

RECONSTRUCTIVE UROLOGY

Engineering of a vascularized scaffold for artificial tissue and organ generation

Mertsching H, Walles T, Hofmann M, Schanz J, Knapp WH

Fraunhofer Institute for Interfacial Engineering and Biotechnology, Stuttgart, Germany, Tissue Engineering Network, Hannover Medical School, 30659 Hannover, Germany

Biomaterials 2005 Jun 22; [Epub ahead of print]

Tissue engineering is an emerging field in regenerative medicine to overcome the problem of end-stage organ failure. However, complex tissues and organs need a vascular supply to guaranty graft survival and render bioartificial organ function. Here we developed methods to decellularize porcine small bowel segments and repopulate the remaining venous and arterial tubular structures within these matrices with allogeneic porcine endothelial progenitor cells. Cellular adherence and vitality was characterized by quantitative 2-[(18)F]-fluoro-2'-desoxy-glucose (FDG) positron emission tomography (PET) and subsequent immunohistological work up. The generated matrices showed insulin-dependent FDG uptake predominantly in the region of the former vascular structures. Stain for vitality and the specific endothelial markers CD31, VE-Cadherin and Flk-1 matched this functional finding. Providing evidence for vitality up to 3 weeks post reconstitution and typical endothelial differentiation, these results indicate that our generated matrix allows the generation of complex bioartificial tissues and organs for experimental and future clinical application.

Editorial Comment

So far, one of the limiting factors in using cultivated tissue flaps or in vitro generation of whole organs was vascularization. Bioartificial grafts will usually become necrotic in the centre before sufficient revascularization takes place whenever a graft is implanted into the donor organism. The authors referring their results from Stuttgart, Germany and belong to one of the most advanced institutions dealing with biomaterials for regenerative medicine. They have shown that by using allogeneic porcine endothelial progenitor cells vascularization of acellular tissue flaps became possible. The achievements of this study were twofold: The authors were able to show that an endothelial differentiation was possible from their progenitor cells, and that with the help of progenitor cells differentiating into endothelial cells revascularization became possible as well. Once we achieve the goal of a "fast-track" revascularization of artificially cultivated flaps, we will be able to use much larger tissues and only then, we will be able to think about urinary bladder off the shelf.

Dr. Arnulf Stenzl

*Professor and Chairman of Urology
Eberhard-Karls-University Tuebingen
Tuebingen, Germany*

Urethral sensitivity in incontinent women

Kinn AC, Nilsson BY

Department of Surgical Science, Division of Urology, Karolinska University Hospital, Karolinska Institute, Stockholm, Sweden

Eur Urol. 2005; 48: 116-20

Objectives: The aim of this study was to ascertain whether frequent voiding and urge incontinence are associated with supersensitivity to electrical stimulation in the posterior urethra.

Methods: Current perception thresholds (CPT) were tested at four stimulus frequencies (1, 3, 20, and 100Hz; duration 0.5ms) using a square-wave constant current electrical stimulator connected to ring electrodes on a urethral catheter. The strength of the current at the first tingling sensation was regarded as the CPT. CPT analysis and cystometry were performed on 61 women (ages 28-89 years).

Results: CPTs were significantly higher at lower than at elevated stimulus frequencies, and they were also generally higher in old than in younger patients. Seven women repeated the CPT test after two months, and the thresholds were unchanged. There were no significant differences in sensitivity between patient groups with stress incontinence, urge, or mixed symptoms. Moreover, CPT was not significantly related to bladder volume at first sensation of filling.

Conclusion: Measuring CPT is an easy and reproducible method of testing urethral sensibility, but our results do not support the suspicion that urethral hypersensitivity is involved in increased voiding frequency and urge incontinence.

Editorial Comment

This paper was initially designed to study urethral sensitivity in women with stress urinary incontinence, urge incontinence or combined symptoms. Among other things, these authors were able to demonstrate a direct correlation between median sensory thresholds of the urethra and different age groups. There had been previous reports about a decrease of muscle cells (1) in the urethral sphincter with increasing age but there are to my knowledge no previous reports about a decreasing sensitivity of the urethral mucosa in older women. When we do a urethra-sparing cystectomy both in male and female patients, functional results tend to be less favorable in patients beyond 75 yrs. However, we know that some patients will have perfect results despite an age over 75 yrs. It has further been demonstrated that preservation of autonomic nerves, which most probably contain afferent sensory nerve fibers from the urethral mucosa, will improve not only sexual function but also urinary incontinence (2).

What we can learn from this paper for our elderly patients which are candidates for an orthotopic neobladder to the urethra is that preservation of autonomic nerves to the urethra may improve the functional outcome in old patients (for example those older than 70 yrs). It may also give us a hint how we can select patients who may be borderline candidates due to either their age or the status of their pelvic floor.

If we can standardize a preoperative evaluation, including sensory thresholds and contractility, we may be able to sort out those patients that will be continent despite an advanced age and/or radiation or other factors considered to be a contraindication for an orthotopic neobladder. These tests may also be a diagnostic help for urologists in their decision on how to treat patients with urinary incontinence. As an example, those with perfect sensitivity but decreased contractility may benefit from pelvic floor supporting surgery whereas those with a decreased or absent sensitivity of the urethra but perfect contractility might have better results with physical therapy and related forms of treatment.

References

1. Strasser H, Tiefenthaler M, Steinlechner M, Bartsch G, Konwalinka G: Urinary incontinence in the elderly and age-dependent apoptosis of rhabdosphincter cells. *Lancet*. 1999; 354 (9182): 918-9.
2. Turner WH, Danuser H, Moehrle K, Studer UE: The effect of nerve sparing cystectomy technique on postoperative continence after orthotopic bladder substitution. *J Urol*. 1997; 158: 2118-22.

*Dr. Arnulf Stenzl
Professor and Chairman of Urology
Eberhard-Karls-University Tuebingen
Tuebingen, Germany*