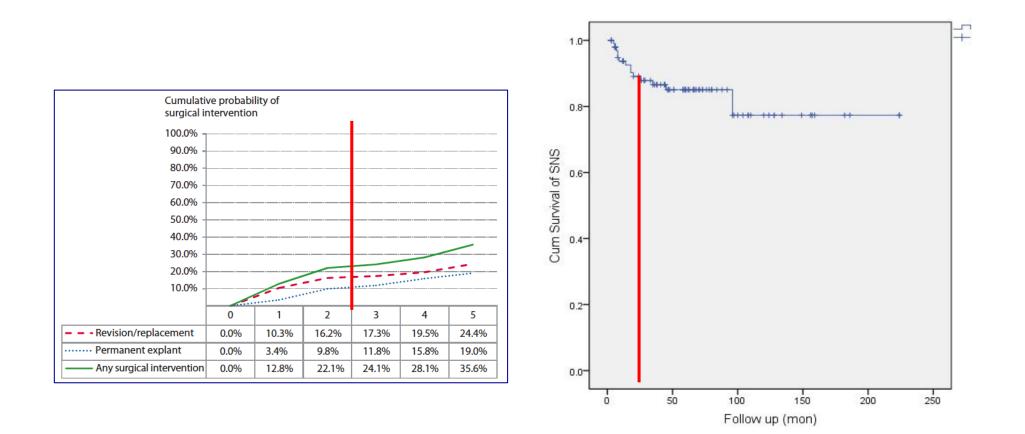


- Loss of efficacy typically occurs within the first
 2 years of the treatment [1]
- The mean time to definitive failure was 13.6 months (range 3–42.4) [2]



[1] Maeda Y et al, Br J Surg. 2011;98:140-147 [2] Melenhorst J, et al. Colorectal Dis. 2007;9:725-30

Loss of Effectiveness



Hull et al. Dis Colon Rectum 56, 234-45, 2013



Reasons for Loss of Effectiveness

Technical failure

- High (>4000 Ω) or low impedance (<50 Ω), lead migration
- Fibrosis around the lead



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Reasons for Loss of Effectiveness

Technical failure

EDIZINISCHE FAKULTÄT

- High (>4000 Ω) or low impedance (<50 Ω), lead migration
- Fibrosis around the lead
- New or progressive metabolic or neurologic issues
- "Accommodation" by the nervous system (steady increase of the amplitude)

Pettit. Int Urogynecol J 2010, 21 (Suppl 2):S491–S496; Siegel S, et al. Female Pelvic Med Reconstr Surg. 2018;24:267-271; Maeda Y et al. Br J Surg. 2011;98:140-147; Maeda Y et al. FRIEDRICH-ALEXAN Ann Surg. 2014;259:1126-31

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Reasons for Loss of Effectiveness

Technical failure

EDIZINISCHE EAKULTÄ

- High (>4000 Ω) or low impedance (<50 Ω), lead migration
- Fibrosis around the lead
- New or progressive metabolic or neurologic issues
- "Accommodation" by the nervous system (steady increase of the amplitude)
- Insufficient test duration and waning placebo effect
- No clear-cut definition of treatment success, symptoms fluctuate over time, changing patient expectation (change with increased confidence and activity)

Pettit. Int Urogynecol J 2010, 21 (Suppl 2):S491–S496; Siegel S, et al. Female Pelvic Med Reconstr Surg. 2018;24:267-271; Maeda Y et al. Br J Surg. 2011;98:140-147; Maeda Y et al. FRIEDRICH-ALEXAN Ann Surg. 2014;259:1126-31 UNIVERSITÄT ERLANGEN-NÜRNBERG

rsitätsklinikum gen

Prevention for Loss of Effectiveness

- Commonly used cut-off for chronic implant and considered successful treatment: 50 %
- If cut-off for the improvement of incontinence episodes required to avoid lack of efficacy over time: > 90% during test stimulation
- A highly selective patient population leads to better success rates, but will exclude many patients who may have a clinical benefit



Predictors for Poorer Efficacy

 Ø age, gender, duration of symptoms, main causes of FI, type of FI (i.e. active or passive), baseline symptom
 scores or medications taken.

Only loose stools and a history of diarrhea

Presence of an internal rectal prolapse (III,IV)

- Treatment success rates tended to be less favorable in men compared with women (1 y vs 5 ys: 89% and 44% vs 92% and 64%)
 - etiological profile of refractory FI in men was different from that in women, including predominantly anal surgery and LARS



Gallas et al. Colorectal Dis. 2011 13:689–696 Prapasrivorakul S et al. Int J Colorectal Dis. 2015 30:229-34 Brochard Cet al. Neuromodulation. 2019;22:745-750.

Failed SNM: What to do ?

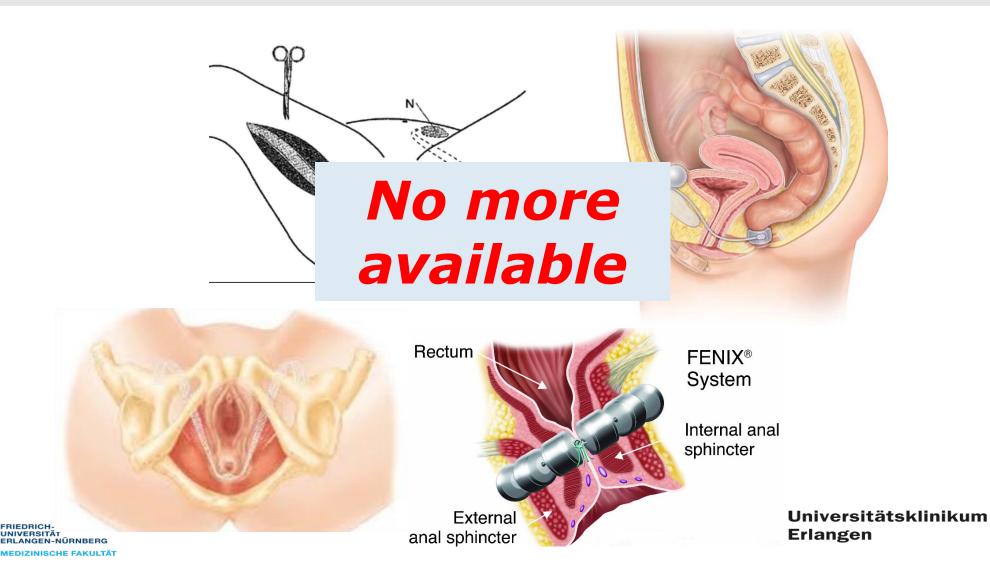
Reprogramming

Adjuvant therapies

- Medication, transanal irrigation
- Bulking agents / gatekeeper
- Revision surgery
 - Fresh nerve roots
- Surgical alternatives
- Stoma



Failure of SNM: Surgical Alternatives



Failure of SNM: Surgical Alternatives

Sphincteroplasty

Sphincter augmentation

- Gatekeeper
- Bioinjectables

Sphincter replacement

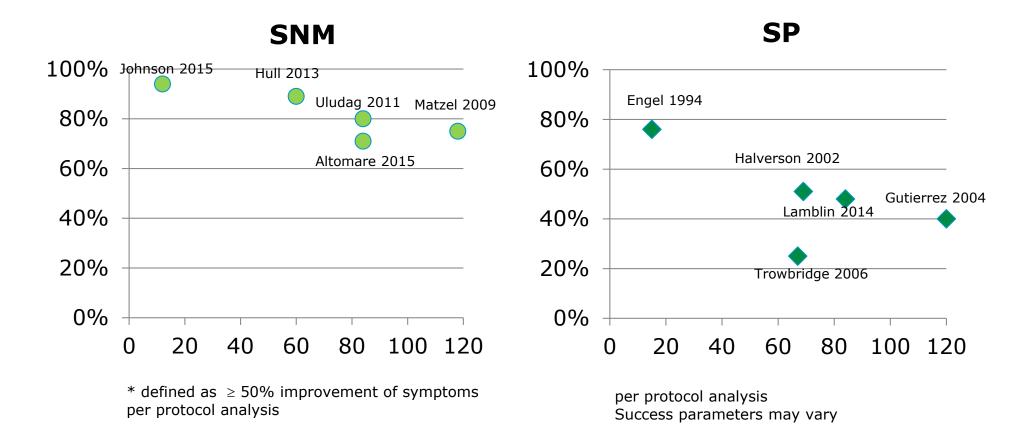
AMI Band

Stoma

Colostoma



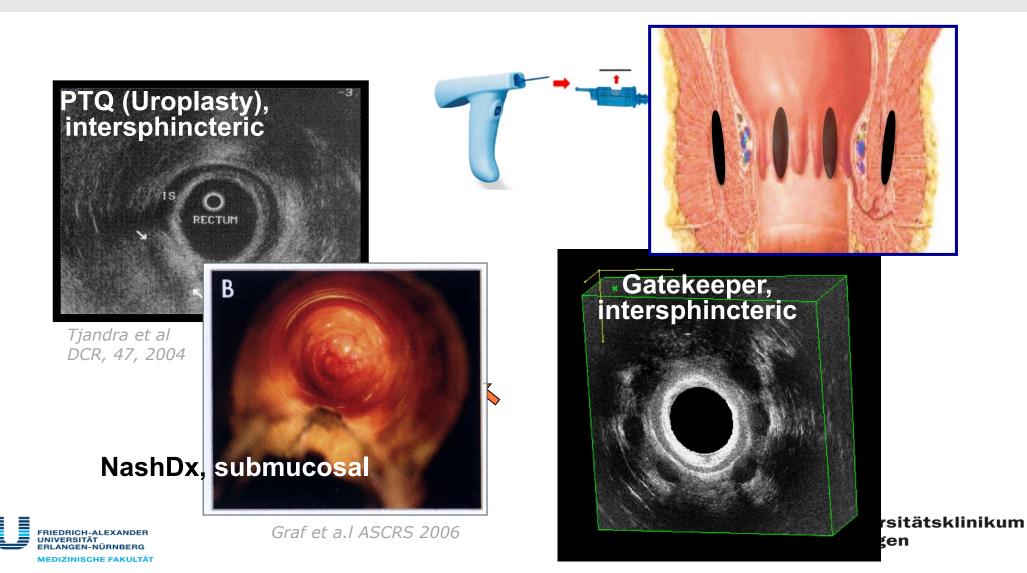
Long-term : SNM and Sphincteroplasty





5th International Consultation on Incontinence, Paris February, 2012.

Injectables / Bulking Agents



Failure of SNM: Surgical Alternatives

Sphincteroplasty

Sphincter augmentation

- Gatekeeper
- Bioinjectables

Sphincter replacement

AMI Band

Stoma 🛛

Colostoma



SNM Longterm Outcome: Summary

- First line: conservative treatment
- Longterm: Sustained clinical benefit: Incontinence, QoL
- Reproducable results
- Central role in current treatement algorithms "Surgical treatment for FI"
- Maintainence needed



Thank you

