

A Novel Neuroprosthesis to Restore Bladder Function after SCI

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Neural Control of Micturition

Normal Condition

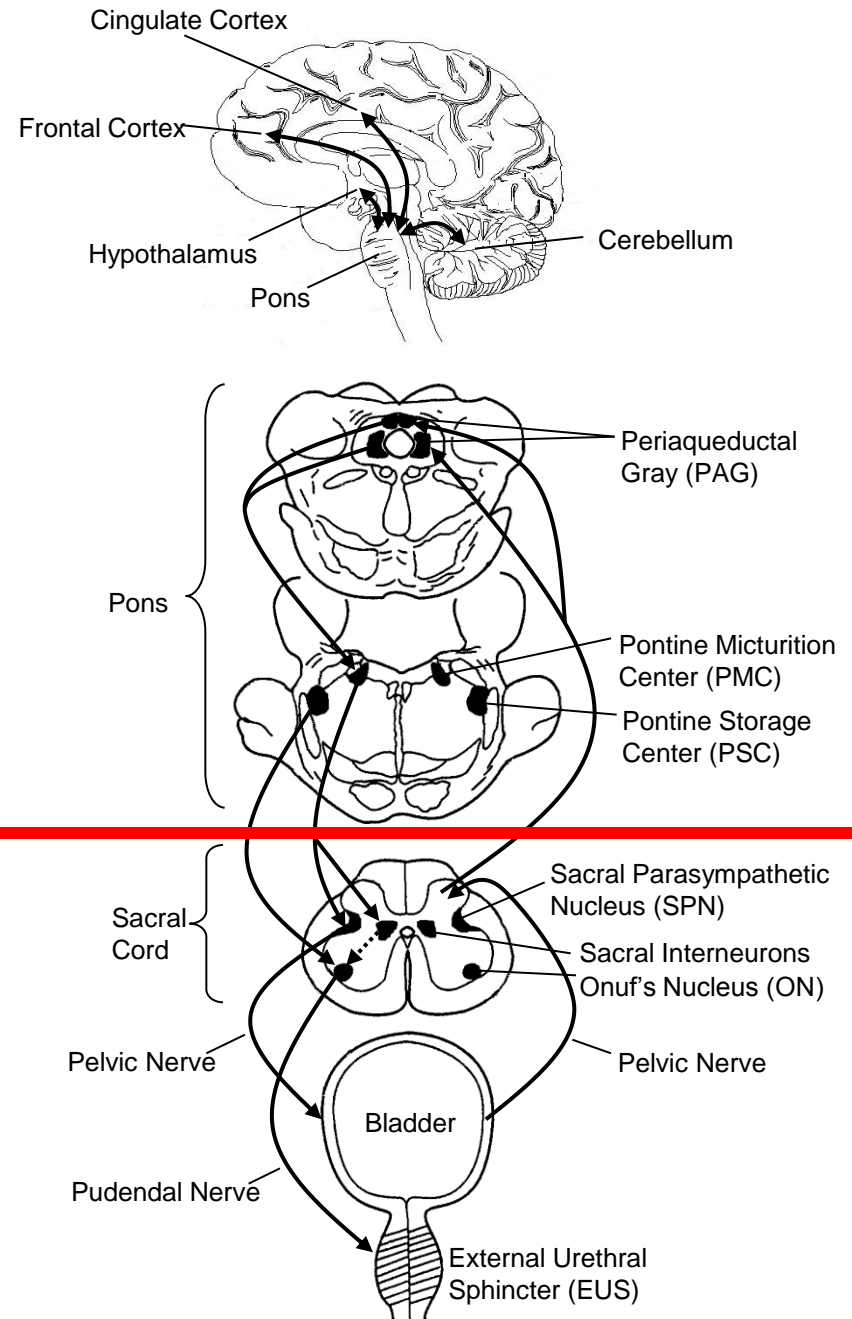
Urine Storage
Bladder: **relax**
EUS: **contract**

Voiding
Bladder: **contract**
EUS: **relax**

After Spinal Cord Injury

Urine Storage
Bladder: **contract**
i.e. detrusor hyperreflexia (DH)
EUS: **contract**

Voiding
Bladder: **contract**
EUS: **contract**
i.e. detrusor sphincter dyssynergia (DSD)



Detrusor Hyperreflexia

1. Bladder hypertrophy
2. Low bladder storage capacity
3. Frequent incontinence
4. Transient high intravesical pressure
5. Risk of kidney damage

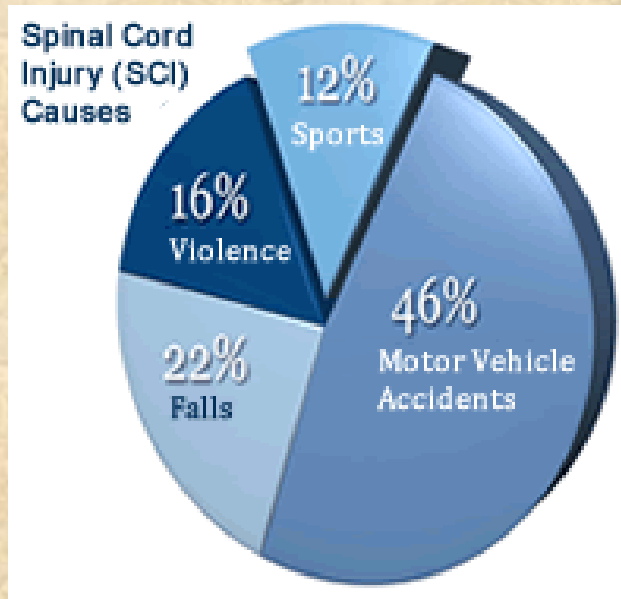
Detrusor Sphincter Dyssynergia

1. Large residual volume of urine
2. Daily urethral catheterization
3. Frequent bladder/urethra infection
4. High intravesical pressure
5. Vesicoureteral reflux and renal failure in the long-term

SCI Fact Sheet (from CDC)

1. 200K SCI currently in US
2. 12K – 20K new SCI per year
3. Medical cost \$15K - \$30K per year
4. Life medical cost \$0.5 - \$3 MM per SCI

5. Causes:



Treatment for Micturition Dysfunction

Implantable devices

Sacral Neuromodulation
InterStim® Stimulator
Medtronic Inc. USA

Minimal surgery to implant a tined lead at the S3 sacral foramen

Only treat DH

For both spinal cord injured and spinal cord intact patients

Sacral Anterior Root Stimulation
Brindley Stimulator
Finetech Medical Ltd. UK

Major spinal surgery to implant electrode on S2-4 anterior root

Treat both DH and DSD

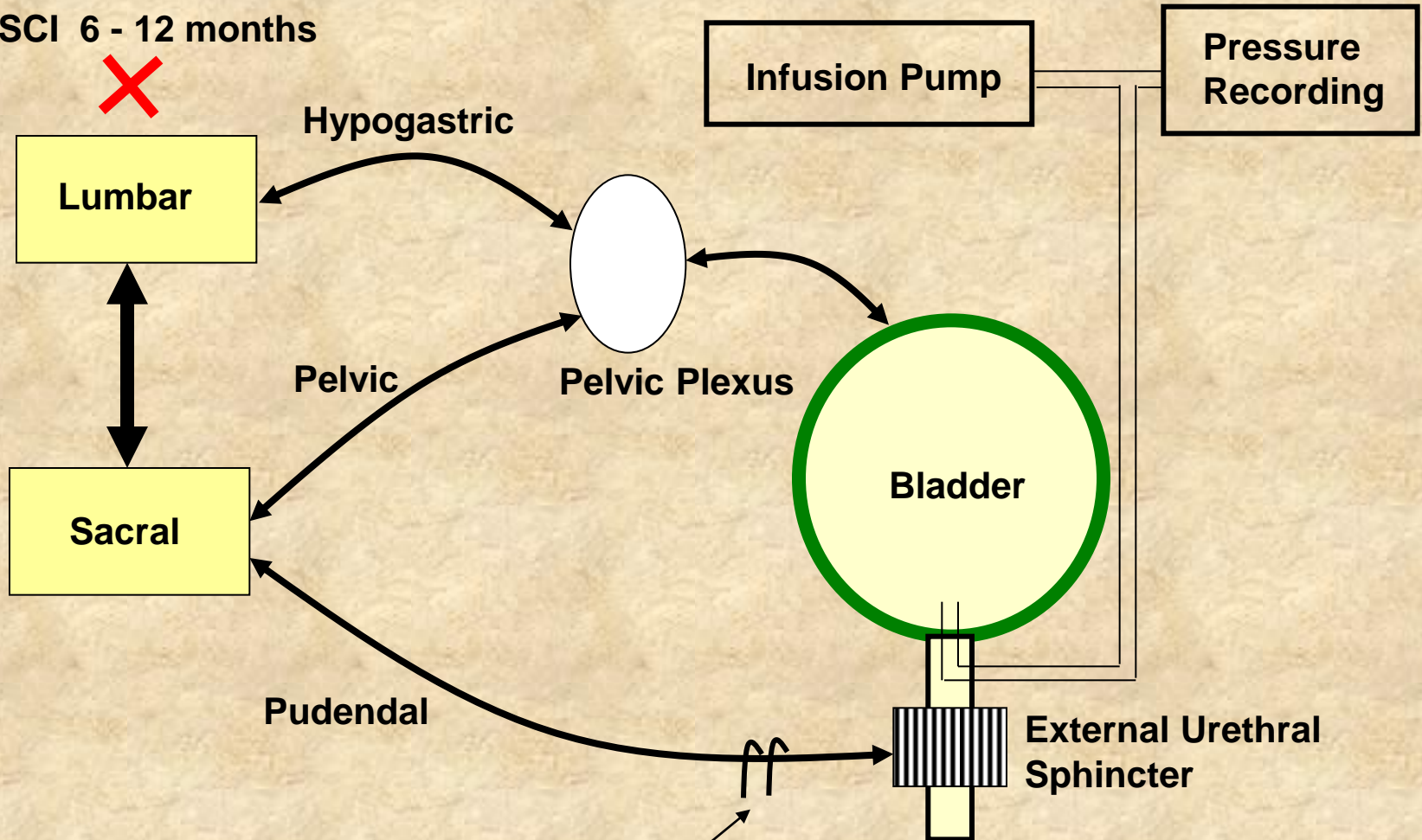
Requires dorsal rhizotomy
Eliminates reflex defecation and sexual functions

Can we treat both DH and DSD without rhizotomy?

**Pudendal-to-Bladder Reflexes
in Chronic SCI cats**

Pudendal Nerve Neuromodulation of Bladder Activity

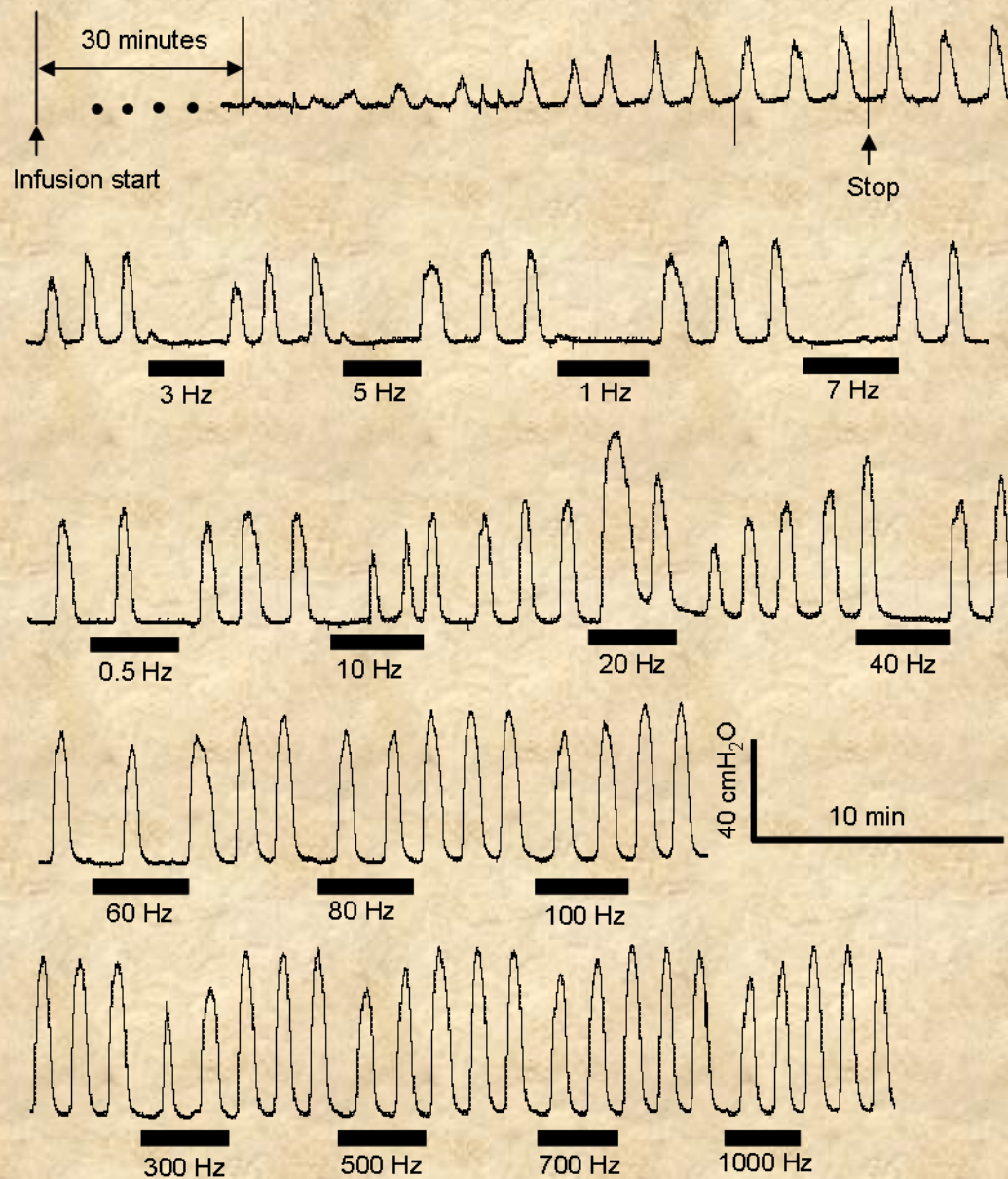
SCI 6 - 12 months



Electrical Stimulation at 0.5 – 1000 Hz

1. Inhibitory at 3-7 Hz
2. Excitatory at 20 Hz

Frequency Dependence - Isovolumetric



Stimulation:

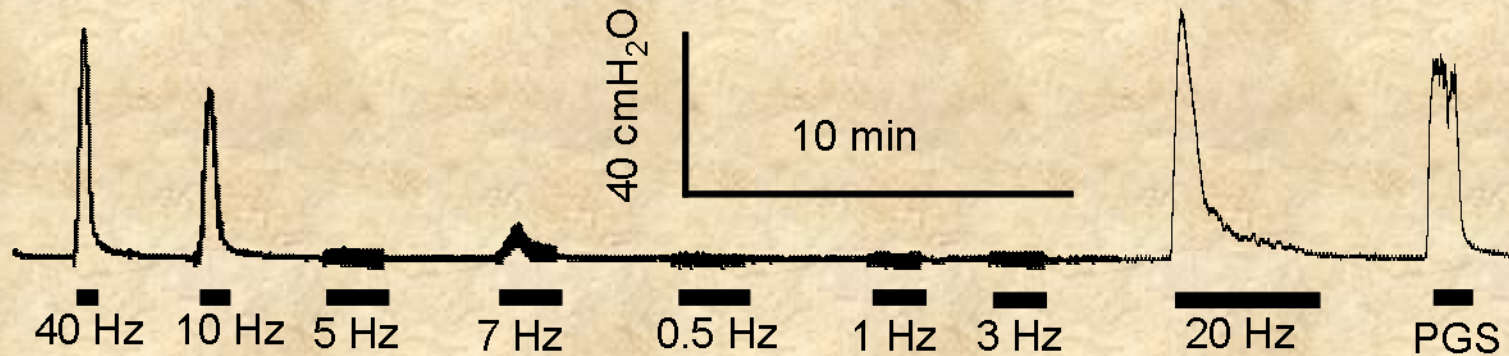
0.1 ms

0.5 V

Bladder Volume:

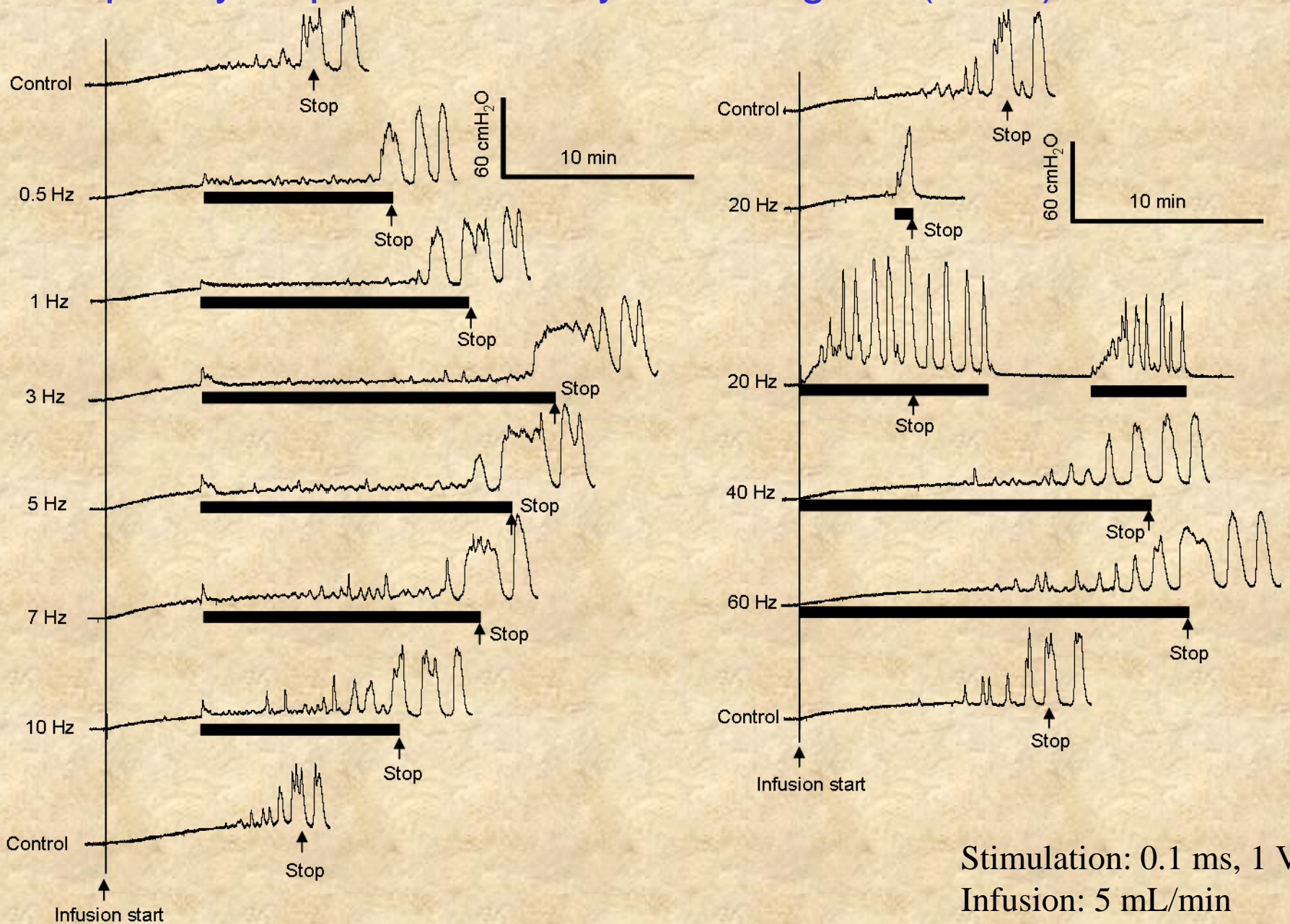
110 mL

Frequency Dependence - Isovolumetric

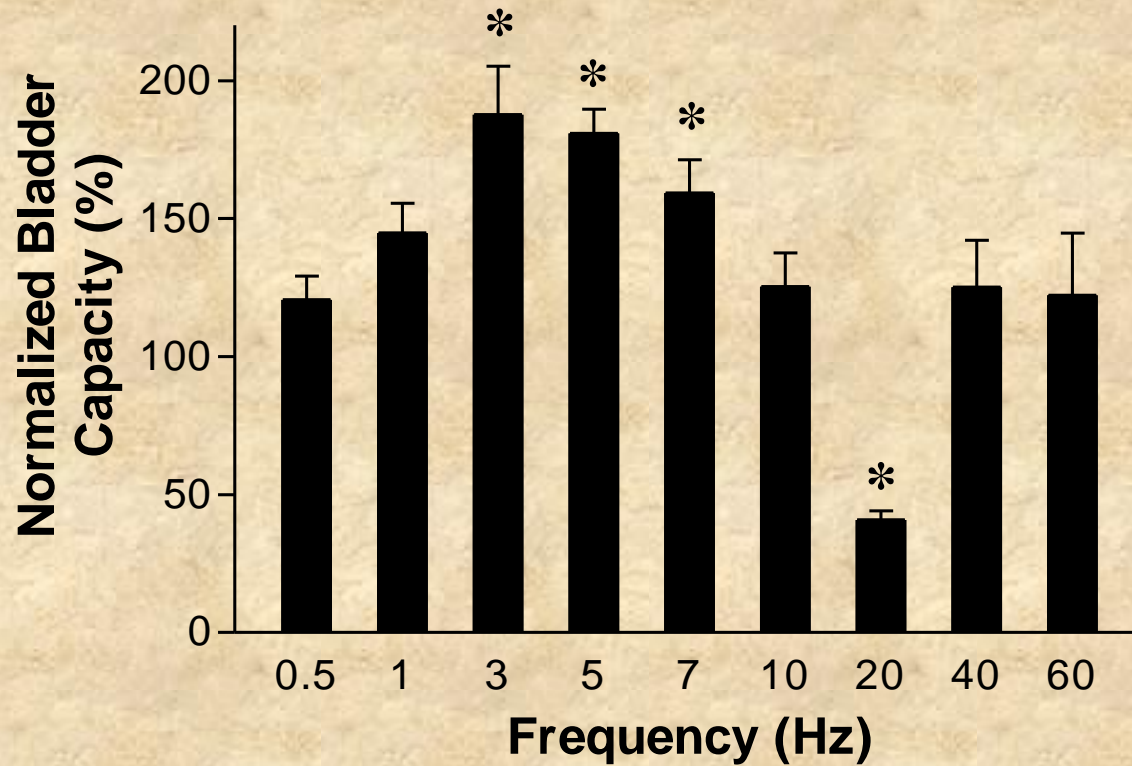


Stimulation: 0.1 ms, 10 V.
Bladder Capacity: 80 mL
Bladder Volume: 50 mL

Frequency Dependence – Cystometrogram (CMG)



Frequency Dependence - Bladder Capacity



Stimulation: 0.1 ms, 0.7-2 V

Infusion: 5 mL/min

N = 3

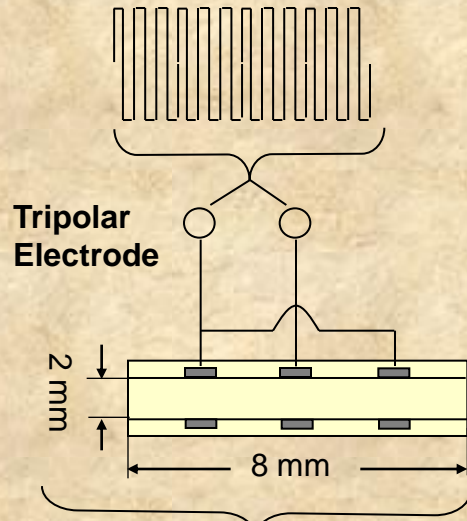
Summary

- At 3-7 Hz pudendal nerve stimulation can inhibit bladder activity, increase bladder capacity, and treat DH.
- At 20 Hz pudendal nerve stimulation can excite bladder and induce large bladder contraction, but co-activation of the sphincter (DSD) will prevent voiding.

Blocking Pudendal Nerve by Biphasic High-Frequency (6-10 kHz) Electrical Current

Pudendal Block to Relax EUS

Blocking Stimulation

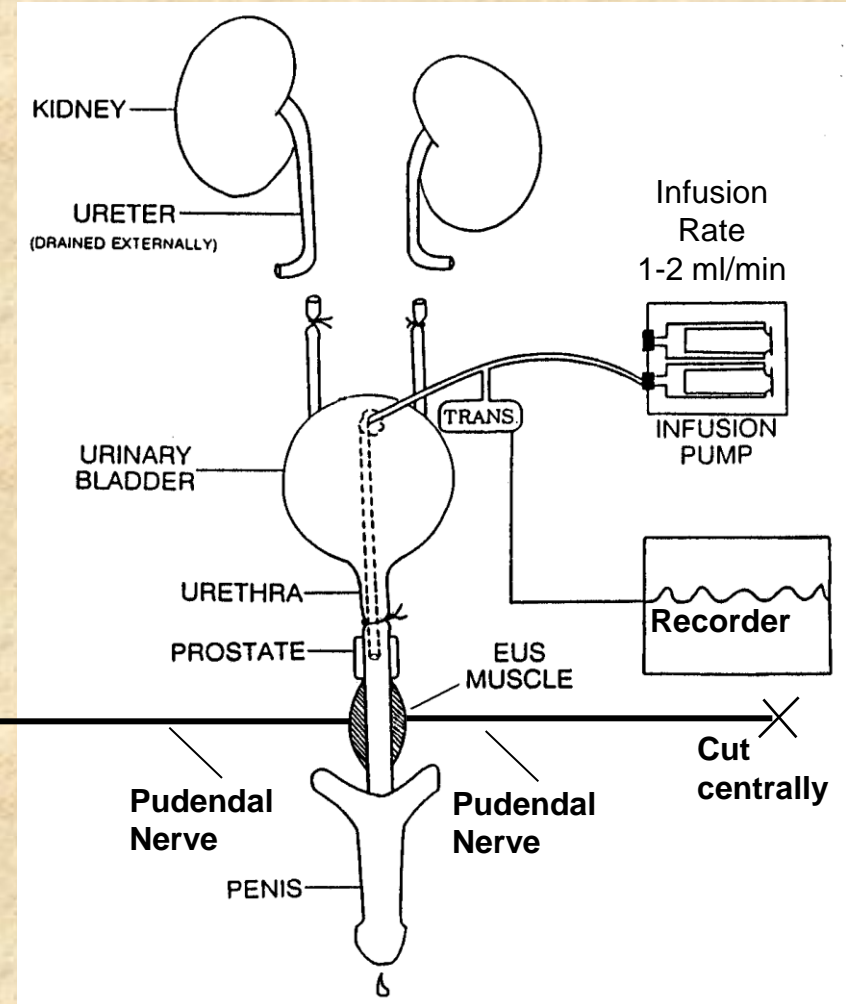


Blocking Frequency
6-10 kHz

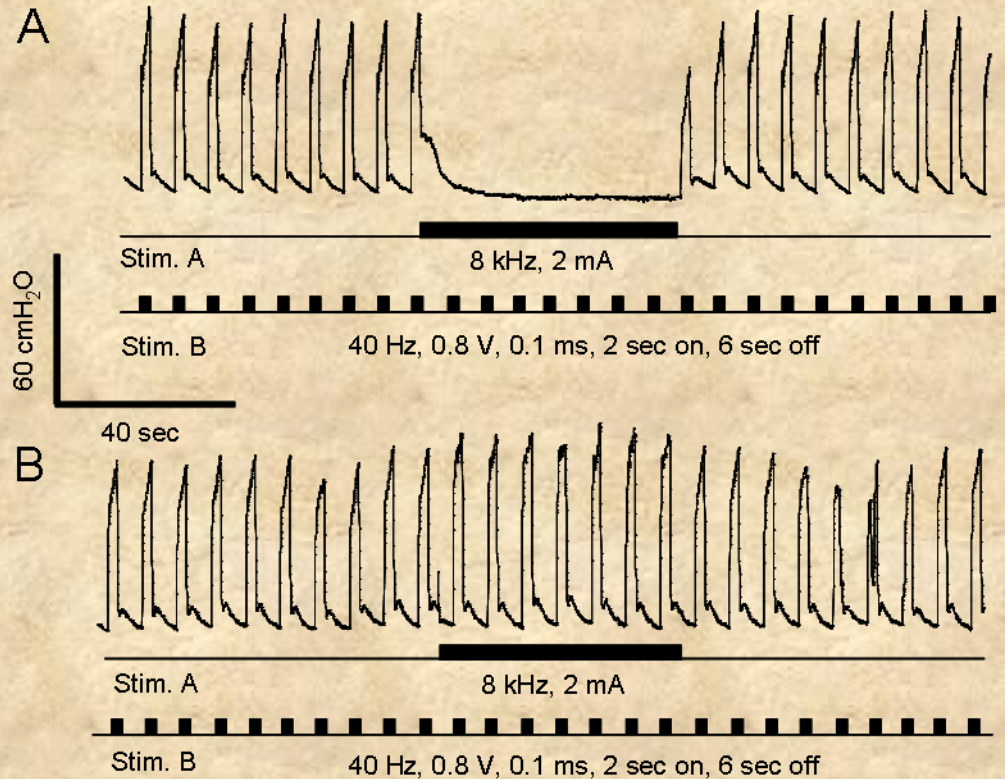
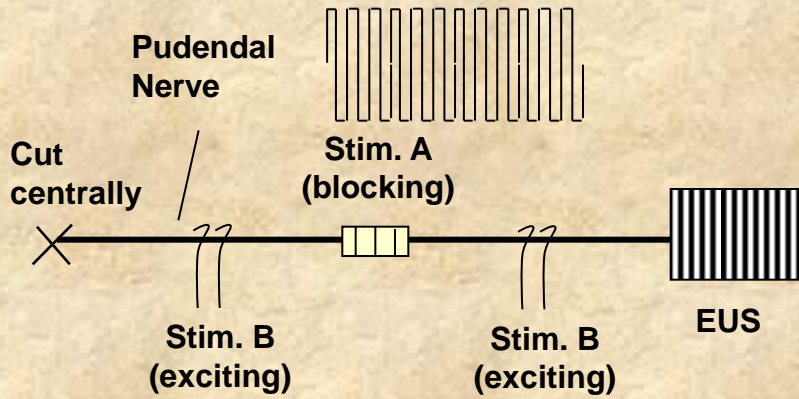


Stim. A 7K Hz, 4 mA, 0.05 ms

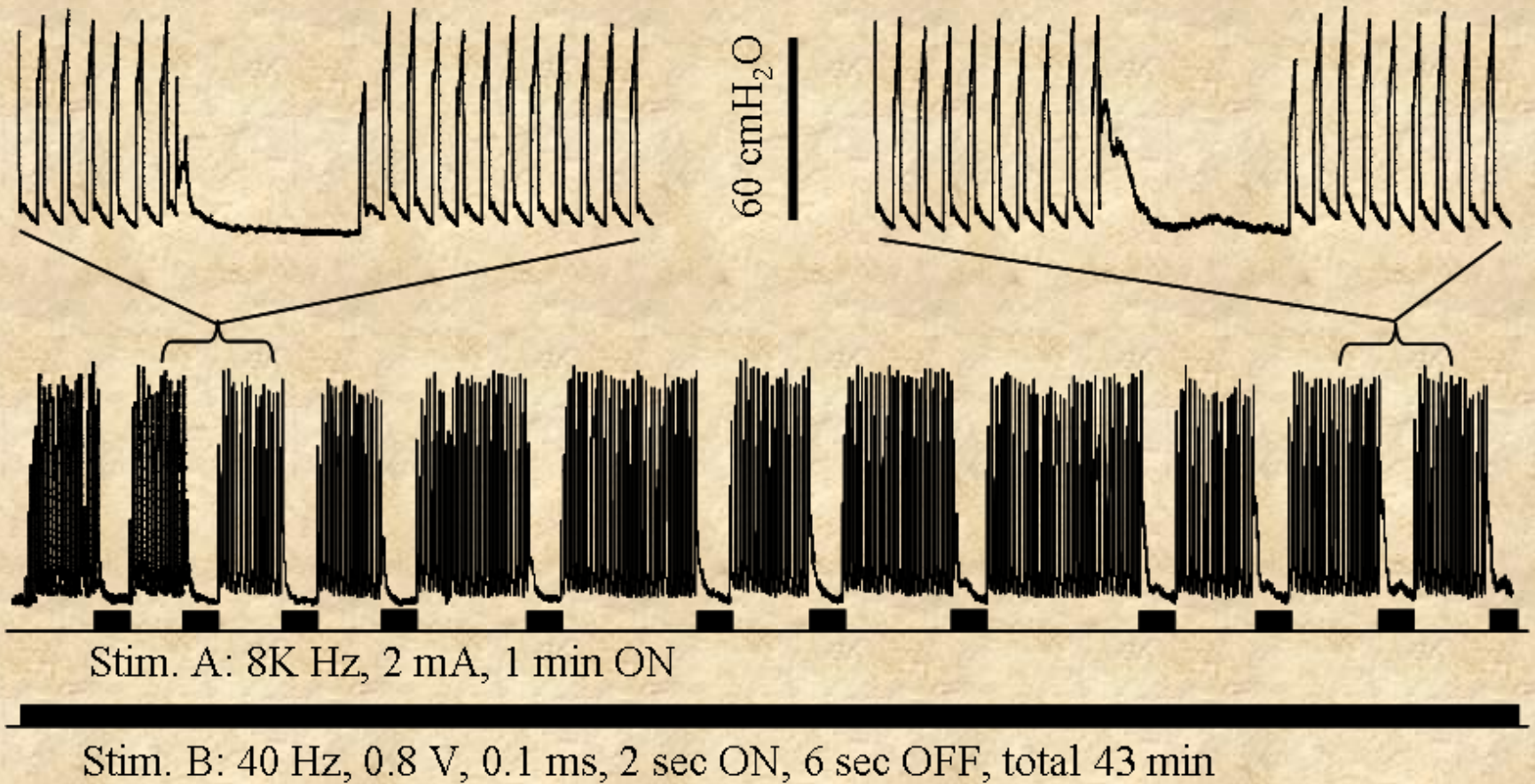
Stim. B 40 Hz, 3 V, 0.2 ms



Pudendal Nerve Block or Muscle Fatigue?



Nerve Conduction after Repeated Pudendal Block



Summary

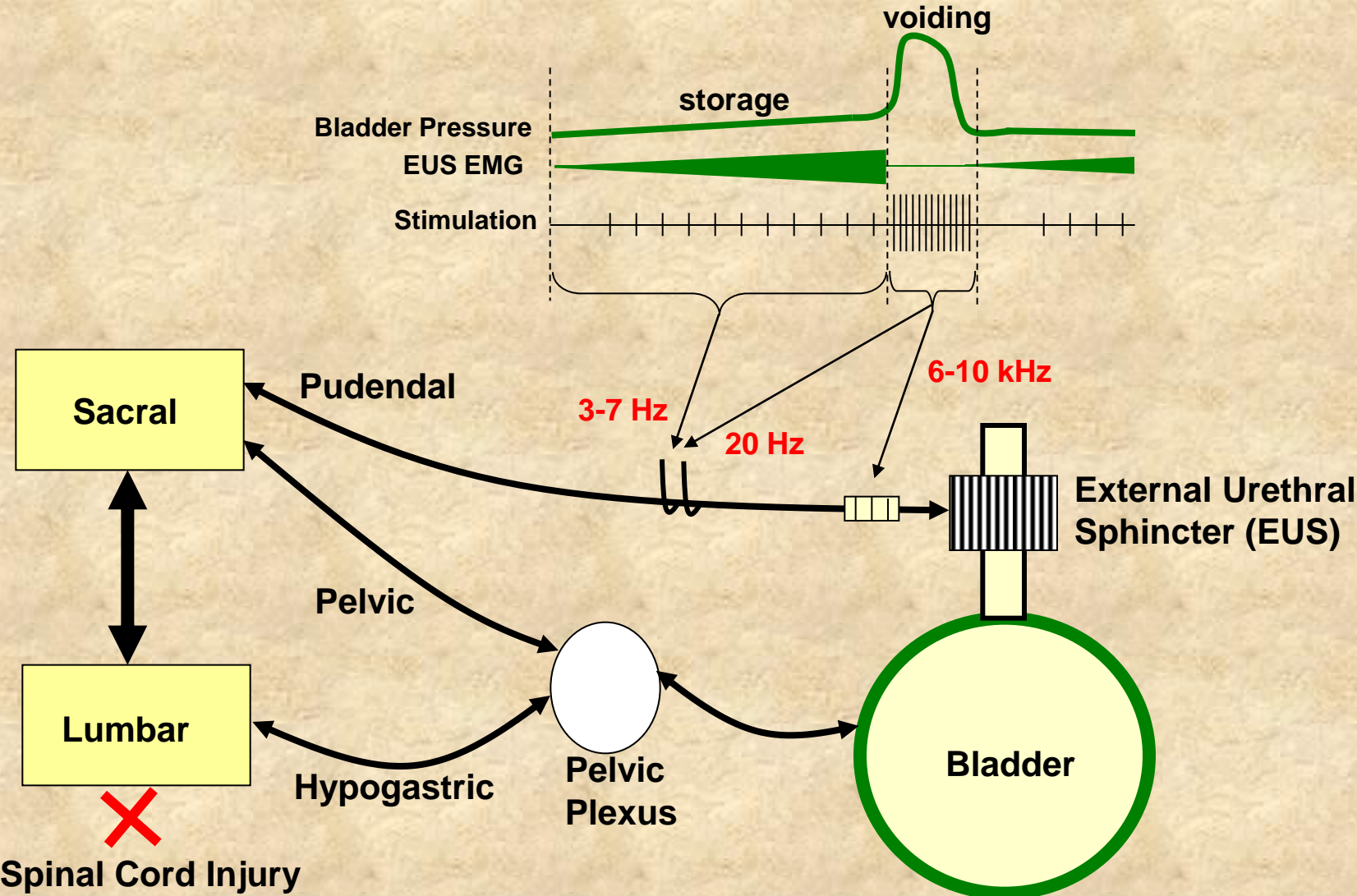
High-frequency (6-10 kHz) biphasic electrical stimulation can block pudendal nerve conduction and reduce urethral resistance.

Question:

Can this high-frequency stimulation be used to treat DSD?

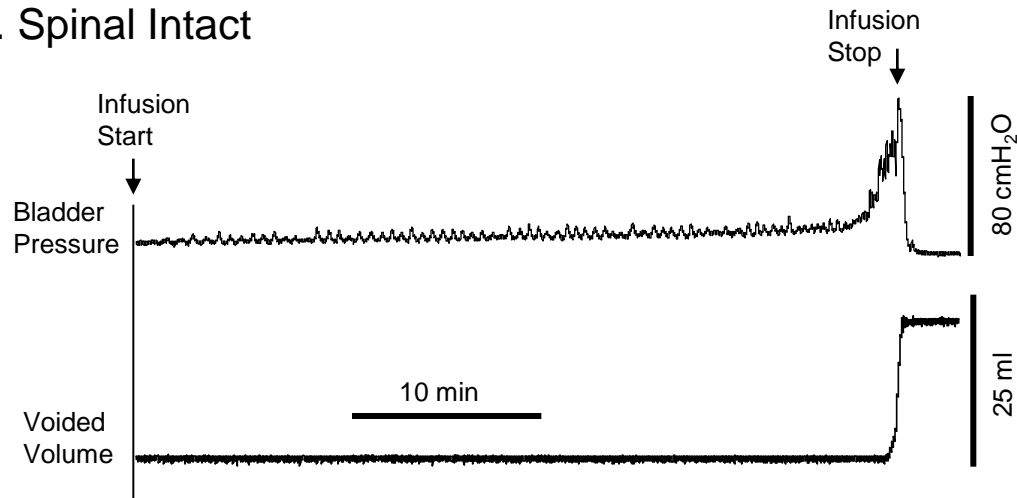
**Voiding in Chronic SCI Cats
by Stimulating and Blocking Pudendal Nerves**

Control Bladder and EUS by Pudendal Nerve Stimulation and Blockade after Spinal Cord Injury



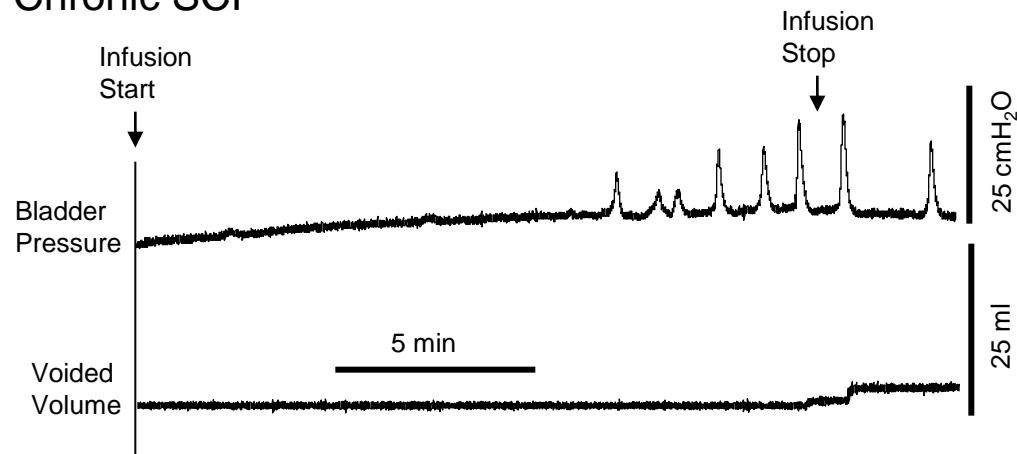
Voiding Induce by Bladder Distension

A. Spinal Intact



Voiding efficiency: 95.2%
Infusion rate: 0.5 ml/min
Total infused: 21 ml

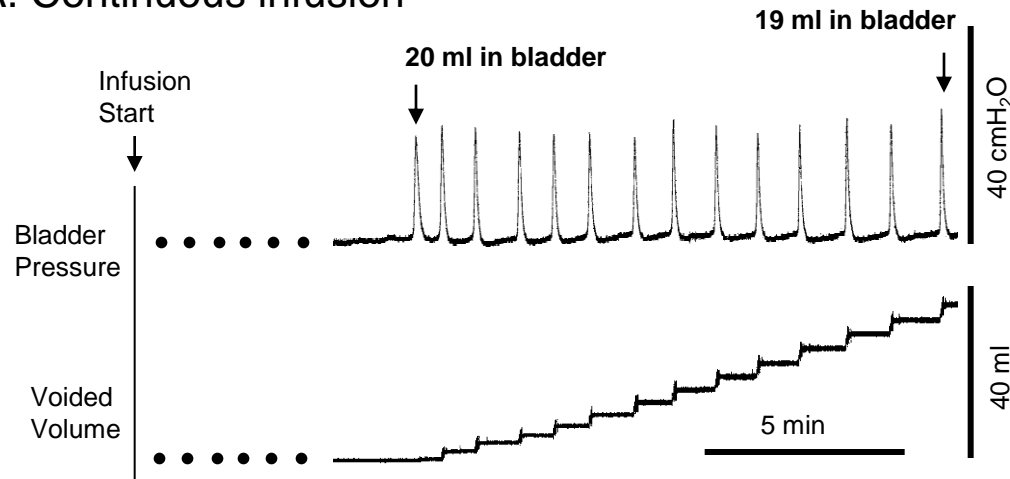
B. Chronic SCI



Voiding efficiency: 5.4%
Infusion rate: 4 ml/min
Total infused: 74 ml

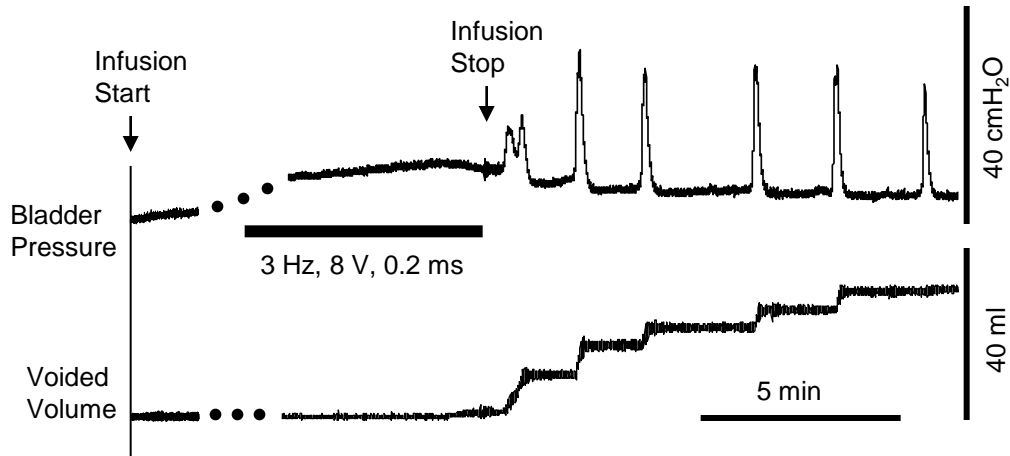
Voiding Induce by Continuous Infusion in SCI Cats

A. Continuous infusion



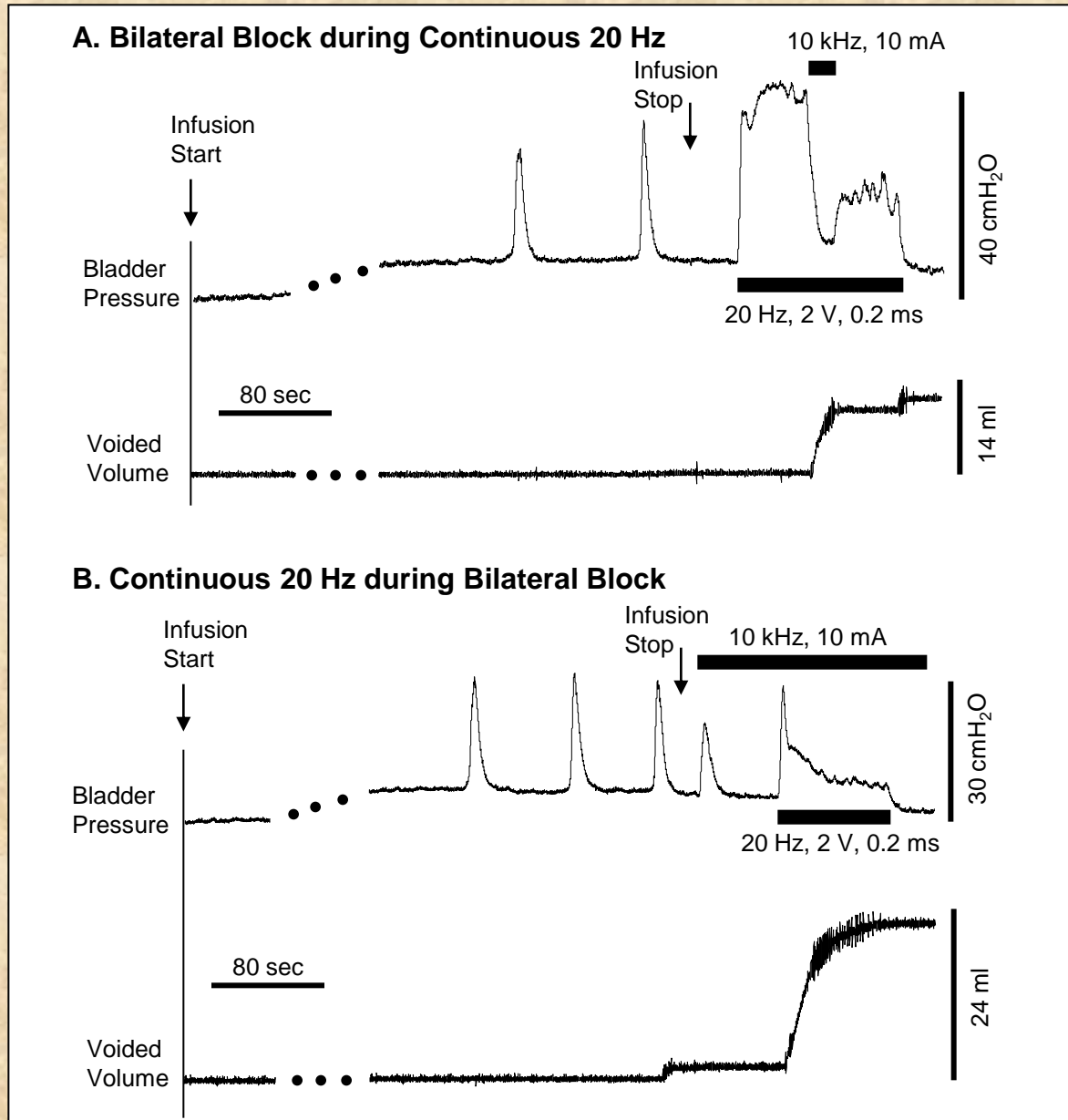
Total infused: 57 ml
Total voided: 38 ml

B. Larger bladder volume



Voiding efficiency: 25%
Total infused: 124 ml
Total voided: 31 ml

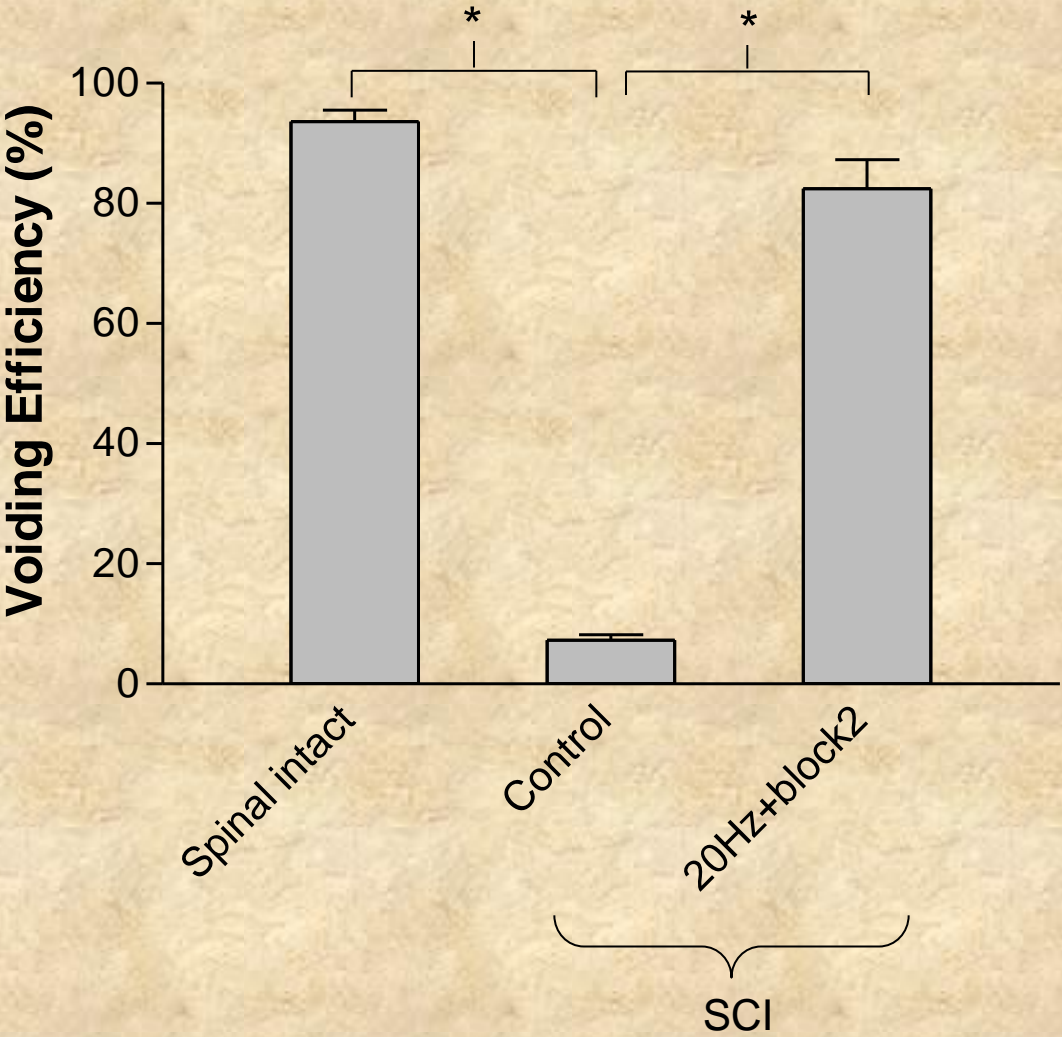
Voiding Induce by Stimulating and Blocking Pudendal Nerves



Voiding efficiency: 50%
Total infused: 24 ml
Total voided: 12 ml

Voiding efficiency: 88%
Total infused: 25 ml
Total voided: 22 ml

Voiding Efficiency



Summary

- Voiding efficiency induced by bladder distension is very low in SCI cats compared to the normal cats.
- 20 Hz pudendal nerve stimulation by itself failed to induce voiding.
- Efficient voiding can be induced in SCI cats by 20 Hz pudnedal nerve stimulation combined with 10 kHz nerve block bilaterally.

Design and Development of a Small Implantable Pudendal Nerve Stimulator

US patent application # US/2009/0036945
Methods and Systems for Achieving a Physiological Response
by Pudendal Nerve Stimulation and Blockade
Filing Date: August 1, 2008. Publication Date: February 5, 2009.

An Implantable Bladder “Pacemaker”

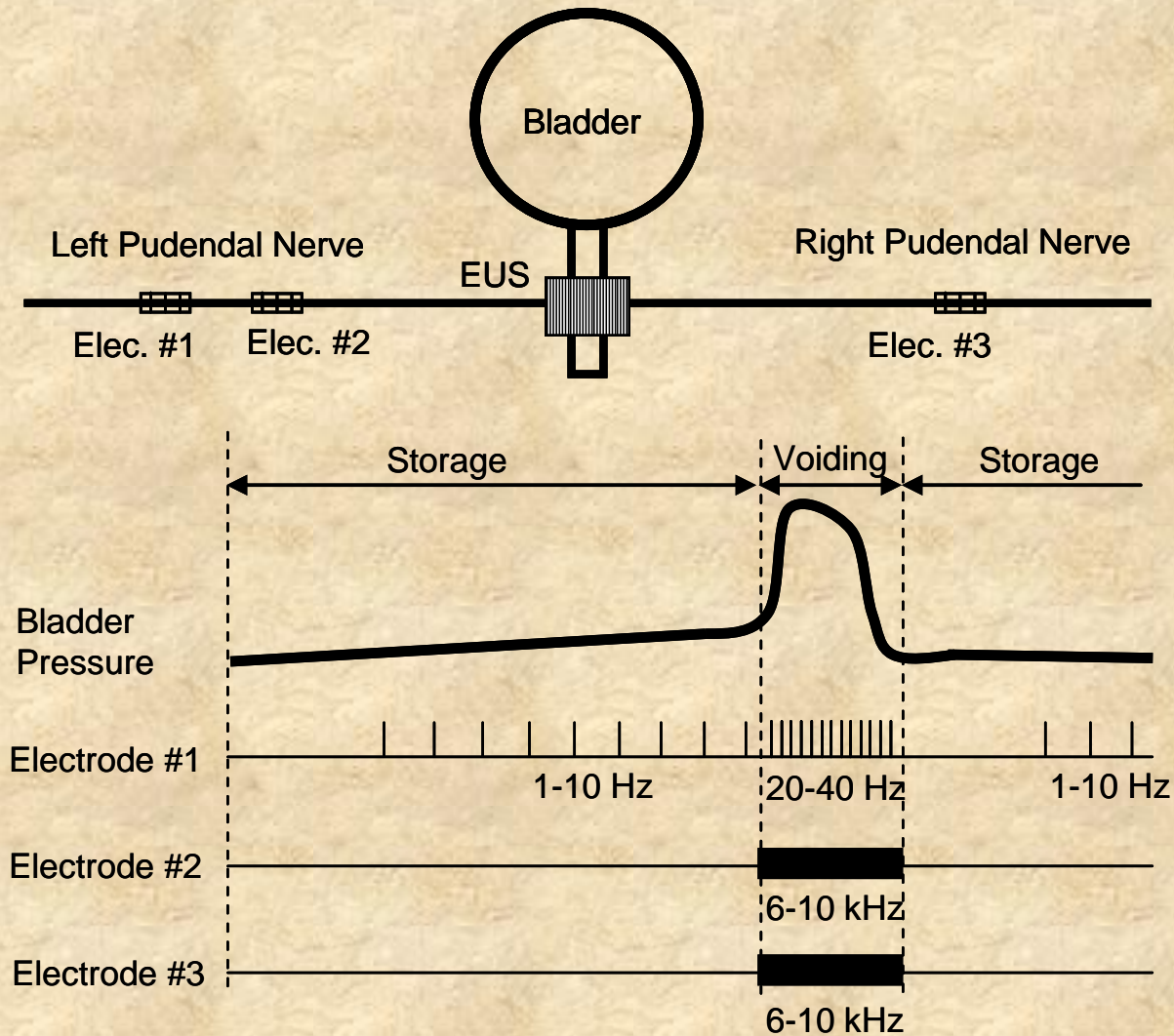
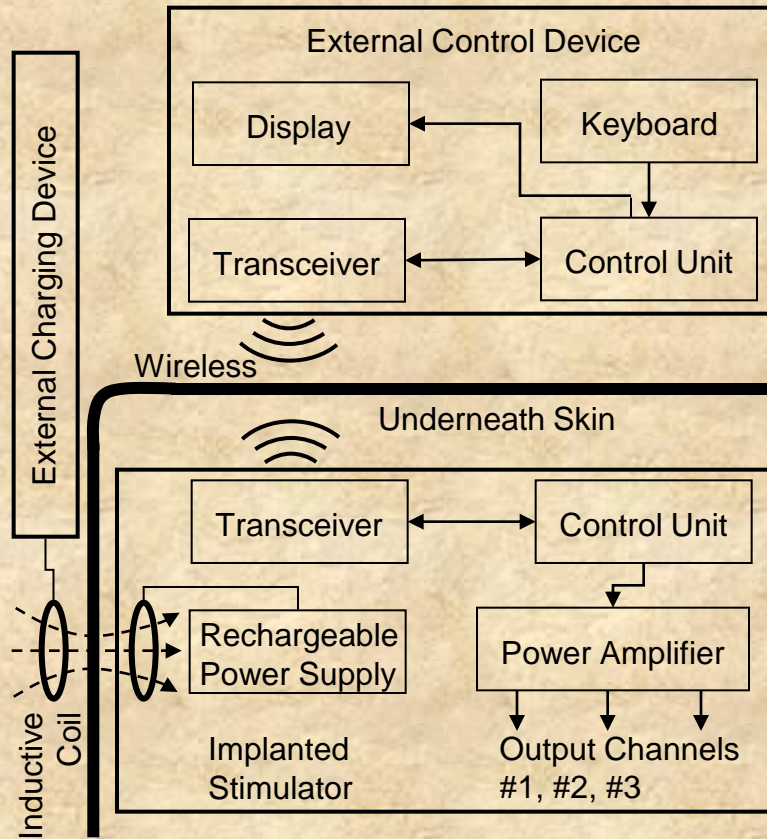


Figure 1: Our strategy to restore normal functions of the lower urinary tract after SCI. EUS – External Urethral Sphincter.

An Implantable Bladder “Pacemaker”



External Handhold Device

Setting the storage/voiding mode
Setting each channel individually
Wearable

Implanted Stimulator

Channel #1: 1-10 Hz or 20-40 Hz
Channel #2/3: 6-10 kHz
Small Size: < 5x5x1 cm
Power Supply: > 5 years, wireless charging
Communication: wireless

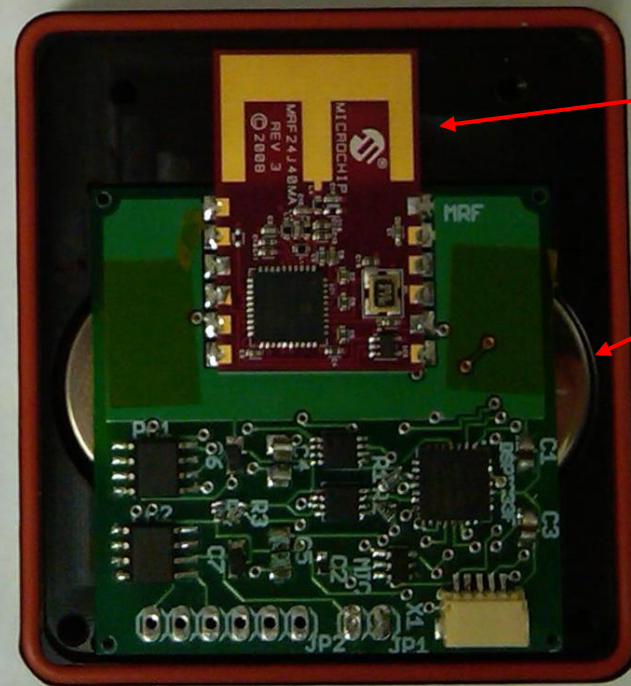
Figure 11: Diagram of the control device and the implantable stimulator.

An Implantable Bladder "Pacemaker"

Wireless controlled, battery powered
But not wireless charged



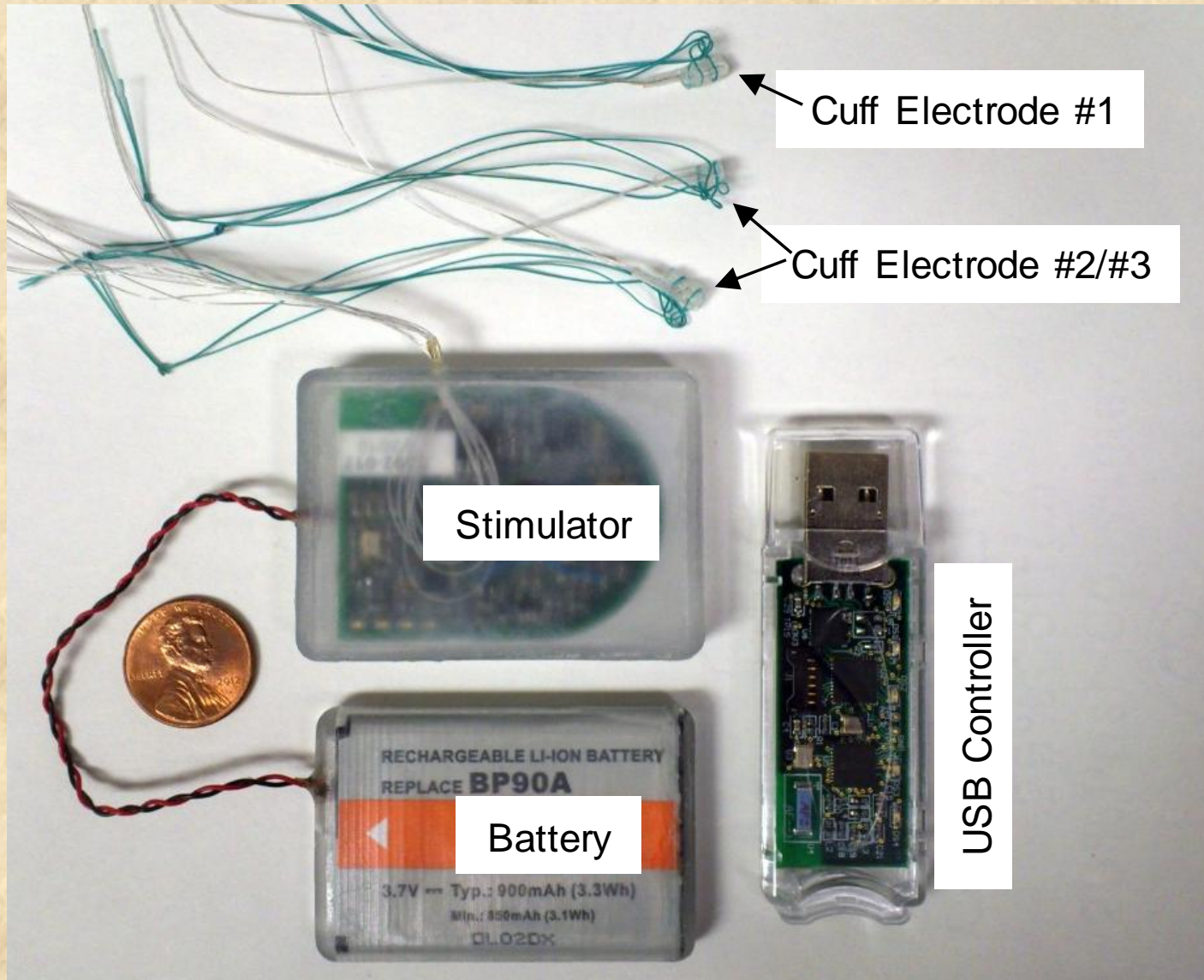
Version #1



Antenna

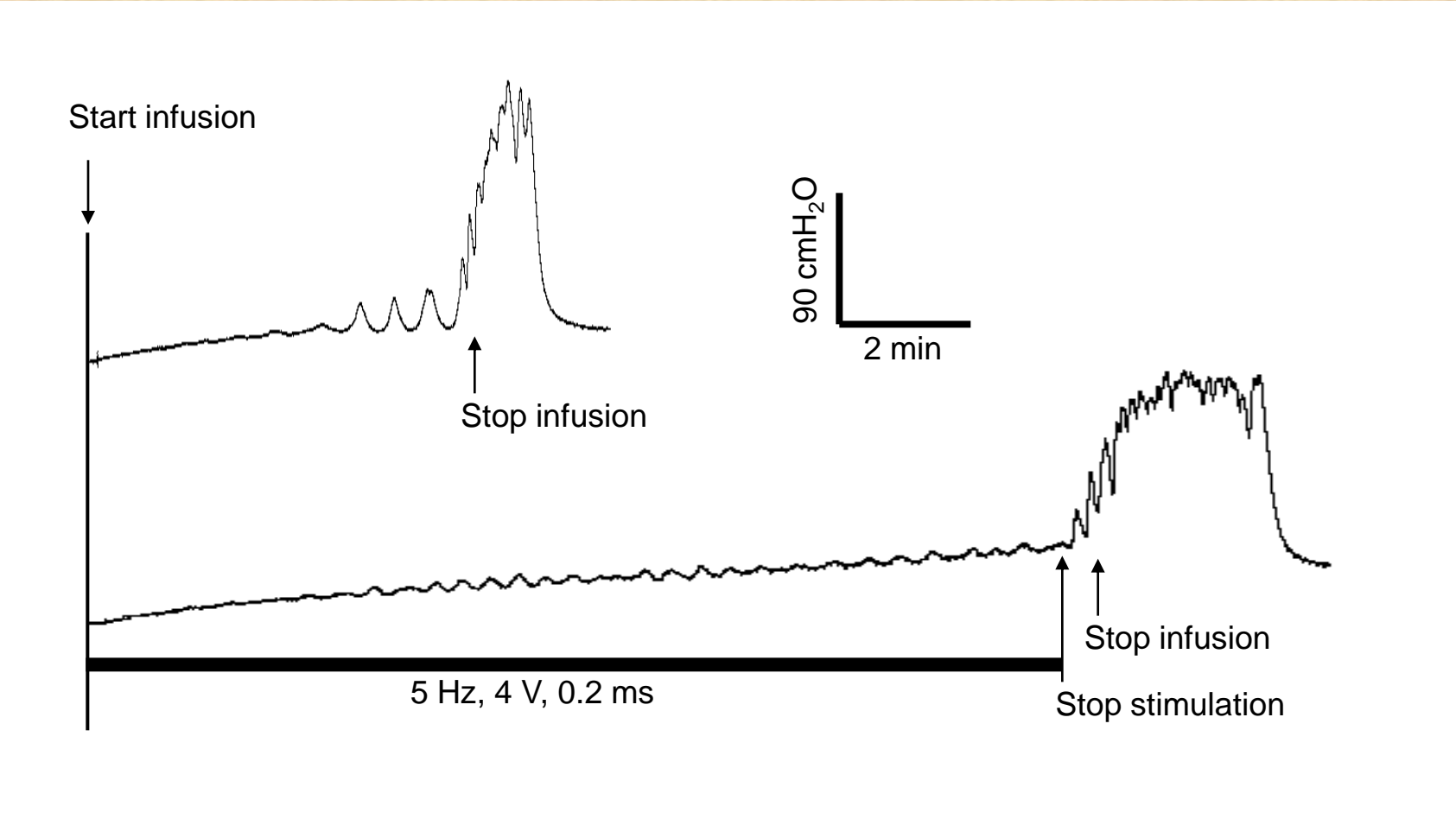
Battery

An Implantable Bladder “Pacemaker”

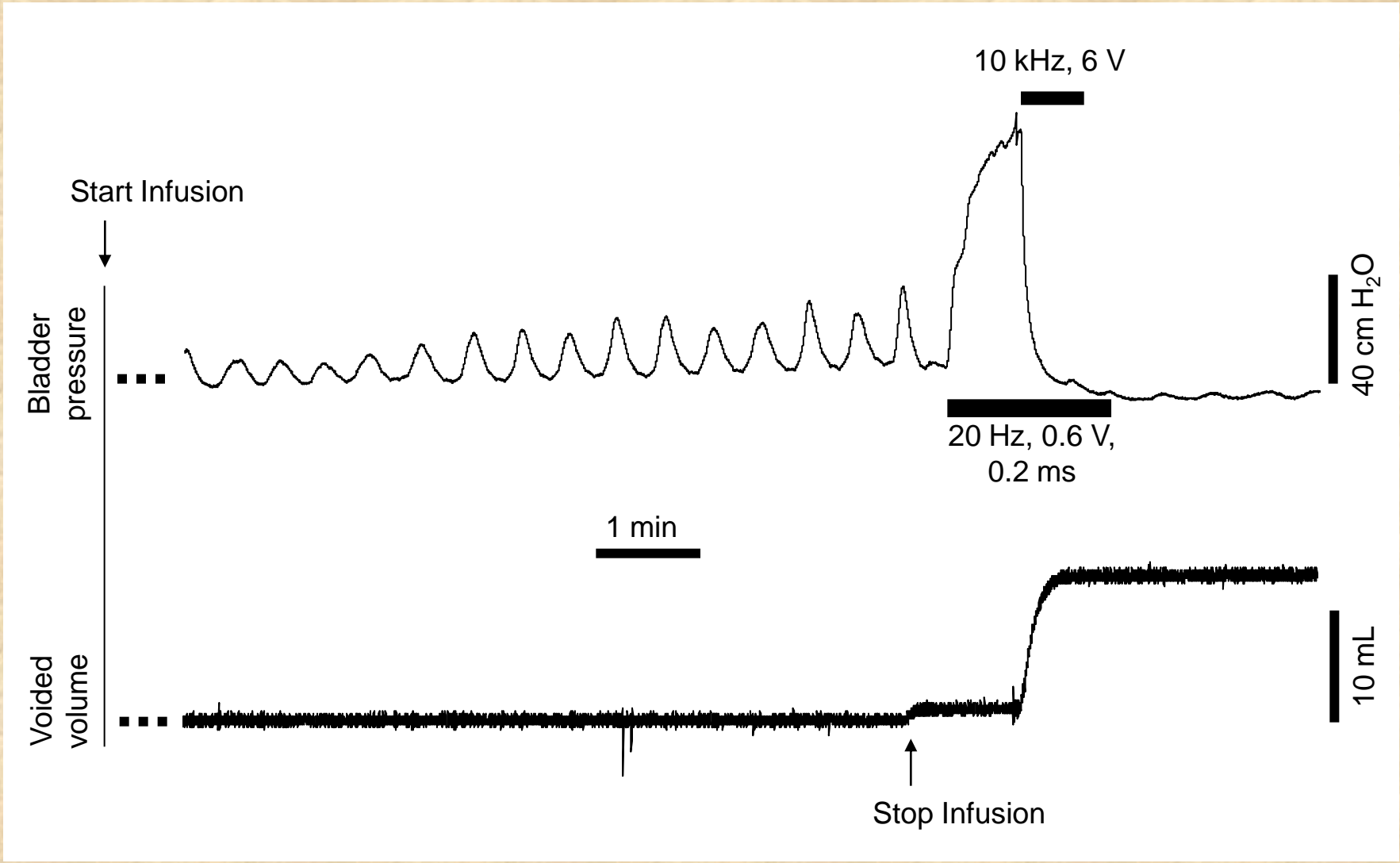


Wireless controlled, wireless charged, battery powered, implantable stimulator

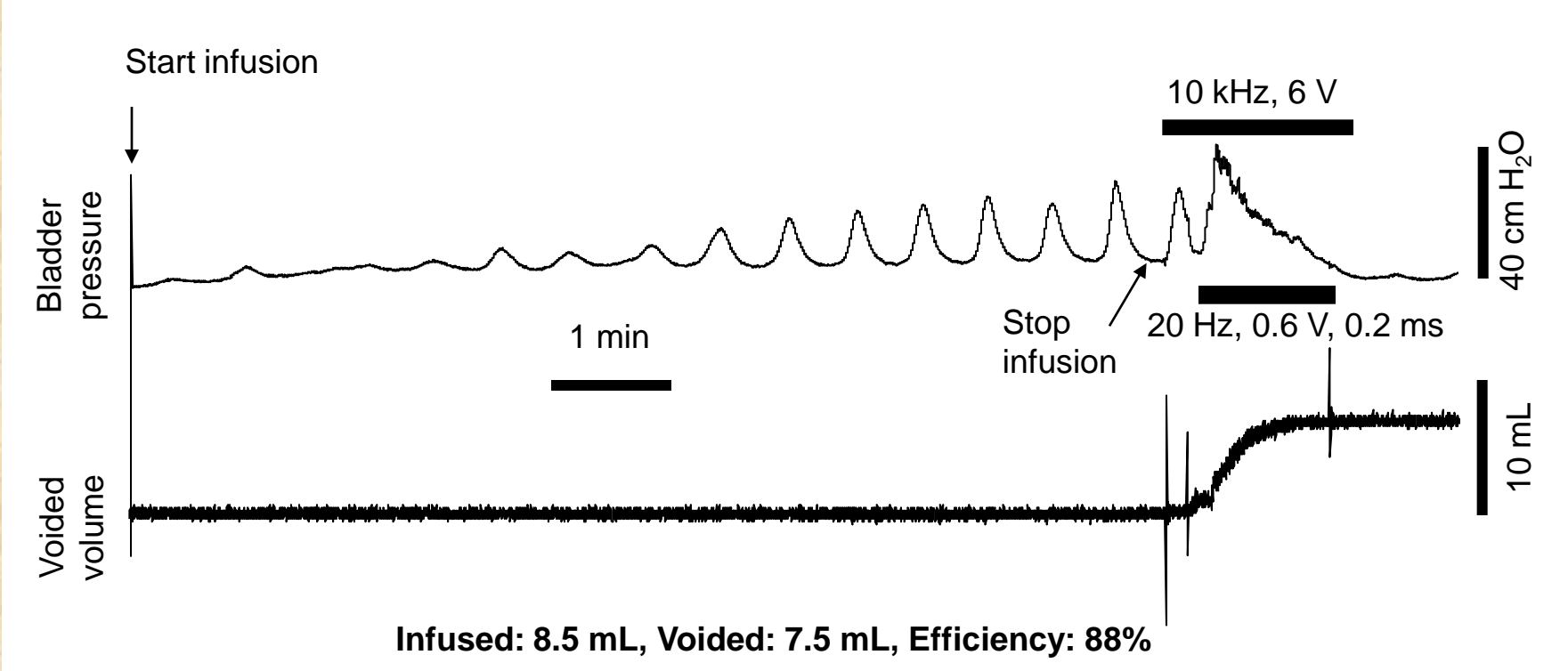
Bladder "Pacemaker" – Improving Storage



Bladder "Pacemaker" – EUS Blockade



Bladder "Pacemaker" – Low Pressure Voiding



An Implantable Bladder “Pacemaker” in Human

- Develop the bladder “pacemaker” for FDA IDE approval
- Clinical trial in human SCI subjects
- Additional funding

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