

ABSTRACT:

We aimed to test selected novel treatment modalities for pelvic floor dysfunctions and genitourinary syndrome of menopause. Both conditions are common in female, they negatively affect their quality of life, and current treatment options are not optimal.

We started our research with an extensive literature search. First, we summarized the information on animal models for, and the utility they may have in the investigation of the pathophysiology of POP and novel therapies. We systematically searched 7426 articles from which 51 fulfilled the inclusion criteria. From all screened animals, only the non-human primate develops POP spontaneously, however their use is controversial. We concluded that many studies have methodological shortcomings and lack standardization in reporting outcomes. Also, several other animals can be used as a model of surgery for POP, each of them with different purposes. For our later research we chose the rat model to simulate POP repair with synthetic mesh.

We also systematically reviewed the literature on the objective effects of non-ablative Er:YAG LASER on the skin and vaginal wall. We identified 7187 articles of which we included 15 in our review, including four that tested Er:YAG LASER on vaginal tissue. Er:YAG LASER energy induces measurable changes in the deeper skin or vaginal wall by a process of cell activation, production of extracellular matrix and tissue remodelling, however the evidence level was low with serious risk of bias in most articles, and a wide spectrum of outcome measures. This review helped us to build the design of an animal study. We also reviewed the literature on LASER therapy for POP and UI. We included 31 studies on 1530 adult women. All studies reported an improvement of POP or UI after LASER use, but the quality of studies was mostly poor and risk of bias serious. We identified only one randomised controlled trial and two controlled cohort studies in urinary incontinence and using standardized validated tools. The risk of bias in the RCT was low; the controlled studies had a serious risk for bias. Unfortunately, there was a wide heterogeneity of LASER settings, application protocols and outcome measures. That review helped our group designing three RCT, one in GSM, one in POP and one for urinary incontinence; work that will be reported by one of my successors.

In the experimental part of my thesis, I conducted two animal translational studies. In the first we did a randomised controlled trial aiming to measure effects of non-ablative Er:YAG LASER on vaginal atrophy in the ewe menopausal model, as compared to sham and oestrogen application. We demonstrated that both the vaginal epithelial thickness as well as the vaginal compliance were modified by LASER and SHAM manipulation to a similar extent, but less than what was observed following systemic oestrogen replacement.

In the second experiment we preclinically tested a polyvinylidene fluoride (PVDF) mesh, used for POP surgical repair. We implanted the material in the rat incisional abdominal hernia model. We compared outcomes to those obtained after implantation of a structurally identical mesh but made from polypropylene (PP). Main outcome measure was biomechanical behaviour of explants, next to host inflammatory response and tissue integration. Biomechanical testing showed no difference between the two materials. Also, the host response and tissue integration were almost identical, and both implants caused ultimately some degree of muscle atrophy in later time points. In conclusion, we first demonstrate there is no difference in host response to implants either made from PP or PVDF when they have the same textile properties.

In conclusion, treatment of GSM, POP, and UI with Er: YAG laser is not supported by good quality evidence. Second, in the ovine menopause model laser therapy has an effect that is no different from that of sham manipulation, and both have less effects than systemic oestrogens. Third, in the rat model, implants that have an identical textile structure but that are made from a different polymer (PVDF or PP), hence have a different weight, generate the same biomechanical properties, host response and tissue integration. Both induce muscle atrophy on the medium term.