



ADAPTIVE REGULATION OF REGENERATED BLADDER SIZE AFTER IMPLANTATION WITH TENGION NEO-BLADDER AUGMENT™ EARLY CLINICAL OUTCOMES AND PRECLINICAL EVIDENCE

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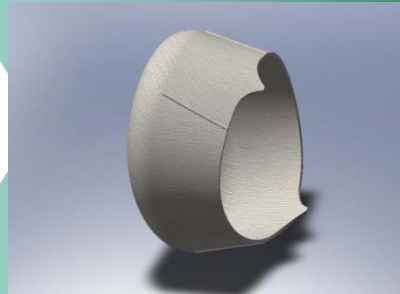
Urinary Bladder Regeneration

An organ regeneration technology platform

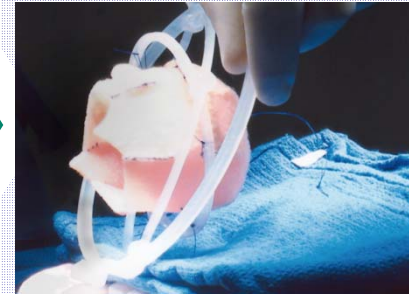
Autologous Cells



Scaffold



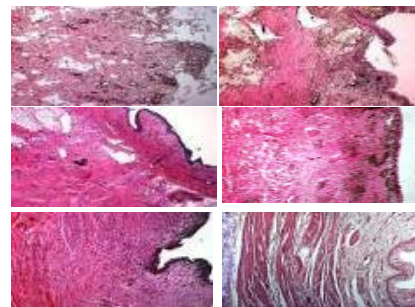
Neo-Bladder Construct



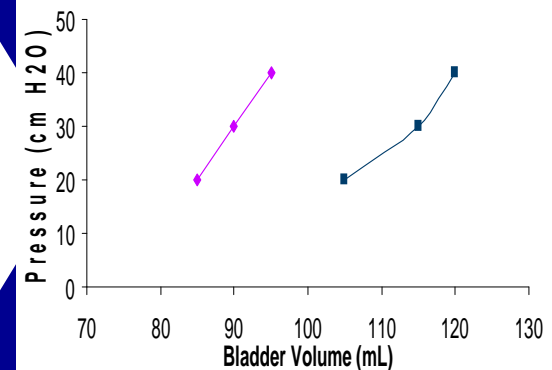
Surgical Implantation



In-vivo Regeneration



Improved Bladder Function



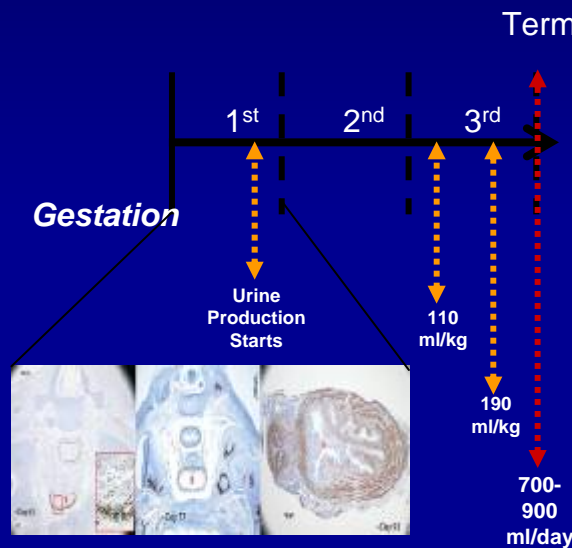
*Oberpenning et al, Nature Biotechnology, 1999

Human Urinary Bladder Capacity Development

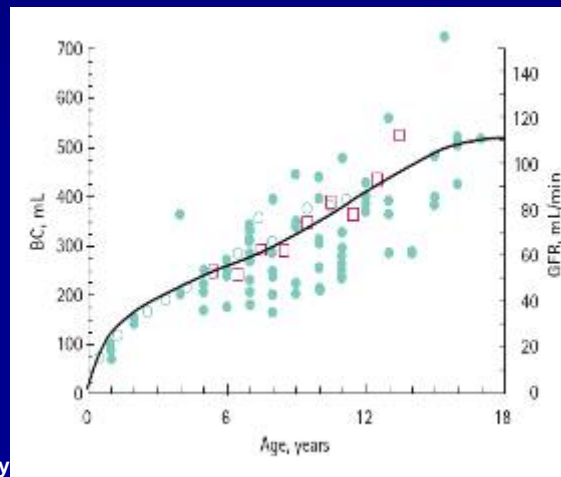
Role of cycling in bladder development



Increased urine production drives increased bladder capacity

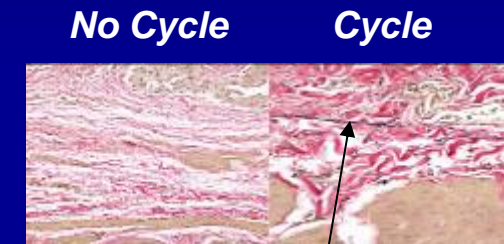


Pre-natal Period
Trimesters



Post-natal Period
Birth to adolescent

Elastin Fiber Development



Elastin fibers

- Muscle and elastic fibers increase while collagen is reduced
- Sphincter tone develops near term to facilitate cycling dynamics
- Bladder capacity increases with age and urine output



Regenerated Bladder Capacity

Neo-Bladder Replacement – Bioresponsive and functional

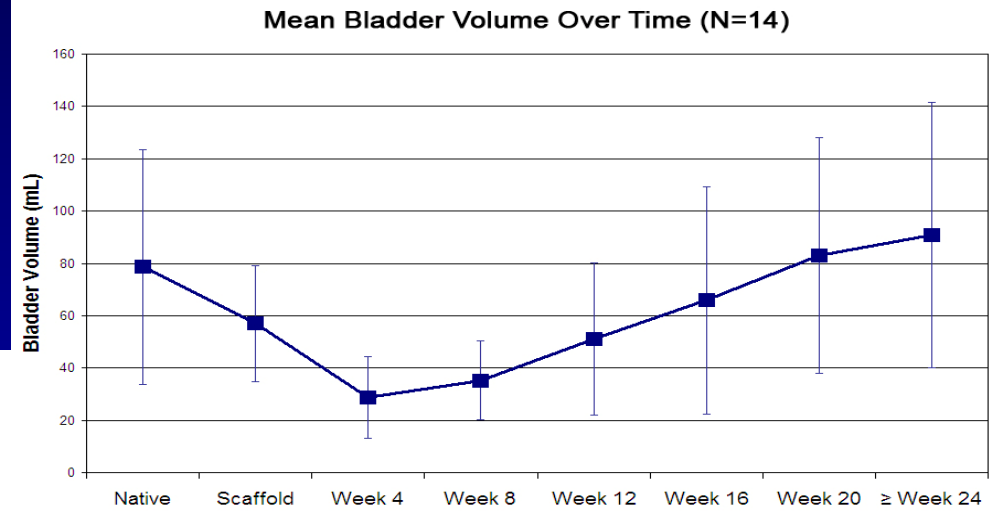
- Bladder capacity regenerated to baseline by 6 mo post-implantation.

Percent Change from Baseline Capacity

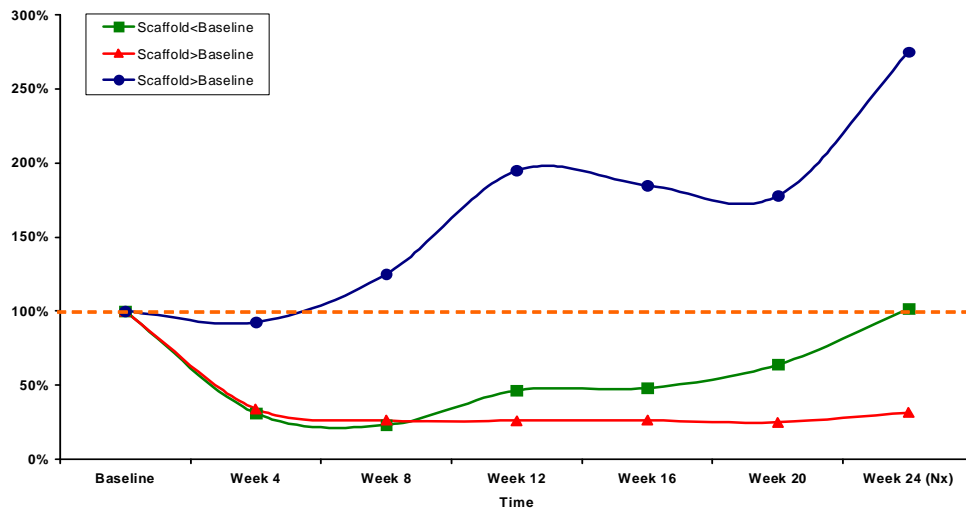
Large animal – Regenerated bladder size increased

Consonant animal – Regenerated bladder size remained same

Small animal – Regenerated bladder size decreased



Percent (%) Change from Baseline Capacity



- Bladder capacity develops with animal size and growth.

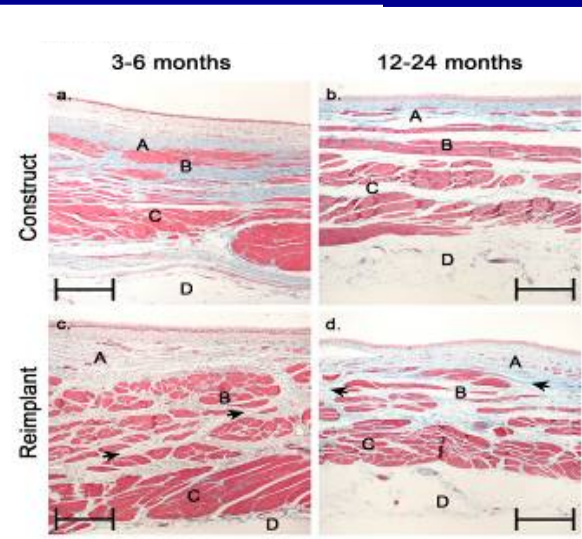
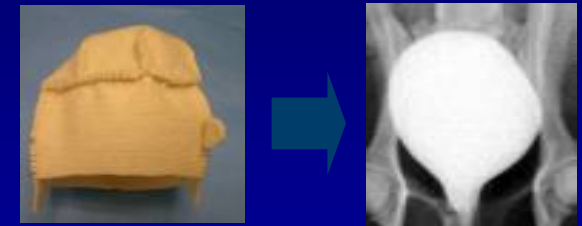
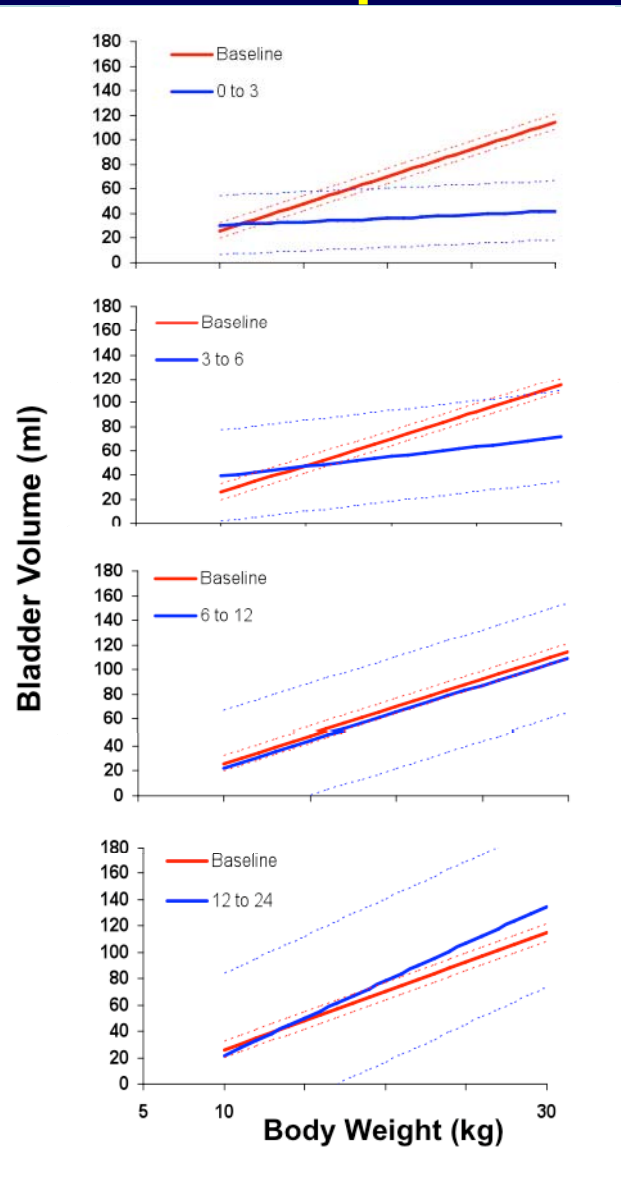
Jayo et al. Regen. Med 3(5)
2008

Neo-bladder Augment™



Regeneration of bio-responsive organs

- Neo-bladder Augment™
 - All animals healthy and continent, no indication of urological disease
 - All augmented bladders normal histology and function out to 2 years.
 - Urodynamics stable after 6 mo (capacity) and 9 mo (compliance) and durable to 2 years.
 - Neo-bladder showed adaptive response with age – normal bladder capacity:body wt.
 - No indication of abnormal urological or systemic findings to date.





Autologous Neo-Bladder Augment Construct **Pediatric clinical program, phase 2 clinical trial design**

- Open-label, uncontrolled
- 10 subjects (age 3-21) with neurogenic bladder secondary to myelodysplasia refractory to medical management including CIC and anti-cholinergic drugs
- Enrollment criteria: Most severe need for augmentation, as defined by:
 - Bladder pressure ≥ 40 cmH₂O at or below estimated bladder capacity for age, or
 - New-onset of upper urinary tract changes (hydronephrosis, vesicoureteral reflux)
- Primary endpoint:
 - Changes in bladder compliance as measured by urodynamics 12 months
- Secondary endpoints:
 - Changes in bladder pressure and capacity at 12 months
 - Changes in bladder compliance, pressure and capacity at 6, 9, 36 and 60 months
 - Safety, including known early and late complications of enterocystoplasty
- Exploratory outcomes:
 - Frequency and severity of incontinence episodes
 - Functional capacity and detrusor pressure at functional capacity



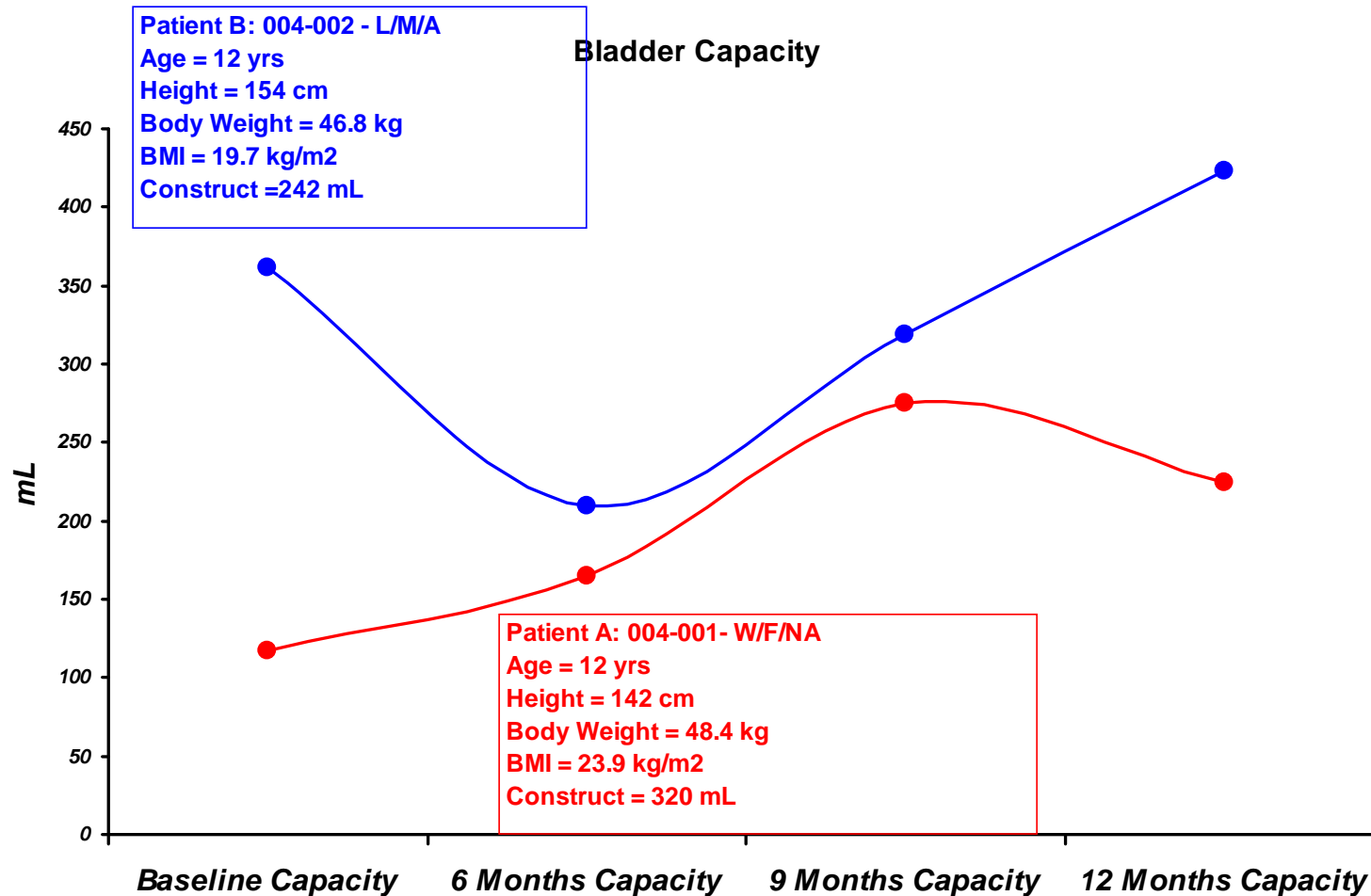
Case study: Bioresponsive Regeneration in Patients

<i>Patient</i>	<i>Male</i>	<i>Female</i>
<i>Age (yr)</i>	12	12
<i>BMI</i>	19.7	23.5
<i>Construct Size (ml)</i>	242	320
<i>Baseline capacity (ml)</i>	362	118
<i>Capacity at 12 months (ml)</i>	423	225
<i>% change from baseline</i>	17%	92%



Neo-Bladder Construct is Bio-responsive

Capacity is responsive to each patient's need





Conclusions

- **Autologous neo-bladders regenerated and grew appropriately to the recipient's body size in animals and humans.**
- **Neobladders elicited by Tengion Autologous Neo-Bladder Augment™ implantation are bioresponsive to the needs of the recipient.**