MOTILITY

Cell therapy shows promise for women with anal incontinence caused by obstetric trauma

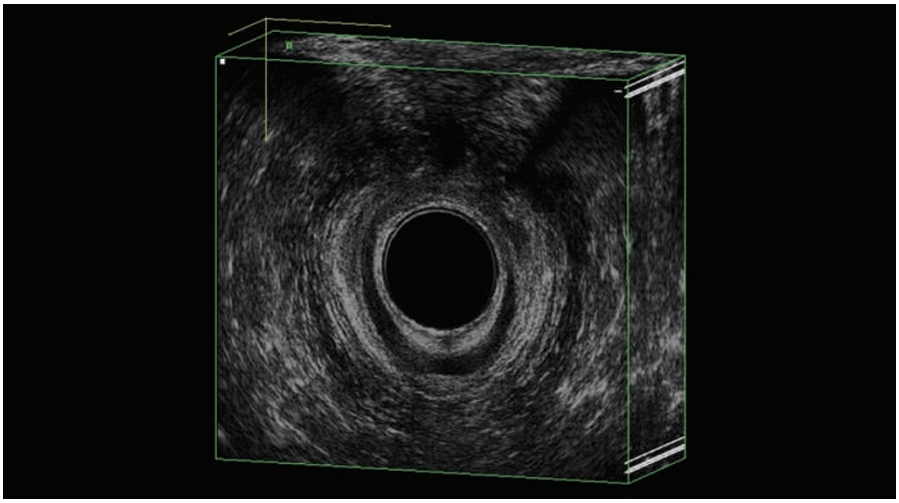
Injection of muscle-derived cells into the anal sphincter has potential as a new treatment option for women who develop anal incontinence after vaginal delivery, according to the findings of a pilot study by Andrea Frudinger and colleagues.

Anal incontinence often devastates patients' lives and treatment options are limited. Surgical intervention is required in many cases because conservative measures can be ineffective. In some cases, permanent colostomy is required. The success of nonsurgical alternatives, such as injection of silicone into the anal sphincter complex, has been variable.

Obstetric trauma is thought to be the most common cause of anal incontinence, with the external anal sphincter being disrupted by a third-degree tear in up to one-third of women after vaginal delivery. "I have been following women who have severe obstetric perineal trauma since 1993," says Frudinger, "…and was looking for [an anal incontinence] treatment that was less invasive and more successful." The successful treatment of stress urinary incontinence with autologous myoblasts and fibroblasts injected into the urinary sphincter inspired Frudinger *et al.* to try a modified approach for anal incontinence.

The 10 women selected for treatment were chosen from a group of participants recruited prospectively from a pelvic-floor outpatient clinic. All had third-degree or fourth-degree obstetric tears and had tried conservative treatments, but had not gained any significant clinical benefit; none had undergone surgery. Evidence of severe anal incontinence to gas and solids (Wexner incontinence score ≥9) was validated by incontinence diary records, and quality of life monitored. Anal endosonography confirmed that the women all had an anterior defect in the external anal sphincter.

Autologous myoblasts were cultured from striated muscle biopsy samples taken from the patients' pectoralis muscles and then harvested ready for implantation.



Courtesy of A. Frudinger. An ultrasound image of a defect of the external and internal anal sphincter (between 10 o'clock and 3 o'clock).

For 10 weeks before treatment (and 28 days after), the patients underwent anal electrical stimulation (15 min per day) to try to enhance myoblast integration.

Next came myoblast injection. "It is critical to bring the cells into the correct structure and height of the anal canal," says Frudinger, who worked with engineers to develop an ultrasound probe and injection device for the task. Armed with the new device, the group used ultrasound guidance to ensure cells were injected into the anal sphincter defect and hypothesized that "…the engineered cells would integrate into their surroundings and restore functionality to the damaged striated muscle…"

Treatment conferred significant and sustained improvements in quality of life—overall and for lifestyle, coping and embarrassment. There was also a significant reduction in the number of bowel movements and incontinence scores over time and at 1 year postimplanation. No adverse effects were reported.

"Now, 2 years after implantation [the patients] are still continent and live a 'new life'," says Frudinger. "Previously these women were isolated, always cautious about their food intake and planned their days around their bowel movements."

The authors could not, however, provide a physiological explanation for the improvements. Although the function of the external anal sphincter improved significantly at 1 month and 6 months postimplantation, at 12 months there was no difference from baseline. They acknowledge that a placebo effect may have occurred, but stress that the study size was too small to draw any conclusions. They also highlight the need to study the survival, distribution, integration and functional contribution of the myoblasts.

Frudinger and colleagues believe their study provides the first evidence that this procedure is feasible, well tolerated and safe, and have a double-blind, placebo-controlled, dose-finding study planned for the summer. As they conclude, "If the beneficial results we observed are sustained … then this procedure holds promise as a relatively noninvasive treatment for a common and distressing clinical problem."

Natalie J. Wood

Original article Frudinger, A. *et al.* Muscle-derived cell injection to treat anal incontinence due to obstetric trauma: pilot study with 1 year follow-up. *Gut* **59**, 55–61 (2010)