Letter to the Editor, BJOG Exchange

Re: Vaginal Er:YAG laser application in the menopausal ewe model: a randomised estrogen and sham–controlled trial

Dear Editor,

As authors of several published clinical studies using the same technology for the treatment of genitourinary syndrome of menopause (GSM) in women, we read with interest the recently published study from Mackova and colleagues [1].

We compliment the sophisticated design and methodology used in the study, however, we believe that the sheep model is simply not adequate to investigate GSM symptom relief, for several obvious reasons, the two most important being:

1) a sheep is an animal without natural menopause; therefore, it is impossible to compare the symptoms of induced-menopause after ovariectomy in sheep to those of menopause in women and,

2) it is impossible to measure quality-of-life-related symptom severity, nor their relief after treatment, in sheep.

GSM is a complex condition affecting 70% of postmenopausal women, who suffer from several symptoms severely affecting their quality of life.

Let us illustrate the complexity of the condition by focusing on only one of the symptoms of GSM – vaginal dryness. The physiology of vaginal lubrication is strongly connected to sexual pleasure and regulated by a complex interplay of different psychological and physiological factors. In premenopausal women this is orchestrated by circulating estrogen. Vasodilatation caused by an upstream signaling mechanism leads to increased capillary pressure and liquid flow to the vaginal mucosa. As always in nature, there are different pathways to achieve the same result, and to compensate for the absence of estrogen, the master regulator, new treatments are finding ways to achieve similar results independently of estrogen. Er:YAG laser with SMOOTH mode stimulates tissue turnover and also induces vasodilatation and angiogenesis, resulting in increased vaginal lubrication and better tissue quality. Several published studies have shown that multiple GSM symptoms are greatly reduced when using Er:YAG SMOOTH laser and that the results are comparable and last longer than local vaginal estrogens[2–5]. Even if there would be no change in vaginal epithelial thickness, the treated women reported excellent symptom relief, which should be the ultimate goal of any GSM treatment.

However, we have also shown that treatment with the same Er:YAG laser that was used in the Mackova et al. animal study, does in fact greatly increase epithelial thickness in women. Our most recently published study[3] has shown a 3x increase in epithelial thickness, measured 3 months after completed laser treatment, in a group of women with severe vaginal atrophy. They have reported significant

decrease in GSM symptoms, including vaginal dryness, which was reduced from 8.5 at baseline to 1.8 at the 3-month follow-up, as measured on a 0-10 VAS scale. The women were extremely satisfied with the result and the reduction of symptoms significantly improved their quality of life. Although the thickness of their vaginal epithelium greatly increased, we cannot say that this is the only reason for the relief of symptoms, as there are probably other factors at play, as for example, increase in angiogenesis, blood flow and improved vasodilatation. The mechanisms of action of the Er:YAG SMOOTH laser are still not completely clear. But what we know so far is that it is a safe treatment which greatly benefits women.

One must remember to be extra careful when extrapolating the results of animal model studies to human conditions, especially so with respect to conditions that significantly affect quality of life. We should rather trust the women.

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1. Mackova, K. *et al.* Vaginal Er: YAG laser application in the menopausal ewe model: a randomised estrogen and sham–controlled trial. *BJOG An Int. J. Obstet. Gynaecol.* (2020).

2. Gaspar, A., Brandi, H., Gomez, V. & Luque, D. Efficacy of Erbium:YAG laser treatment compared to topical estriol treatment for symptoms of genitourinary syndrome of menopause. *Lasers Surg. Med.* **49**, 160–168 (2017).

3. Gaspar, A., Silva, J., Calderon, A., Di Placido, V. & Vizintin, Z. Histological findings after non-ablative Er:YAG laser therapy in women with severe vaginal atrophy. *Climacteric* **23**, S11–S13, (2020).

4. Gambacciani, M. *et al.* Long-term effects of vaginal erbium laser in the treatment of genitourinary syndrome of menopause. *Climacteric* **21**, 148–152 (2018).

5. Gambacciani, M. *et al.* Sexual function after vaginal erbium laser: the results of a large, multicentric, prospective study. *Climacteric* **23**, S24–S27 (2020).