



Aşırı Aktif Mesanede Nöromodülasyon

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Ondokuz Mayıs Üniversitesi Tıp Fakültesi –Samsun
14 Mayıs 2016 TÜAK Kayseri Toplantısı

Sunu Planı :

Nöromodülasyon

Uygulanması

Üroloji Pratigi

Botulünüm toksin ile karşılaştırma

Nörostimülasyon

- 1864: Budge ve ark. Sakral spinal kordun uyarımı ile mesanede kontraksiyon
- 1954: Boyd ve ark. mesaneye ilk direkt stimülasyon
- 1982: Tanagho ve Schmidt SNS implantasyonu



Nörostimülasyon

- Sakral
 - Pudendal
 - Posterior tibial
- 
- Santral- Periferal
- Elektrod
 - Patch

Sakral Nöromodulasyon

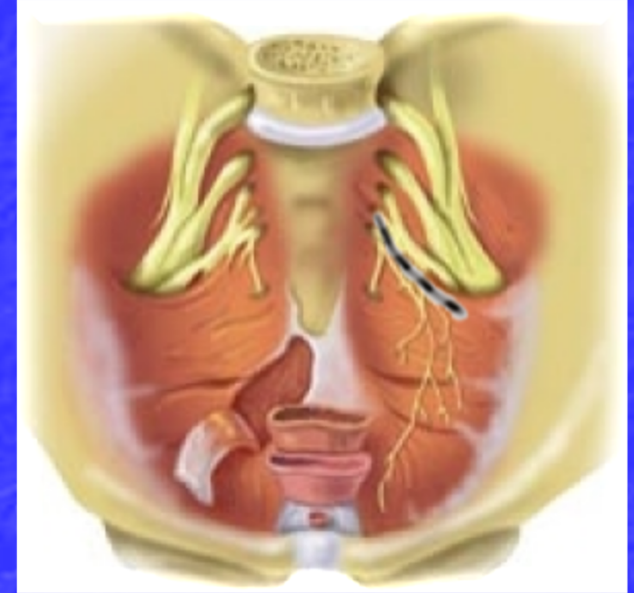
İmplant edilen bir sistem yardımıyla,

-mesane,

-sfinkter ve

-pelvik tabanı

etkileyen nöral refleksleri kontrol eden sakral sinirler stimule edilmektedir.

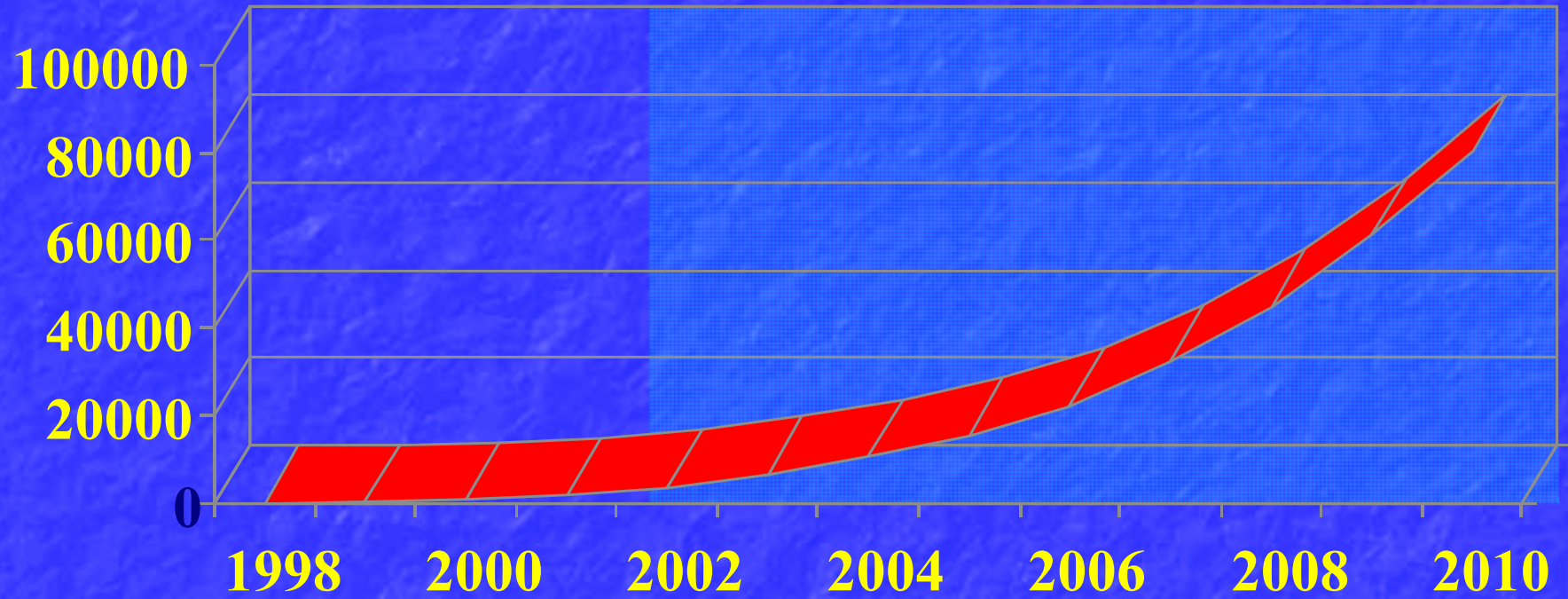


SNM; FDA:

- 1997'de urge inkontinans
- 1999'da obstrüksiyona bağlı olmayan üriner retansiyon ve sıkışma-sıklık sendromu için FDA onayı almıştır.

InterStim Tedavisi

Dünya Geneline Kümülatif Kullanımı



85.000' den fazla hastaya uygulanmıştır.

Sakral Nöromodulasyon

UUI ve AAM' de Etki Mekanizması:

- Üretral sfinktere giden liflerin aktivasyonu ile **detrusörün refleks gevşemesi**
- Uyarıcı ve baskılayıcı refleksler arasında dengenin sağlanması
- Afferent liflerin selektif aktivasyonun **spinal ve supraspinal seviyede oluşturduğu inhibisyon**
- Mesane pregangliyonik lifler inhibisyonu
- **Spinotalamik yoldan ağrı blokajı**
- Efferent inhibitör yolların tetiklenmesi
- Arka boynuzda GABA aktivasyonu
- Beyin sapı inhibisyonu

Etki

- Üriner NGF de azalma

Shalom ve ark. Am J Obstet Gynecol 2014

- Komplet SCI de etkisi yok

Schurch ve ark. World J Urol 2003

Hohenfellner ve ark. Urology 2001

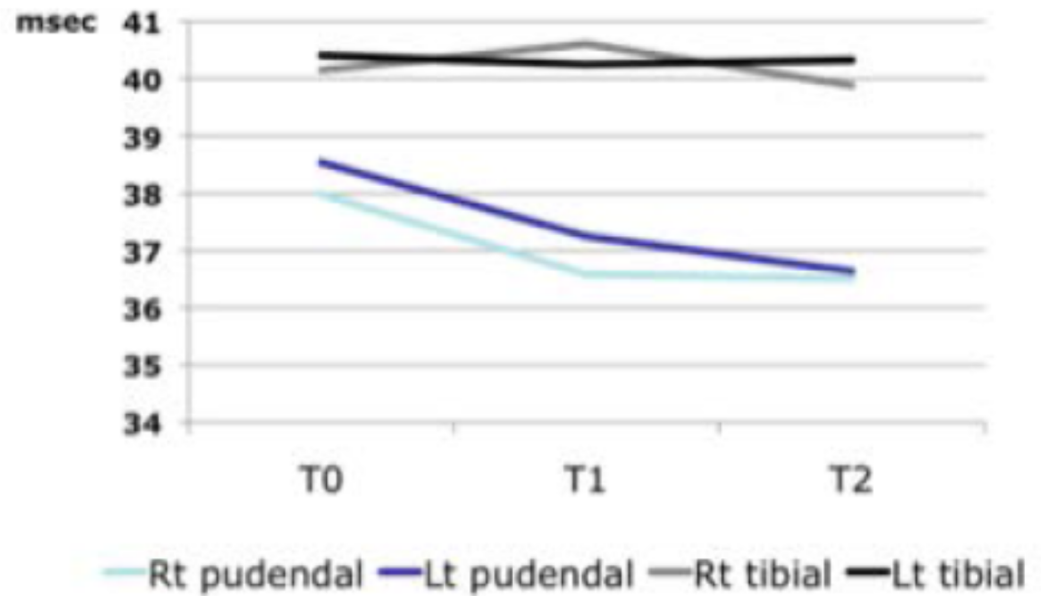
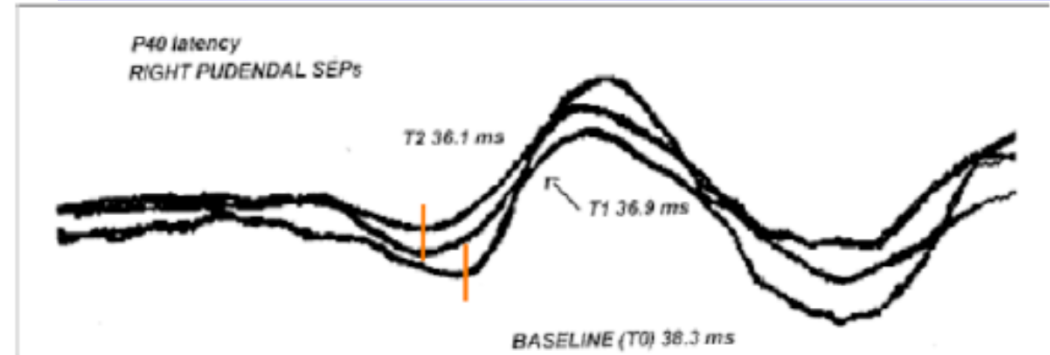
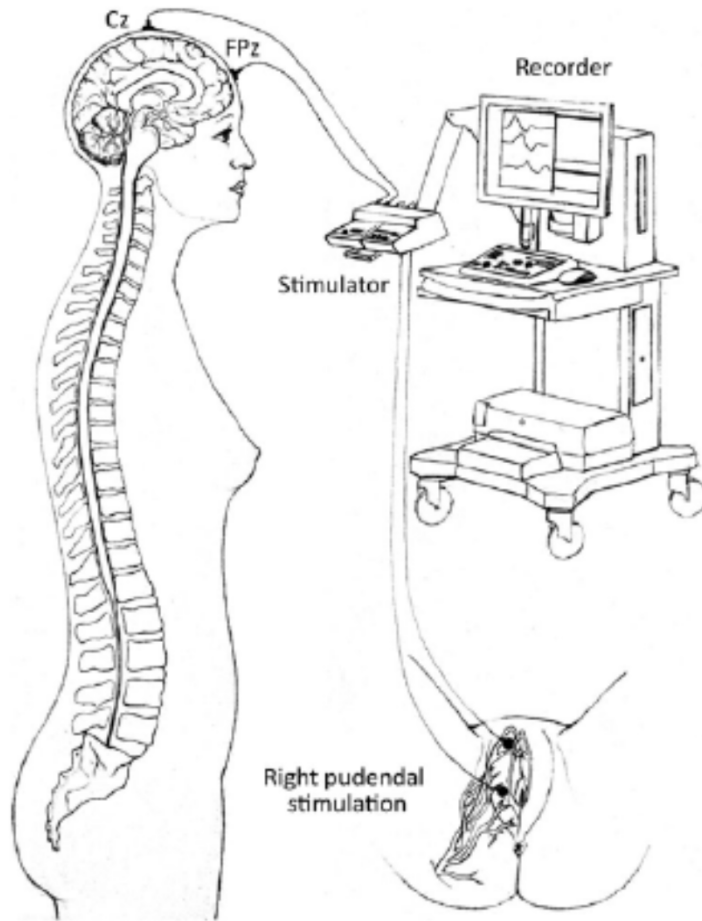
- İnkomplet SCI de ilk idrar hissi volümünde %102 artış, mesane kapasinde %125 artış

Chartier-Kastler et al. J Urol 2000

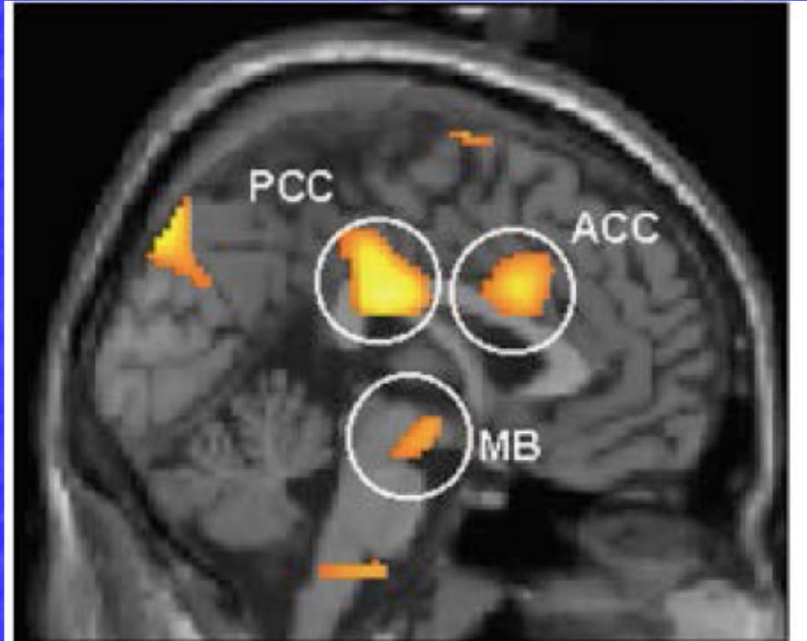
- İnkomplet SCI hastalarında iyi cevap

Lombardi ve ark. Spinal Cord 2009

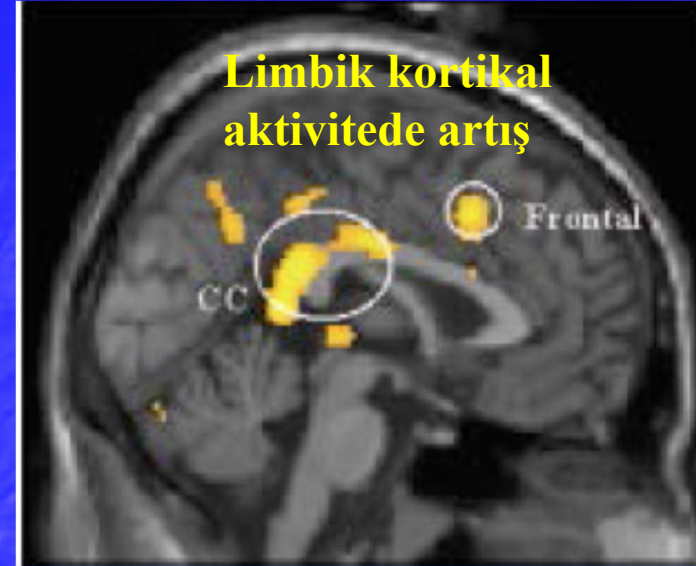
Kronik S3 stimölasyon



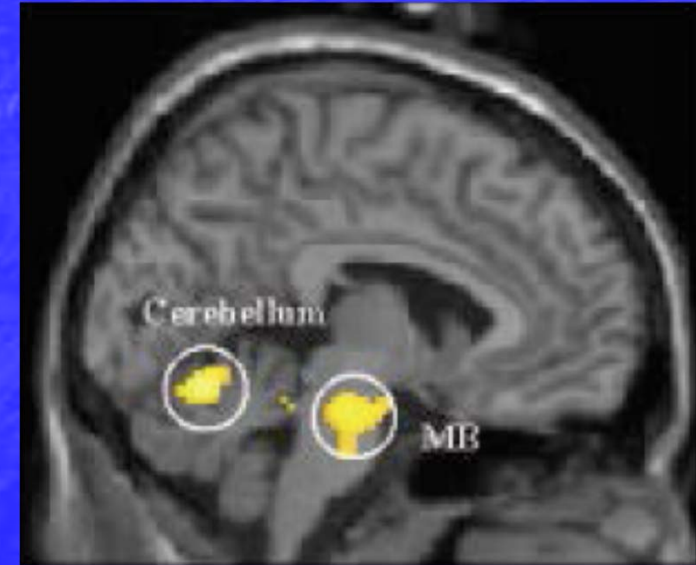
- Pudendal sinir afferent iletiminde modölasyon



Normal Fonksiyon



SNM
kapalı



SNM
açık

Fowler's Sendromu

Dasgupta ve ark. J Urol 2005¹¹

- Muhtemelen **aberran nöral aktiviteyi düşürerek** hastaların pelvik tabanı algılamalarına yardımcı olur
- Pelvik taban kaslarının istemli kontrolüne olanak sağlar.

Spinal korda giden afferent yollarının uzun süreli nöromodülasyonu ile **miksiyon refleksi** üzerinde aşırı bir **inhibisyon yapan**, pelvik tabanıda içeren **patolojik refleks inhibe** olmaktadır

Endikasyonlar

- Aşırı Aktif Mesane
- Nörojen Mesane
- Non obstrüktif üriner retansiyon
- İnterstisyel sistit

Kontrendikasyonları

- Genel durum bozukluğu
- Girişim yerinde enfeksiyon
- Rektal prolapsus
- Ventriküler stimülatör gerektiren kardiyak rahatsızlığı olan hastalar
- Test basamağına yetersiz yanıt veren hastalar
- Mental kapasitesi yeterli olmayan hastalar
- Potansiyel Ürolojik KE
 - BPH
 - Üretral darlık
 - Kanser
 - Mesanede yapısal anomali
- Sakrumda kemik anomalisi



İmplantasyon

- Test Periyodu

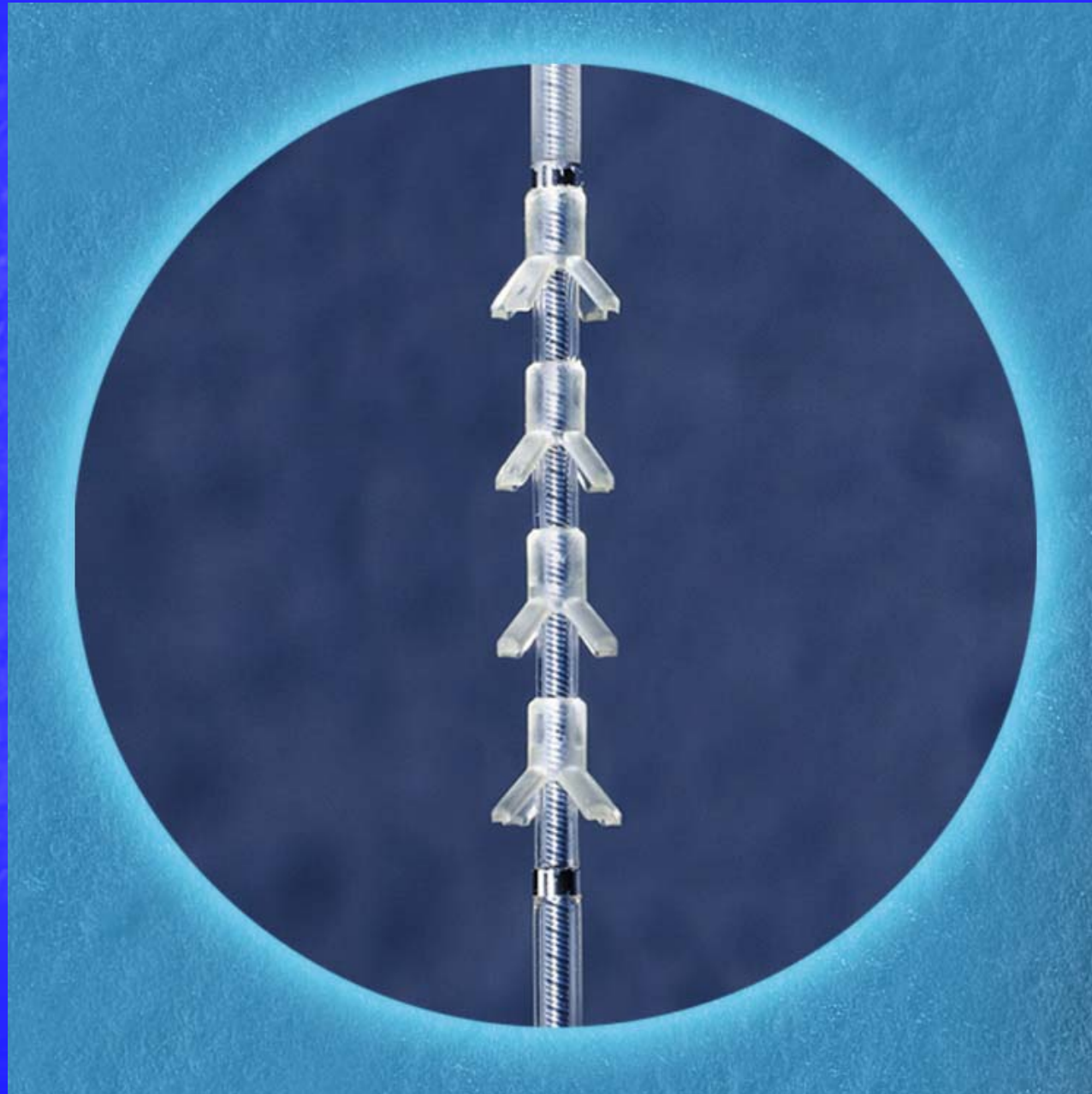
- PNE & Stage I

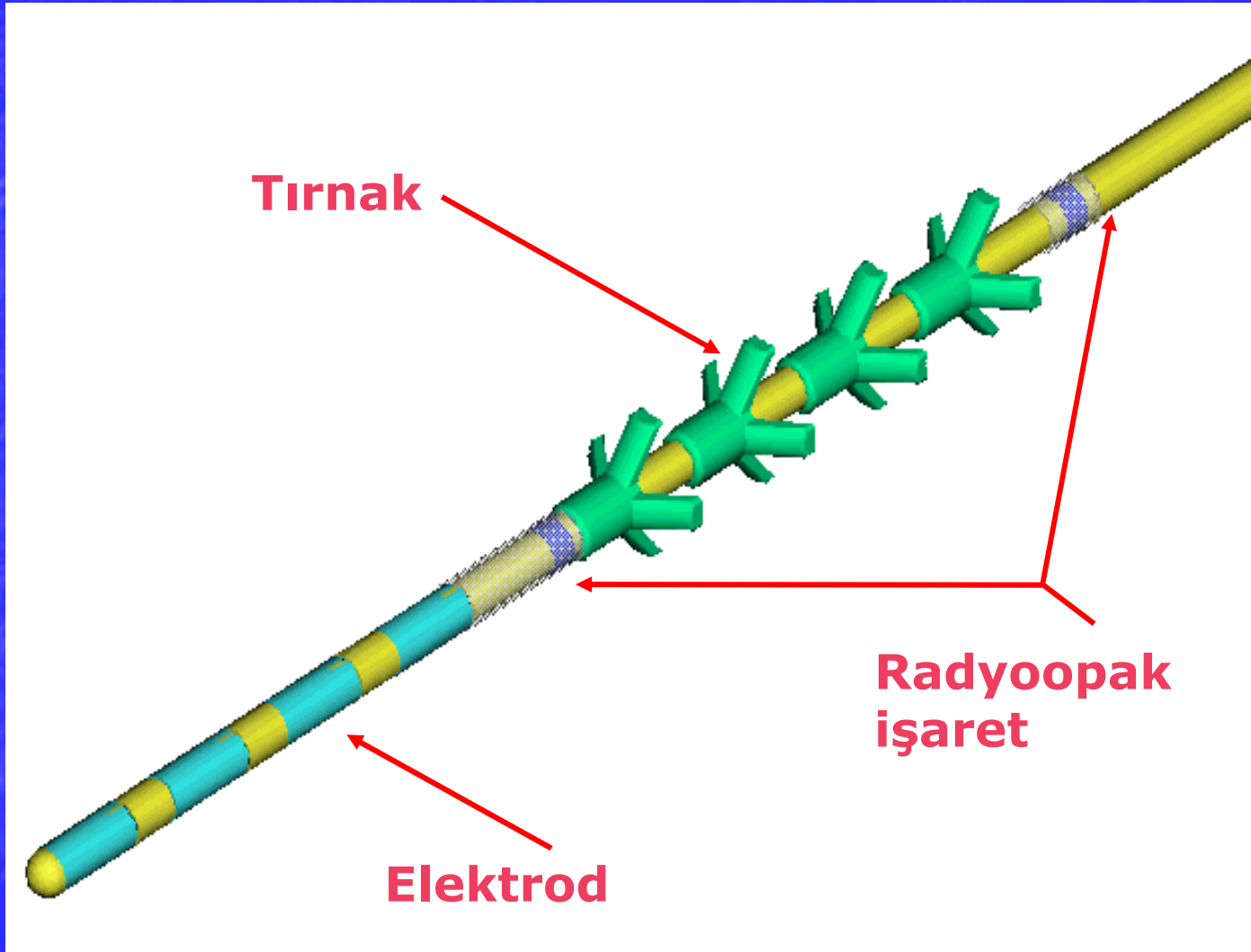
- Pozitif cevap quadripolarlarda daha fazla
 - Pozitif cevap test süresi arttıkça daha iyi
 - Test pozitifliği uzun dönem başarı için prediktif

- İmplantasyon

- %50 iyileşme



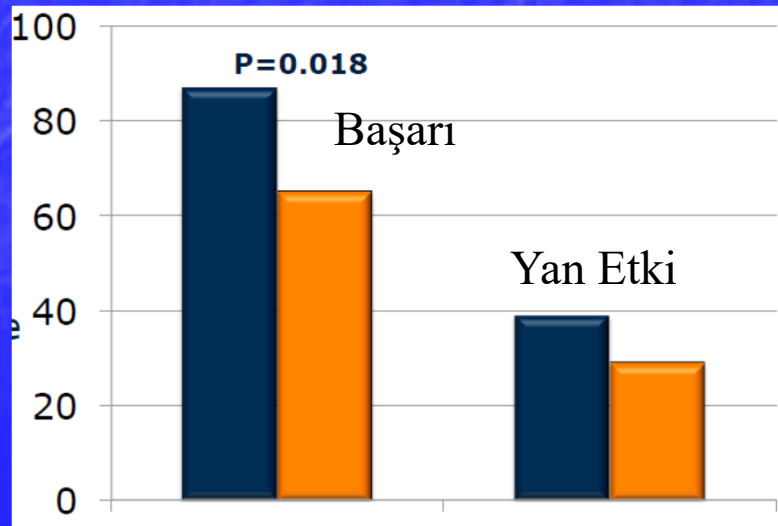




PNE	Hasta Sayısı	Pozitif Cevap
<i>Schmidt et al 1999</i>	155	63%
<i>Weil et al 2000</i>	65	68%
<i>Jonas et al 2001</i>	177	38%
<i>Everaert et a 2004</i>	114	37%
<i>Kessler et al 2007</i>	185	43%
Toplam Stage I	696	50%
<i>Spinelli et al 2005</i>	65	77%
<i>Borawski et al 2007</i>	17	88%
<i>White et al 2009</i>	221	91%
Toplam	303	88%

İyi hasta & Kötü Hasta

- İdiyomatik AAM
- Non obstrüktif Retansiyon
- Semptom süresi kısa olan
- DM
- Yaşlı Hasta
- Sling sonrası AAM
- Psikiyatrik sorunlar



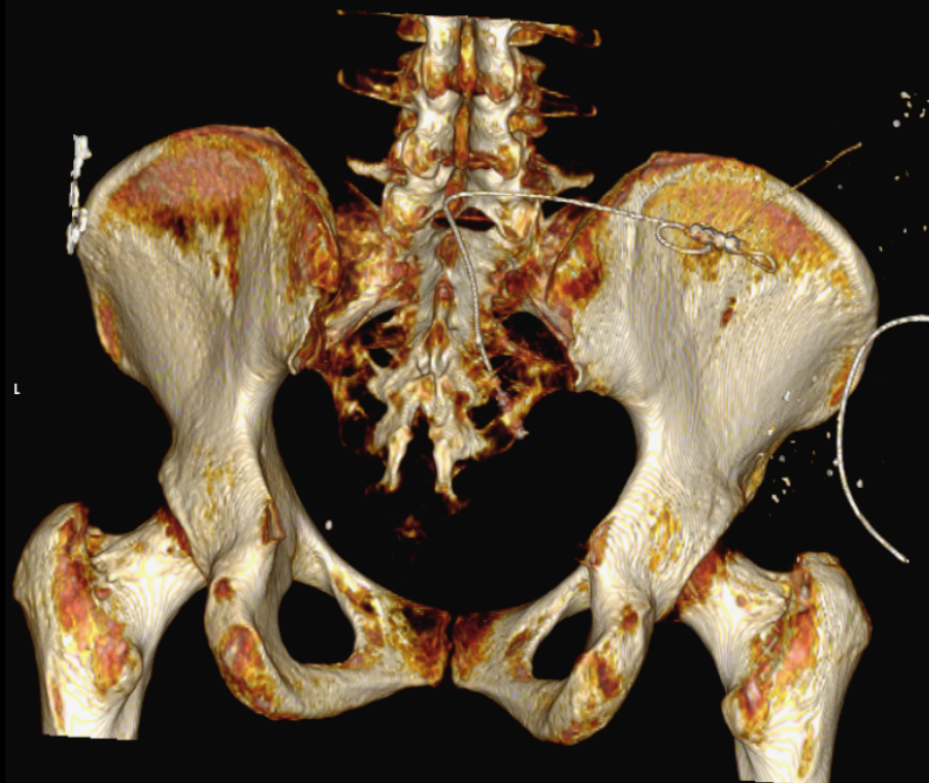
White ve ark. J
Urol 2009

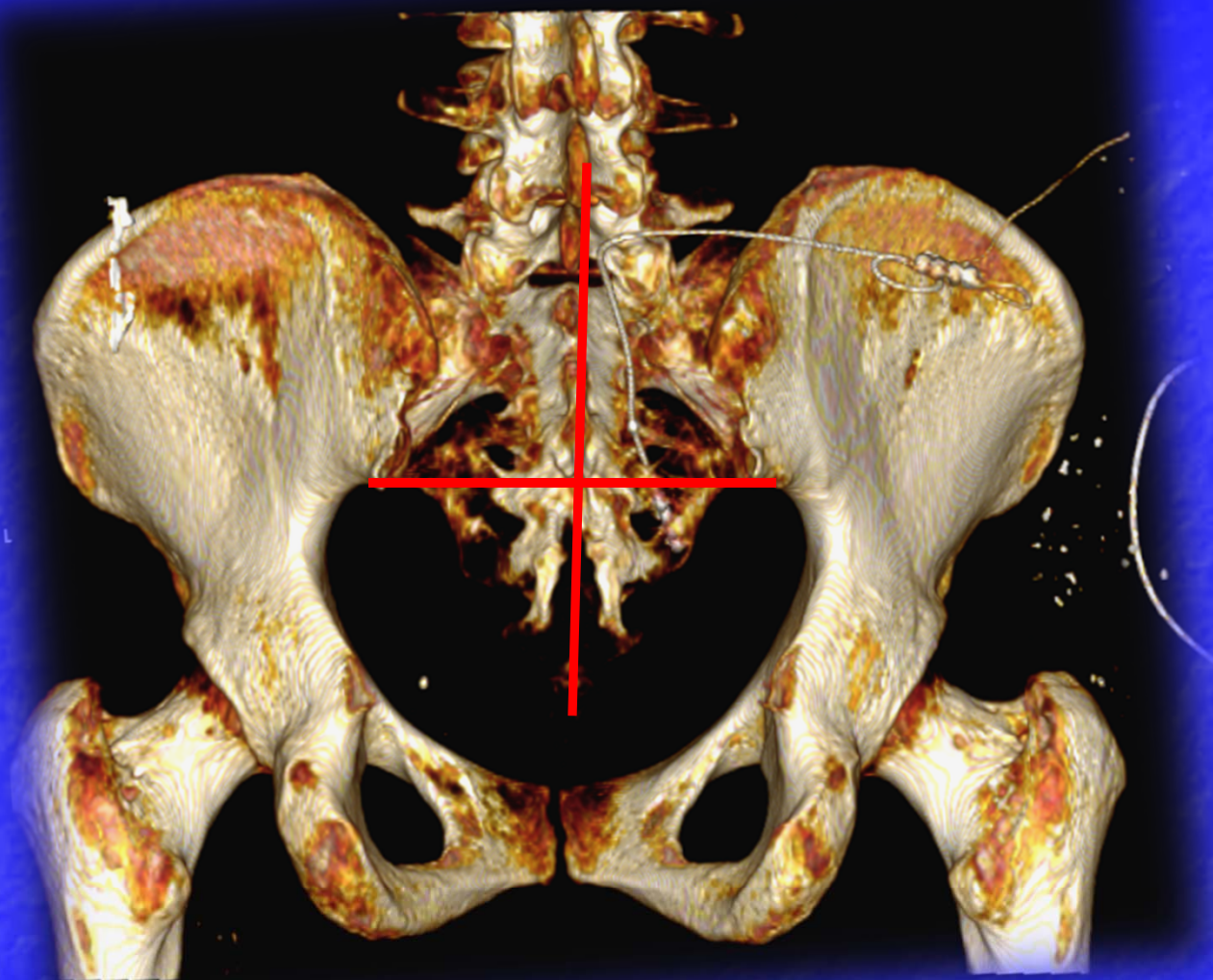
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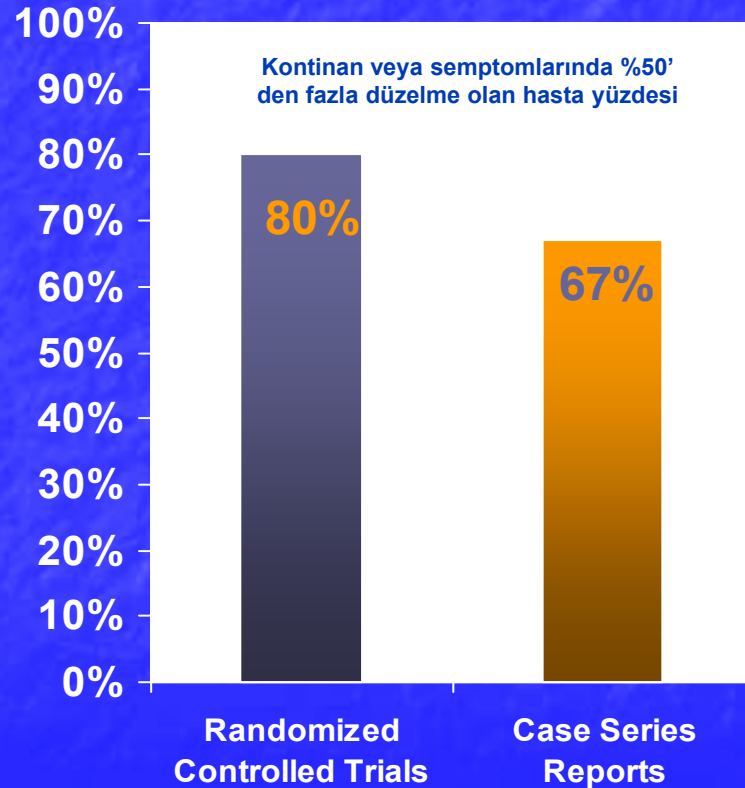




Efficacy and safety of sacral nerve stimulation for urinary urge incontinence: a systematic review.

Brazzelli M¹, Murray A, Fraser C.

- Sistematik Literatür Derlemesi: UUI
- Randomize kontrollü çalışmalar ve vaka serileri



34 klinik çalışmada, 1.827 implantasyon sonucunda, InterStim Tedavisinin UUI' da etkin bir tedavi yöntemi olduğu gösterilmektedir.

TABLO 2. Randomize kontrollü çalışmalarda 6 aylık sonuçlar (Kür: %90'dan fazla düzelme, Düzelme: %50'den fazla semptomlarda iyileşmeyi ifade etmektedir).

<i>Çalışma</i>	<i>n/toplam n (%yüzde)</i>		
SNM Grubu	Kür	Düzelme	Toplam İyileşme
<i>Weil ve ark.(25)</i>	9/16 (56)	5/16 (29)	%85
<i>Schmidt ve ark.(26)</i>	16/34 (47)	10/34 (29)	%76
<i>Weil ve ark.(27)</i>	0 (0)	5/5 (100)	%100
Geciktirilmiş Grup			
<i>Weil ve ark.(25)</i>	1/22 (5)	0/22 (0)	%5
<i>Schmidt ve ark.(26)</i>	0/42 (0)	2/42 (5)	%5
<i>Weil ve ark.(27)</i>	X	X	X

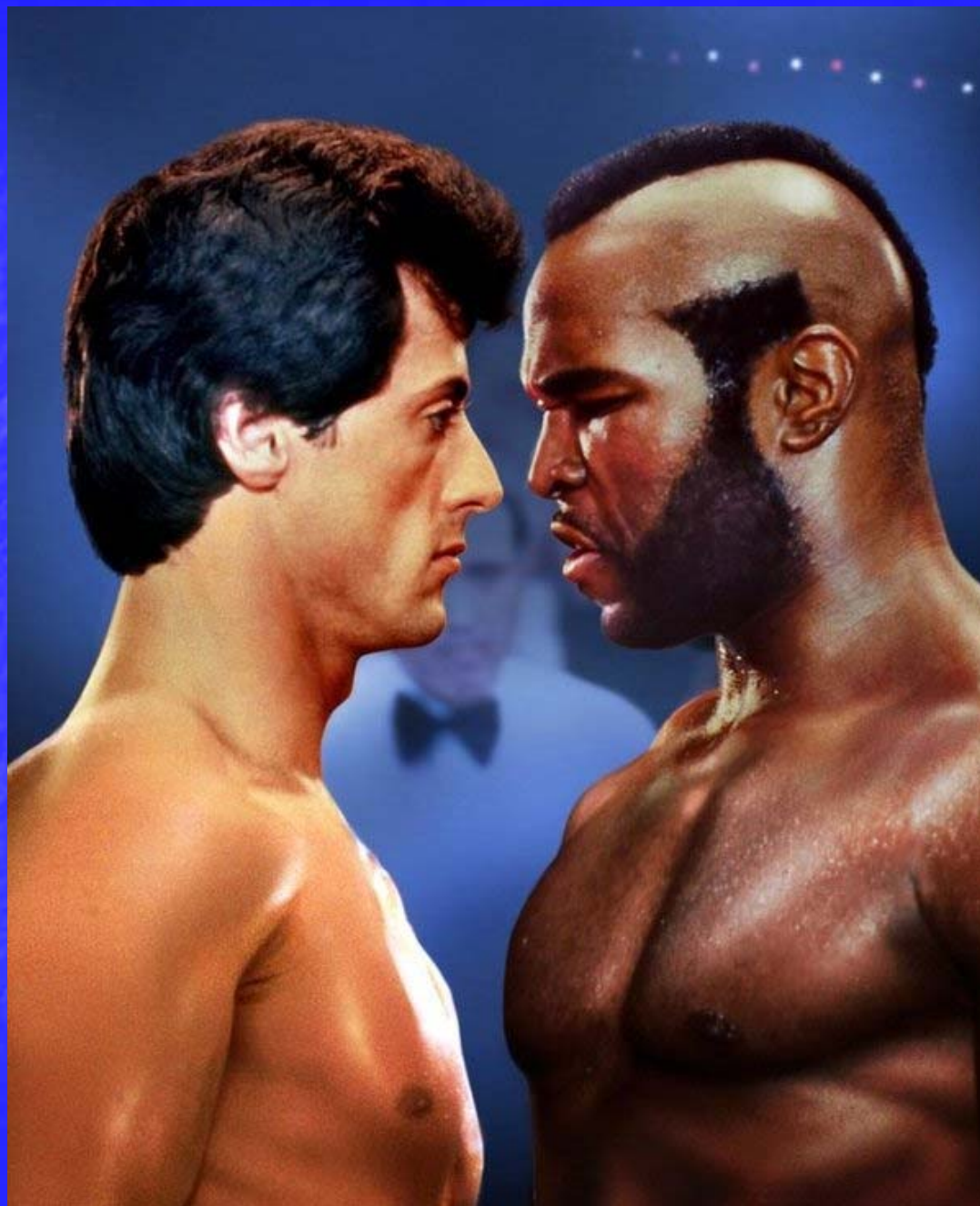
TABLO 3. Randomize kontrollü çalışmalar: kaçırma sayısı, miktarı, mesane kapasitesi.

<i>Çalışma</i>	<i>n</i>	<i>SNM</i>		<i>p</i>	<i>n</i>	<i>Kontrol</i>		<i>p</i>
Kaçırma Sayısı/gün								
<i>Weil ve ark.(25)</i>	21	13,5 ± 7,5	1,4 ± 3,3	<0,0005	22	13,5 ± 7,8	11,2 ± 5,6	anlamsız
<i>Schmidt ve ark.(26)</i>	34	9,7 ± 6,3	2,6 ± 5,1	<0,0001	42	9,3 ± 4,8	11,3 ± 5,9	0,002
Ped adet/gün								
<i>Weil ve ark.(25)</i>	21	8,7 ± 6,8	0,7 ± 1,3	<0,0005	22	8,7 ± 7,1	6,8 ± 4,0	anlamsız
<i>Schmidt ve ark.(26)</i>	34	6,2 ± 5,0	1,1 ± 2,0	<0,0001	42	5,0 ± 3,7	6,3 ± 3,6	0,003
Kaçırma Derecesi								
<i>Weil ve ark.(25)</i>	21	2,1 ± 0,6	1,6 ± 1,7	anlamsız	22	2,1 ± 0,6	2,1 ± 0,6	anlamsız
<i>Schmidt ve ark.(26)</i>	34	2,0 ± 0,7	0,8 ± 0,9	<0,0001	42	1,8 ± 0,6	2,0 ± 0,6	0,006
Kapasite ml								
<i>Weil ve ark.(25)</i>	21	266 ± 112	370 ± 91	0,013	23	X	X	-

TABLO 4. SNM vaka serileri ve etkinlikleri

Çalışma	Takip (ay)	(n) Kür/Toplam (%)	(n) İyileşme/ Toplam (%)	(n) Yanıtsız/ Toplam (%)
<i>Ruiz-Cerda ve ark. (32)</i>	6,8	14/25 (55)	2/25 (8)	9/25 (36)
<i>Heesakkers ve ark. (33)</i>	60	X	27/43 (63)	16/43 (37)
<i>Amundsen ve ark. (29)</i>	7,8	2/12 (17)	10/12 (83)	0/43 (0)
<i>Everaert ve ark. (34)</i>	12	X	4/5 (80)	1/5 (20)
<i>Groenendijk ve ark. (35)</i>	6	X	55/84 (65)	29/84 (35)
<i>Hedlund ve ark. (36)</i>	18	8/14 (57)	5/14 (36)	1/14 (7)
<i>Spinelli ve ark. (37)</i>		X	3/3 (100)	0/3 (0)
<i>Caraballo ve ark. (38)</i>	13,4	1/15 (7)	11/15 (73)	3/15 (20)
<i>Janknegt ve ark. (39)</i>	30,8	25/96 (26)	35/96 (36)	36/96 (38)
<i>Bosch ve ark. (40)</i>	47	18/45 (40)	9/45 (20)	18/45 (40)
<i>Grunewald ve ark. (41)</i>	6	6/26 (23)	13/26 (50)	7/26 (27)
<i>Siegel ve ark. (20)</i>	36	19/41 (46)	5/41 (12)	17/41 (41)
<i>Koldewijn ve ark. (42)</i>	29	18/28 (64)	3/28 (11)	7/28 (25)
<i>Hohenfellner ve ark. (32)</i>	13	X	5/5 (100)	0/5 (0)
<i>Shaker ve ark. (30)</i>	18,8	8/18 (44)	4/18 (22)	6/18 (33)
<i>Weil ve ark. (43)</i>	37,8	14/24 (58)	3/24 (13)	7/24 (29)
<i>Dijkema ve ark. (44)</i>	17	6/17 (35)	5/17 (30)	6/17 (35)
Toplam		139/361 (39)	199/501 (40)	163/501 (32)

<i>Yan Etki</i>	<i>n /toplam (%)</i>
Tekrar girişim	282/855 (33)
<i>IPG değiştirilmesi</i>	42/279 (15)
<i>Tümüyle çıkarılması</i>	44/514 (9)
<i>IPG problemleri</i>	18/399 (5)
Elektrot problemleri	129/785 (16)
<i>Ağrı</i>	162/653 (25)
Enfeksiyon	35/727 (5)
<i>Yara yeri problemleri</i>	19/273 (7)
<i>Barsak fonksiyon bozuklukları</i>	20/353 (6)



Botox & Sakral Nöromodülasyon

SNM

- Lisanslı
- Uzun etkili
- Az sayıda RCT
- Az sayıda hasta
- İnvaziv
- Re-operasyon oranı fazla
- Uzun dönemde nöronal etki?
- Kostefektivite ?

BTx

- Lisanslı değil
- Uzun dönem etkisi ?
- Az sayıda RCT
- Az sayıda hasta
- Minimal invaziv
- Geri dönüşümlü etki
- Tekrar enjeksiyon
- Uzun dönemde mesanede etki?
- Tak ihtiyacı
- Antikolinerjiklerle birlikte kullanımı?
- Kostefektivite?

Btx & SNM

Hasta Tercihi

- Balchandra ve ark.
- n: 50
- Antimuskarinik tedaviye dirençli AAM hastası
- Ort. yaş: 61.66 (38-82) yıl
- Botox VE SNM avantaj-dezavantajları anlatılmış
- Hastaların %74' ü botox' u, %26' sı SNM' u tercih etmiş

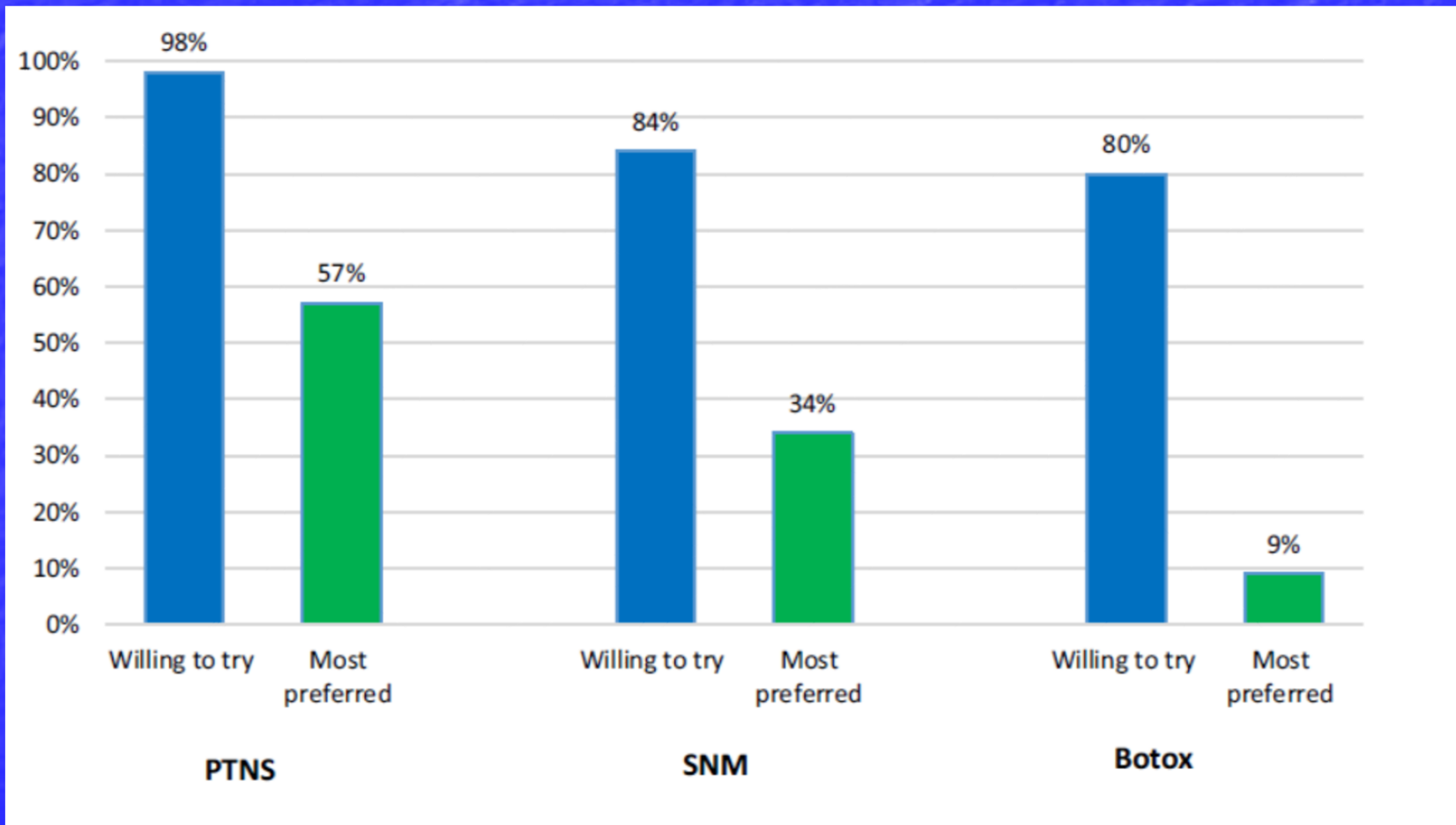
Btx & SNM

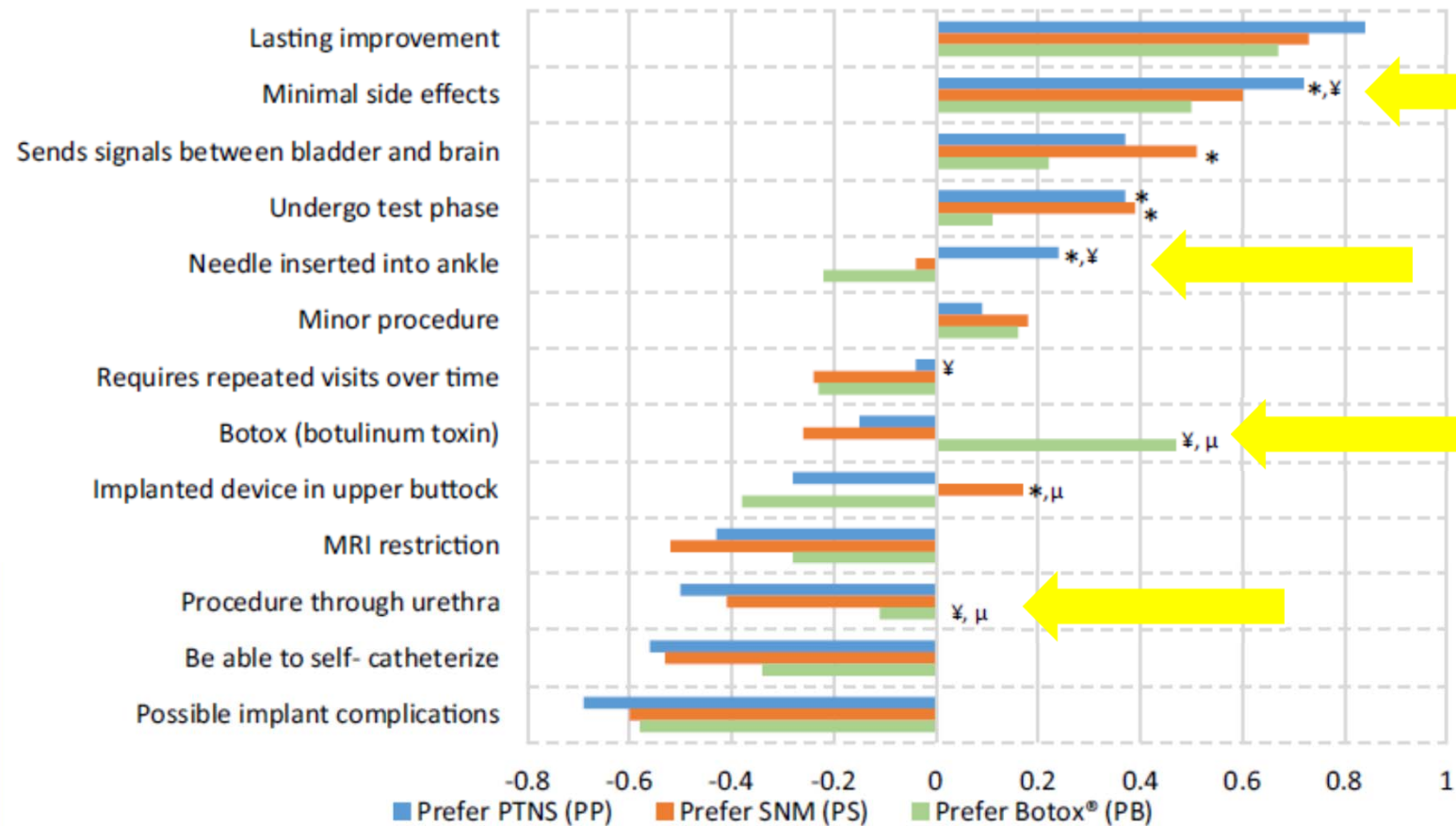
Hasta Tercihi

Neden BTx ?	
Lokal Anestezi	%29
Genel Anestezi	%27
Kısa bekleme süresi	%45
Kısa sürede etkinlik	%43
Popüler	%2,7
Az invaziv	%2,7
Ulaşılması kolay	%2,7
Neden SNM değil?	
İki basamaklı prosedür	%21
Yabancı cisim	%54
6 yıldan sonra pil değişimi	%10
Kumanda çok komplike	%16
Fiziksel kısıtlılık ihtimali	%21
SNM çok invaziv	%23
Sırt sorunlarını artırır	%5

Neden SNM?	
Lokal Anestezi	%30
Pil değişimi	%15
Barsak semptomları için	%23
Uzun etkili daha az invaziv	%7
Kalıcı	%23
Neden Botox değil?	
Tekrar enjeksiyon	%61
Retansiyon, TAK riskleri	%46
Toxin kelimesinden hoşlanmama	%30

- Hashim ve ark.Int Urol Neph.2015
- Web tabanlı anket
- n:139 OAB ilaç kullanan hasta
- 6.1 yıl tanılı
- Ortalama yaş 49 yıl





Research article

Open Access

Treatment success for overactive bladder with urinary urge incontinence refractory to oral antimuscarinics: a review of published evidence

Jonathan D Campbell^{*1,2}, Katharine S Gries¹, Jonathan H Watanabe¹, Arlene Ravelo³, Roger R Dmochowski⁴ and Sean D Sullivan¹

- Tedavi başarıları
- Derleme

Table 1: Complete Continence: Treatment Success Definition by Intervention

Study	Study Design	Sample Size	Study Population	Comparator	Success Evaluated (months)	Success %
Botulinum toxin type A						
Kennelly, Top Spinal Cord Inj Rehabil, 2003 [26]	Open Label	10	NOAB	None	6	80
Reitz, Eur Urol, 2004 [27]	Open Label	200	NOAB	None	4	73
Giannantoni, J Urol, 2004 [28]	RCT	25	NOAB	Intravesically Resiniferation	18	73
Giannantoni, Minerva Urol Nephrol, 2004 [29]	RCT	25	NOAB	Intravesically Resiniferation	12	75.0
Klaphajone, Arch Phys Med Rehabil, 2005 [30]	Open Label	10	NOAB	None	1.5	70
Schurch, J Urol, 2005 [13]	RCT	38	NOAB	Placebo	6	63
Kessler, Neurourol Urodynam, 2005* [31]	Open Label	11, 11	NOAB, IOAB	None	3, 3	72, 91
Popat, J Urol, 2005* [32]	Open Label	3, 4	NOAB, IOAB	None	4, 4	55.2, 57
Werner, Am J Obstet Gynecol, 2005 [33]	Open Label	21	NOAB	None	9	65
Kuo, J Urol, 2006* [34]	Single Blind	35, 40	NOAB, IOAB	None	3, 3	94, 73
Giannantoni, J Urol, 2006 [35]	Open Label	23	NOAB	None	3	78
Karsenty, Urol, 2006 [36]	Open Label	17	NOAB	None	5	100
Sahai, J Urol, 2007 [37]	RCT	10	IOAB	Placebo	3	50
Mascarenhas, Neurourol Urodynam, 2008 [38]	Open label	10	NOAB	None	2	42.8
Sacral neuromodulation						
Bosch, J Urol, 2000 [39]	Open Label	6	NOAB	None	47	80
Chartier-Kastler, J Urol, 2000 [40]	Open Label	9	NOAB	None	43.6	67
Weil, Eur Urol, 2000 [41]	RCT	21	IOAB	Current Management	6	56
Spinelli, J Urol, 2001 [42]	Open Label	96	NOAB	None	18	71
Augmentation cystoplasty						
Chartier-Kastler, Spinal Cord, 2000 [43]	Open Label	17	NOAB	None	75.6	70.5
Ivil, Int Urol Nephrol, 2002 [44]	Open Label	17	IOAB	None	11	83
Khastgir, Eur Urol, 2003 [21]	Open Label	2	NOAB	None	72	100
Quek, J Urol, 2003 [45]	Open Label	20	NOAB	None	96	69
Stoffel, Neurourol Urodynam, 2006 [46]	Open Label	12	NOAB	None	20	88

Btx :
NOAB,

IOAB

SNM

Aug.

50-100

56-80

69-
100

Table 2: $\geq 50\%$ Improvement in Incontinence Episodes or Other Symptoms: Treatment Success Definition by Intervention

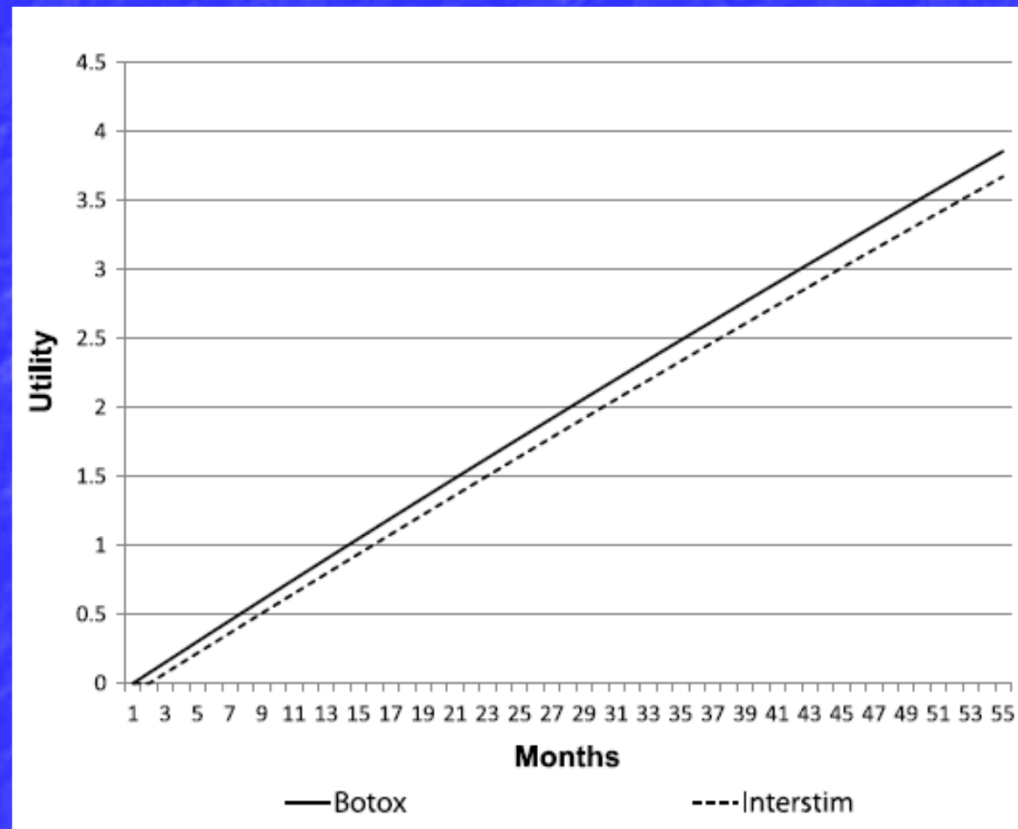
Study	Study Design	Sample Size	Study Population	Comparator	Success Evaluated (months)	Success %
Botulinum toxin type A						
Flynn, J Urol, 2004 [47]	Open Label	7	IOAB	None	3	100
Kuo, Urology, 2004* [48]	Open Label	12, 8	NOAB, IOAB	None	3, 3	66.6, 75
Kuo, Urology, 2005 [49]	Open Label	20	IOAB	None	3	85
Kalsi, Eur Urol, 2006* [50]	Open Label	63, 38	NOAB, IOAB	None	4, 4	86, 79
Kalsi, Ann Neurol, 2007 [51]	Open Label	8	IOAB	None	4	80
Mascarenhas, Neurourol. Urodynam, 2008 [38]	Open label		NOAB	None	2	52.4
Sacral neuromodulation						
Schmidt, J Urol, 1999 [52]	RCT	34	IOAB	Current Management	6	75
Bosch, J Urol, 2000 [39]	Open Label	40	IOAB	None	47	60
Amundsen, Am J Obstet Gynecol, 2002 [53]	Open Label	12	IOAB	None	7	100
Bosch, J Urol, 2000 [39]	Open Label	6	NOAB	None	47	100
Hassouna, J Urol, 2000 [54]	RCT	5	IOAB	Current Management	6	56
Scheepens, Eur Urol, 2003 [55]	Open Label	34	IOAB	None	11	53
Van Voskuilen, BJU Int, 2007 [56]	Open Label	31	IOAB	None	15.5	90
Groenendijk, BJU Int, 2008 [57]	Open Label	67	IOAB	None	6	61
Wallace, Am J Obstet Gynecol, 2007 [58]	Open Label	33	NOAB	None	12.5	84.8
Augmentation cystoplasty						
Blaivas, J Urol, 2005 [59]	Open Label	76	IOAB	None	106.8	97

InterStim Sacral Neuromodulation and Botox Botulinum-A Toxin Intradetrusor Injections for Refractory Urge Urinary Incontinence: A Decision Analysis Comparing Outcomes Including Efficacy and Complications

Jonathan P. Shepherd, MD, MSc, Jerry L. Lowder, MD, MSc,* Wendy W. Leng, MD,†
and Kenneth J. Smith, MD‡*

- «Decision» analiz
- Literatür taranması ve
- Tree Age Pro software
- 54 aylık model

Therapy	Condition	% (n)	Range
InterStim	Dry	36.3 (169/466)	22.2–52.4
	>50% improvement	58.8 (1049/1783)	39.3–92.9
	Respond to stage 1 implant	59.2 (941/1589)	35.8–91.4
	Revision of device	26.9 (206/765)	7.3–33.3
	Explant device	9.1 (76/836)	0–17.9
	Pain at lead site	11.1 (120/1081)	2.5–19.8
	Infection	4.0 (33/831)	0–9.1
	Lead migration	5.4 (67/1249)	0.6–8.6
Botox	Dry	65.4 (240/367)	31.6–90.9
	Symptoms improved/absent	63.5 (122/192)	36.4–75.0
	Need to self-catheterize	37.7 (86/228)	7.7–45.5
	UTI	24.7 (46/186)	9.1–43.8
	Time to reinjection	12.9 mo	6.0–16.1
	Time to Botox failure	8.5 mo	5.0–16.1



Sacral Neuromodulation in Patients with Idiopathic Overactive Bladder after Initial Botulinum Toxin Therapy

Martijn A. C. Smits,^{*,†,‡} Dennis Oerlemans,[†] Tom A. T. Marcelissen,
Philip E. V. Van Kerrebroeck^{§,||} and Stefan G. G. De Wachter^{§,¶}

From the Department of Urology, Maastricht University Medical Centre, Maastricht, the Netherlands

- n:20 hasta
- Btx fayda görmeye 17 hasta
- Kalıcı çözüm arayan 3 hasta
- 23 ay aradaki süreç

Pt No.	Mos BoNTA-SNM	Test Stimulation Result	Leakage Improvement (%)	Frequency Improvement (%)	1-Yr Satisfaction
<i>Successful test stimulation will definitive implant performed:</i>					
1	18	PNE successful	Greater than 50	Less than 50	Unsatisfied
2	25	PNE successful	Greater than 50	Less than 50	Satisfied
3	17	PNE successful	Greater than 50	Greater than 50	Satisfied
4	8	PNE successful	Greater than 50	Less than 50	Satisfied
5	41	PNE successful	Greater than 50	Greater than 50	Unsatisfied
6	11	PNE successful	Greater than 90	Greater than 50	Satisfied
7	21	PNE successful	Greater than 90	Less than 50	Satisfied
8	7	PNE successful	Greater than 90	Less than 50	Satisfied
9	17	PNE successful	Greater than 50	Less than 50	Satisfied
10	31	PNE unsuccessful, TLP 1st stage successful	Greater than 50	Less than 50	Satisfied
11	18	PNE unsuccessful, TLP 1st stage successful	Greater than 50	Less than 50	Satisfied
12	46	PNE unsuccessful, TLP 1st stage successful	Greater than 90	Greater than 50	Satisfied
13	11	PNE successful	Greater than 50	Greater than 50	Unsatisfied
14	11	PNE unsuccessful, TLP 1st stage successful	Greater than 90	Greater than 50	Satisfied
<i>Unsuccessful test stimulation with definitive implant not performed:</i>					
15	29	PNE unsuccessful, TLP 1st stage unsuccessful	Less than 50	Less than 50	
16	18	PNE unsuccessful, TLP 1st stage unsuccessful	Less than 50	Less than 50	
17	53	PNE unsuccessful, TLP 1st stage unsuccessful	Less than 50	Less than 50	
18	18	PNE unsuccessful, TLP 1st stage unsuccessful	Less than 50	Less than 50	
19	31	PNE unsuccessful, TLP 1st stage unsuccessful	Less than 50	Less than 50	
20	27	PNE unsuccessful	Less than 50	Less than 50	

- 14 hastada + cevap IPG implantasyonu
- 5/14 hasta %90 dan fazla UI iyileşme
- 1 yıl sonunda %79 memnuniyet

Kostefektivite

- İspanya ve Fransa çalışması
- Hollanda
- USA
- Kanada

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Cost-Effectiveness of Sacral Neuromodulation Compared to Botulinum Neurotoxin A or Continued Medical Management in Refractory Overactive Bladder

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Table 1 – Treatment transition rates*.

After failure of	Next treatment Line			
	SNM test and permanent implant, %	BoNT-A, %	Cystoplasty, %	OMT, %
SNM test and permanent implant	—	77	5	18
BoNT-A	79	—	5	16
OMT	—	—	—	100

BoNT-A, botulinum neurotoxin A; OMT, optimized medical treatment; SNM, sacral neuromodulation.

* Proportion of patients receiving the next available treatment following a failure of treatment as listed in first left-hand-side column.

■ 10 yıllık model

Table 4 – Cost-effectiveness analyses.

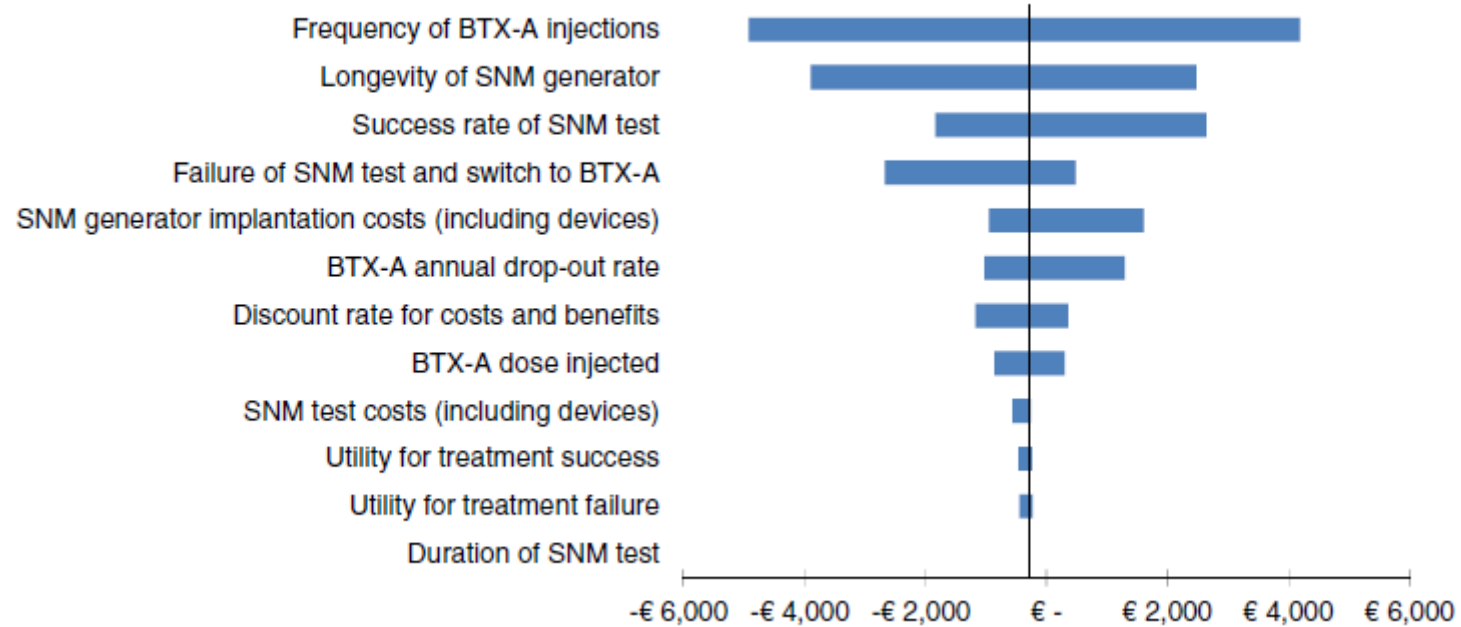
Treatment	Improvement, %	Total per-patient costs, €	QALYs	ICER (cost/QALYs gained), €	Episodes	ICER (costs/episode avoided), €
5 years						
SNM	72.1	19,156	3.69		9561	
BoNT-A	68.6	18,235	3.45		9790	
OMT	0.0	15,932	2.75		16,529	
Incremental: SNM vs. BoNT-A year 5		921	0.24	3775	229	4.02
Incremental: SNM vs. OMT year 5		3223	0.94	3412	6968	0.46
7 years						
SNM	68.8	26,019	5.03		12,976	
BoNT-A	62.9	22,597	4.68		13,389	
OMT	0.0	21,593	3.74		22,486	
Incremental: SNM vs. BoNT-A year 7		3422	0.35	9830	413	8.29
Incremental: SNM vs. OMT year 7		4426	1.29	3433	9509	0.47
10 years						
SNM	62.1	29,166	6.89		17,765	
BoNT-A	55.2	29,458	6.38		18,498	
OMT	0.0	29,370	5.12		30,787	
Incremental: SNM vs. BoNT-A year 10		–292	0.51	Dominant	733	Dominant
Incremental: SNM vs. OMT year 10		–204	1.77	Dominant	13,021	Dominant

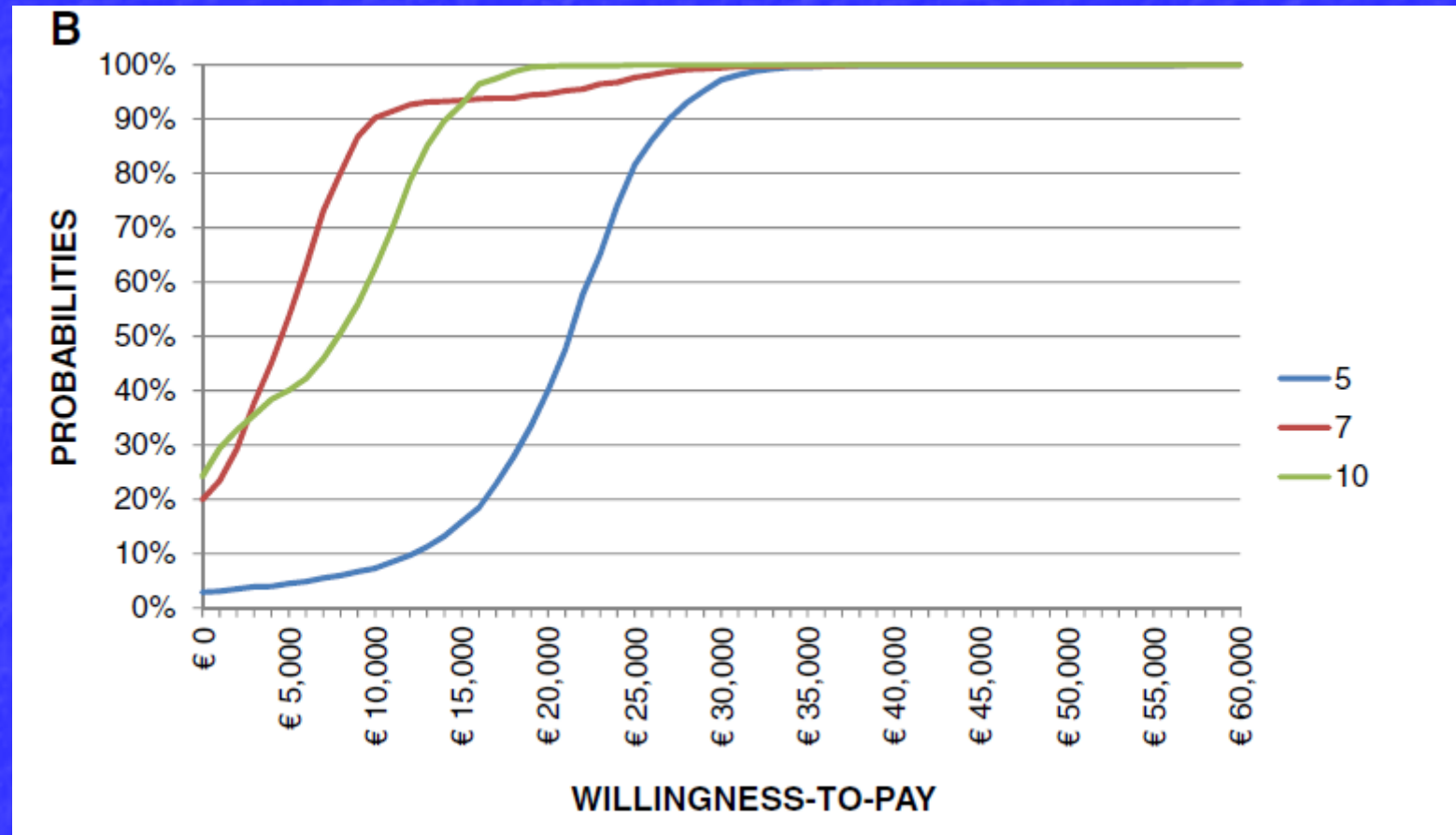
BoNT-A, botulinum neurotoxin A; ICER, incremental cost-effectiveness ratio; OMT, optimized medical treatment; QALY, quality-adjusted life-year; SNM, sacral neuromodulation.

■ SNM 10. yılda kostefektif

Ülke	SNM	Btx	yıl
İtalya	9433 euro Küm: 32,975 euro	1654 Euro Küm: 33,309 Euro	3 yıldan sonra kostefektivite başlıyor 10 yılda kostefektif
USA	22226 \$ başlangıç	1313 Başlandıç	3 yıllık takip SNM pahalı fakat ek tedaviler
İspanya	29166 Euro 10yıllık	29166 Euro 10 yıllık	10 yıllık modelde SNM daha kostefektif
Holanda	11346 euro	1564 Euro / 200 U	5 yıldan sonra SNM kostefektif
Kanada		10.Yılda 9407 \$ daha pahalı	5 yıldan sonra kostefektif

A





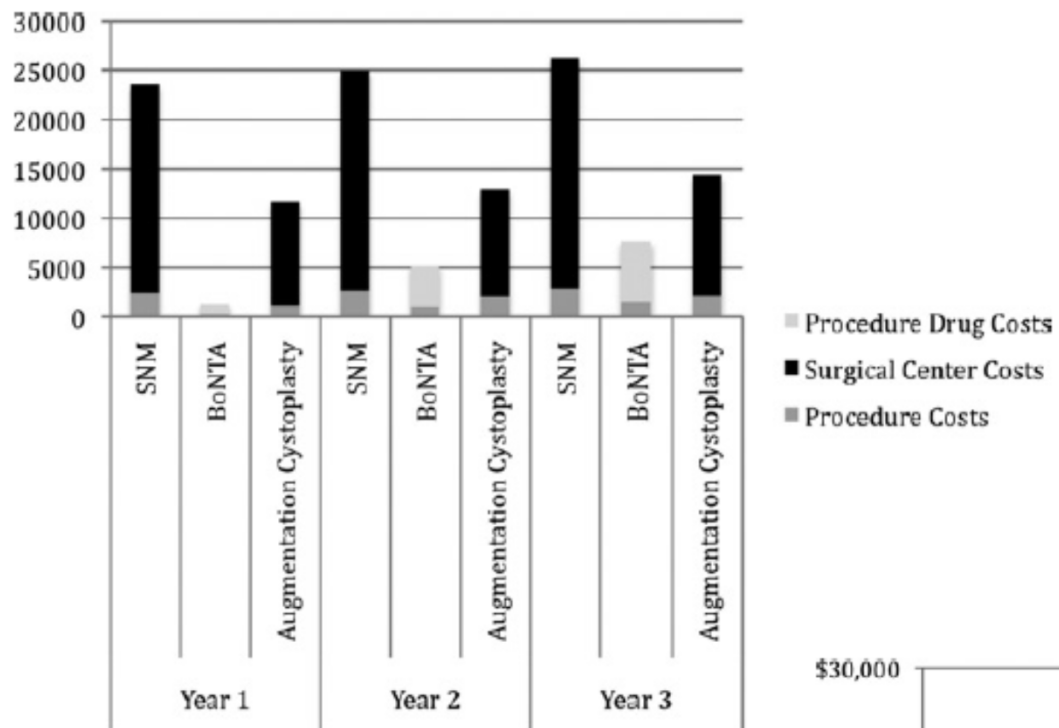


Figure 1. Annual Average Cumulative Cos

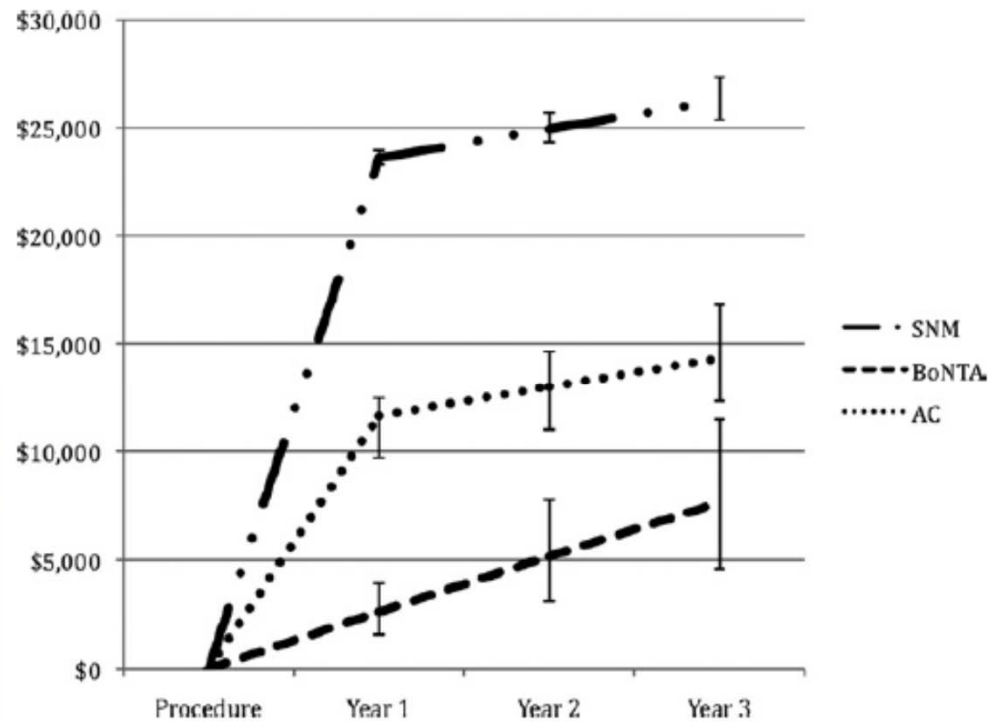


TABLE 2 Results base case and sensitivity analysis

Variable	SNM therapy		BTX therapy		Incremental		ICER €/QALY
	Cost €	QALY	Cost €	QALY	Cost €	QALY	
1 year	20 105	1.66	9 359	1.66	10 745	-0.01	SNM dominated
2 years	21 444	2.51	11 524	2.39	9 920	0.12	84 660
3 years	22 840	3.34	14 173	3.18	8 666	0.16	54 291
4 years	24 288	4.15	16 793	3.96	7 495	0.20	38 327
5 years (base case scenario)	25 780	4.95	19 353	4.72	6 428	0.23	27 991
6 years	27 307	5.73	21 851	5.47	5 456	0.26	20 827
7 years	32 192	6.49	24 289	6.20	7 903	0.29	27 010
8 years	33 763	7.24	26 848	6.92	6 916	0.32	21 502
9 years	35 347	7.98	29 194	7.63	6 153	0.35	17 623
10 years	36 878	8.69	31 485	8.32	5 393	0.37	14 493
PNE test	22 264	4.72	19 189	4.72	3 075	0.00	3 219 121
Bilateral PNE test	22 775	4.72	19 223	4.72	3 552	0.00	3 717 822
Interstim 2	31 111	4.95	19 406	4.72	11 706	0.23	50 974
Bilateral first stage (Interstim 1)	30 366	4.95	19 599	4.72	10 767	0.23	46 888
Bilateral first stage (Interstim 2)	35 696	4.95	19 652	4.72	16 045	0.23	69 870
Local anaesthesia (SNM only)	24 748	4.95	19 304	4.72	5 444	0.23	23 707
Local anaesthesia (BTX only)	25 376	4.95	13 978	4.72	11 398	0.23	49 634
Local anaesthesia (SNM and BTX)	24 343	4.95	13 929	4.72	10 414	0.23	45 350
Drop-out rate 2%	25 765	4.95	19 196	4.79	6 569	0.17	39 265
Drop-out rate 6%	25 791	4.95	19 463	4.68	6 328	0.27	23 121
Utility 'no improvement' 0.80	25 780	5.03	19 353	4.87	6 428	0.17	38 572
Utility 'no improvement' 0.85	25 780	5.09	19 353	4.97	6 428	0.12	52 837
Utility 'no improvement' 0.90	25 780	5.15	19 353	5.08	6 428	0.08	83 847
Utility 'no improvement' 0.94	25 780	5.20	19 353	5.16	6 428	0.04	158 058

BTX, botulinum toxin A; ICER, incremental cost-effectiveness ratio; PNE, peripheral nerve evaluation; QALY, quality adjusted life years; SNM, sacral neuromodulation.

5. Yılda sonra kostefektif

Randall ve ark BJU Int 2010

SHEAMUS vs. THE ROCK

Sheamus and The Rock are two of the most colorful personalities in WWE. Though they have never had an issue, with the World Heavyweight Championship on the line, a match between these fierce competitors would be extremely intense. With fan favorites equally determined to win the title, choosing a side will prove difficult for the WWE Universe.



Sheamus

YEARS ACTIVE: 2009–PRESENT



ATTRIBUTES

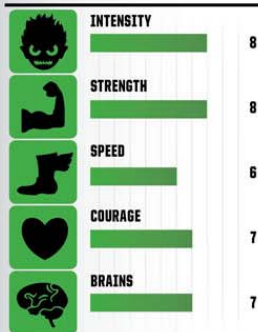
ATTITUDE
DETERMINATION
LOYALTY

The first Irish-born WWE Champion, Sheamus has been fighting professionally for many years, earning a reputation as a happy-but-vicious competitor. He always defends the underdog and fights back against bullies.



SUPERSTAR'S ADVANTAGE
STRENGTH
No stranger to the gym

STATS



INFO

Height 6'6"
Weight 272 lbs.
From Dublin, Ireland
Signature Move High Cross; Brogue Kick; Irish Curse
Career Highlights WWE Champion; World Heavyweight Champion; United States Champion; King of the Ring (2010), *Royal Rumble* Winner (2012)

18

THE SHOWDOWN

The match begins with a friendly, almost joking shove. Then a light slap. And suddenly Sheamus and The Rock both leap into action and the friendliness is dropped. Sheamus levels The Rock with a clothesline, but The Rock springs off his back onto his feet. Sheamus tries a big kick, but misses. The Rock only laughs as he kicks back.

The Rock

YEARS ACTIVE: 1996–PRESENT



ATTRIBUTES

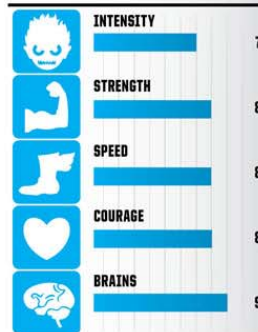
PERSONALITY
HERITAGE
TALENT

Known as "the most electrifying man in all of entertainment," The Rock has made his name known in WWE, in Hollywood, and around the world. A third-generation Superstar (both his father and grandfather were also wrestlers), The Rock will forever be "the people's champion."



LEGEND'S ADVANTAGE
MAN OF THE PEOPLE
Electrifies the audience

STATS



INFO

Height 6'5"
Weight 260 lbs.
From Miami, Florida
Signature Move Rock Bottom; People's Elbow
Career Highlights WWE Champion; Intercontinental Champion; World Tag Team Champion; *Royal Rumble* Winner (2000); WCW Champion

19

Avantajlar



Btx

- Genel ürologlar yapabilir
- Programlama gereksiz
- MRI endişesi yok
- Kolay
- Kısa süre etkinlik
- Kısa dönem güvenlik

SNM

- Uzun Dönem etki
- Uzun dönem güvenlik
- Pre test
- IC konstipasyon, retansiyon
- Ağrı
- Hızlı Balangıç
- Geri dönüşümlü
- Programlanabilir
- Etkinliği ayarlanabilir

The Refractory Overactive Bladder: Sacral NEuromodulation vs. BoTulinum Toxin Assessment: ROSETTA trial^{☆,★}



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Bekleyip Göreceğiz

