

A debilitating condition: «It does not kill you, but takes away your life»

A potential gamechanger in stress urinary incontinence

Stress urinary incontinence is a major health issue that affects over 200 million people worldwide, but is currently not receiving the focus and attention it should. It has a severe impact on physical and psychological health, and imposes a high financial burden on affected individuals, healthcare systems and society. Nevertheless, existing treatment options do not offer a solution for approximately 35% of patients. MUVON Therapeutics, a spin-off from the University of Zurich, is working towards breaking the stigma around stress urinary incontinence and developing a novel regenerative tissue engineering therapy with the goal of providing a safe and effective cure to help these patients regain control.

Stress urinary incontinence

Stress urinary incontinence (SUI) represents an involuntary loss of urine by increased intra-abdominal pressure from coughing, sneezing, laughing or any physical activity. SUI is a highly debilitating condition no one talks about. Yet, it affects the lives of over 150 million women worldwide.

The peak of stress urinary incontinence (SUI) development in women around their mid-forties can be attributed to a combination of factors related to hormonal changes, aging, and life events such as pregnancy and childbirth. Here are some reasons why SUI may become more prevalent during this period:

1. **Pregnancy and childbirth:** The effects of pregnancy and childbirth on pelvic floor integrity can become more pronounced as women age. Multiple pregnancies and vaginal deliveries can lead to stretching and weakening of the pelvic floor muscles and supportive structures. These changes can contribute to

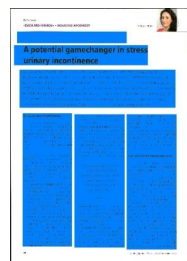
the onset or exacerbation of SUI.

2. **Menopause and hormonal changes:**

Menopause typically occurs in the late forties or early fifties. During this period, there is a significant decline in estrogen levels. Estrogen plays a crucial role in maintaining the health and elasticity of the tissues in the urogenital tract, including the urethra and the pelvic floor muscles. The decrease in estrogen can contribute to weakening of these tissues, making women more susceptible to SUI.

3. **Muscle tone and aging:** As we age, there is a natural reduction in muscle tone and elasticity. The pelvic floor muscles, which play a key role in sustaining continence, can weaken over time. This loss of muscle tone can make it more challenging for the pelvic floor to support the bladder during activities that increase intra-abdominal pressure.

«I am completely satisfied,
no incontinence, also I



*no longer need to use pads,
a clear improvement in
my quality of life and
my well-being.»*

Patient

- Weight changes:** The likelihood of obesity tends to increase with age. Excess body weight can contribute to the development of SUI by placing additional pressure on the pelvic organs and weakening the pelvic floor muscles.
- Connective tissue changes:** The process of aging is associated with changes in connective tissues throughout the body. These changes can affect the integrity of the tissues that support the bladder and urethra, potentially leading to SUI.

It's noteworthy that, while the mid-forties may represent a period when the cumulative effects of these factors become more pronounced, SUI can occur at different ages and for various reasons. Additionally, some women may not experience SUI until later in life. Individual experiences with SUI can vary, and factors such as genetics, lifestyle, and overall health also play a role in its development.

Current SUI treatment solutions

The choice of treatment depends on the severity of the condition, the underlying causes, and individual factors. Non-surgical treatments, such as pelvic floor exercises (Kegel exercises), lifestyle modifications, and behavioural therapies, are often considered as initial management strategies before moving on to surgical interventions. The choice of treatment should be personalized based on the specific needs and circumstances of the individual.

Surgical options typically considered for mild to moderate cases of SUI include in-

jectable bulking agents: substances like collagen or synthetic materials that can be injected into the tissues around the urethra to bulk up the tissue and potentially create a better seal for a couple of months. Another option is the insertion of a midurethral sling (i.e. tension-free vaginal tape [TVT] or transobturator tape [TOT]). These are minimally invasive procedures where a synthetic mesh tape is inserted under the urethra to provide additional support. The

tape acts as a sling, supporting the urethra and preventing involuntary urine leakage during physical activities. In some cases, individuals who have previously undergone sling surgery may experience complications or persistent symptoms. Revision or removal of the sling may be considered to address these issues, bringing along high probability of re-surgery complications.

In summary, all existing treatment options have drawbacks that range from low and short-term efficacy (for conservative treatments) to potentially serious adverse events associated either with invasiveness or the introduction of foreign material (for more potent surgical approaches). Consequently, only around 8% of affected women actively seek treatment, usually after choosing to live with significant symptoms and the associated limitations for years before seeking help.

Socio-economic impact of incontinence

The recently published research on the economic burden of urinary incontinence stated that it reached a staggering 69 billion Euro in 2023 for the EU. These costs include the impact of incontinence on individuals' health, medical consultation costs, absenteeism at work, nursing home admissions, continence pads and the related environmental impact.¹ This equates to roughly half the economic burden of diabetes,



which reportedly cost the EU about 149 billion Euro in 2019, and two thirds of the economic burden of cancer, which cost the EU about 100 billion Euro in 2020. The economic burden for females was four times higher than for males. Without better awareness, prevention, treatment and resource-wise use of continence technologies when UI cannot be cured, the economic burden will most likely increase.

One standout achievement that deserves special recognition is this year's unwavering commitment by key stakeholders to address the issue of incontinence. This joint decision by 22 scientific, professional, patient and non-profit organisations to sign a manifesto advocating for policy changes is a bold step forward and represents a testament to our belief in the positive impact that policy reforms can have on the lives of individuals dealing with incontinence.

The MUVON Project

Tissue engineering holds significant promise for patients in various medical fields, offering innovative solutions for regenerating damaged tissues and organs. This interdisciplinary field combines principles of engineering, biology, and materials science to create functional biological substitutes that can restore or enhance tissue function. For over a decade, pre-clinical and proof of concept studies were conducted in the tissue engineering and stem cell laboratory at the University of Zurich. Based on these results, the Swiss authorities gave their approval for a phase I clinical trial of the first-in-class tissue-engineering therapy, focusing on the treatment of stress urinary incontinence in women, which was completed in 2021.² To ensure that this promising therapy and technology is developed further clinically as well as commercially and made available to the millions of patients in need, we decided to intensify our

efforts and founded MUVON Therapeutics. The company is currently being accelerated by the Wyss Zurich Translational Center, which enabled the setup and initiation of the ongoing phase II clinical trial (<https://muvon-studie.ch/>) at the University Hospital in Zurich.

The first-in-class tissue-engineered regenerative approach consists of four steps. The therapy uses a population of the patient's own muscle precursor cells, isolated from a small biopsy (short outpatient procedure) and expanded under good manufacturing (GMP) conditions. After reaching a therapeutic meaningful number of viable cells, the tissue-engineered product is injected (a second short outpatient procedure) into the urinary sphincter muscle of the same patient (autologous approach) with highest possible precision, thus aiming to regenerate damaged skeletal muscle tissue, consequently increasing the muscles contraction strength (Fig. 1). This revolutionary personalized regenerative tissue-engineered approach is now in a larger advanced clinical trial and has the potential to bring hope for a long-term safe and efficient cure for millions of patients.

The novel MUVON approach offers a low-risk, minimally invasive treatment for moderate to severe SUI that aims at regenerating the urinary sphincter muscle, thus potentially providing a cure for this highly prevalent disease, allowing patients to regain control and live to their full personal and professional potential. ■

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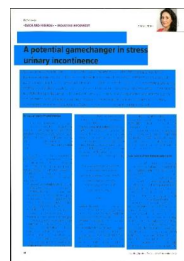
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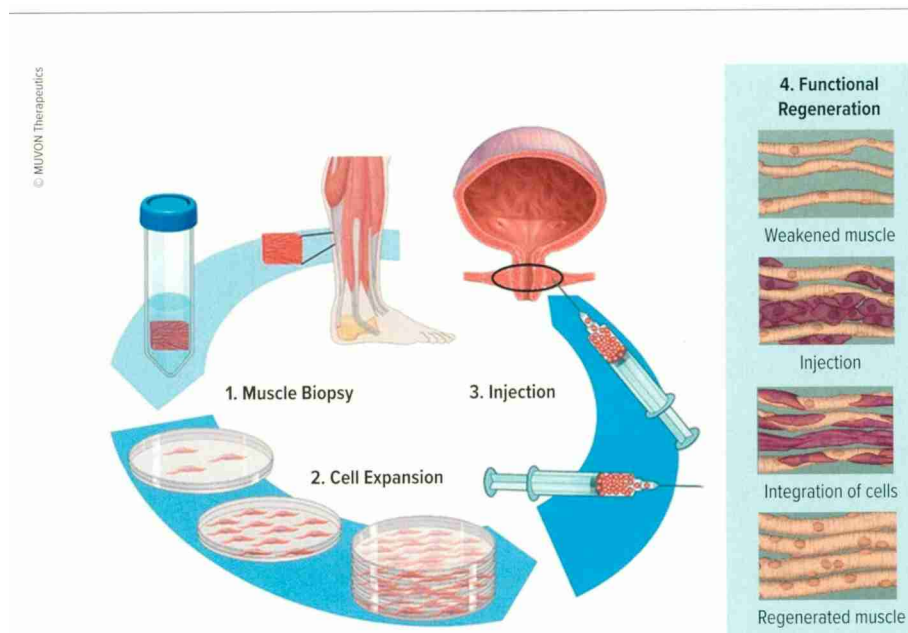


Fig. 1: Tissue-engineered regenerative approach in patients with SUI