INTRODUCTION

TURP and open simple prostatectomy are still considered the standard treatment for benign prostatic obstruction (BPO) by most urologists [1]. However, in recent years the laser treatment of BPO has been gaining increased acceptance, and various laser devices have been introduced to treat patients and thus achieve comparable operative results but decreased morbidity [2–4]. Despite increasing numbers of patients treated with laser-based techniques, a detailed scientific evaluation of the introduced laser devices is rare [5–7]. Ablation capacities, extent of coagulation and of the necrotic tissue zone needs to be determined to combine efficient treatment with the greatest safety possible for the patient. To compare and judge the possibilities and limitations of different laser systems, ex-vivo data need to be available. The purpose of the present ex-vivo study was to evaluate the ablative and coagulative capacities of the 120-W thulium:yttrium-aluminium-garnet (Tm-YAG) 2 μm continuous-wave laser under standardized experimental conditions and compare it to the previously introduced 70-W device.

MATERIALS AND METHODS

Laser ablation was performed using a 120-W 2 μm continuous-wave Tm-YAG laser (RevoLix™, Lisa Laser Products, Katlenburg, Germany). Laser energy is emitted at 2.013 μm in a continuous-wave mode. Output power levels of 70 and 120 W were used in the trial. For the delivery of laser energy flexible 550- and 800-μm optical-core bare-ended fibres were used in a contact mode to vaporize tissue.

The model of an isolated blood-perfused porcine kidney was used to evaluate the tissue ablation capacity and the haemostatic properties, as previously described [8–10]. After catheterization of the renal artery and vein with a 10 F catheter, fresh porcine kidneys were perfused with 0.9% saline until the effluent was clear. Autologous blood was
harvested and anti-coagulated with sodium citrate.

Trials were performed in an acryl basin containing 0.9% saline at 37 °C. All experiments were carried out by the same surgeon. Four experiments were performed for each output power level and fibre, using one porcine kidney per measurement. Before commencing, each kidney was kept in the basin for 30 min to adapt to the temperature. To evaluate tissue ablation, the catheters in the renal artery and vein were removed, the vessels ligated and the capsule was removed. To determine the ablation capacity the kidneys were weighed before and after 10 min of laser treatment to a surface area of 3 cm × 3 cm. The weight difference was taken to be the amount of removed tissue. To achieve reproducible results, the laser fibre was moved in contact mode with a constant drag speed of 1 cm/min over the tissue.

To evaluate the haemostatic properties of the laser devices the kidneys were perfused with autologous blood by a roller pump via the catheter in the renal artery. Blood was drained from the kidneys through the catheter in the renal vein to ensure a clear vision in the basin. The haemostatic properties of the laser devices were determined using the same generator power levels. The perfusion rate was set to 80 mL/min, resulting in a pressure of 110–130 cmH₂O. After removing the renal capsule, a surface area of 9 cm² (3 × 3 cm) was treated. The blood loss was quantified by the weight difference of a swab before and after it was placed on the bleeding surface for 60 s.

Subsequently, samples of the ablated renal tissue were removed, cut on blocks and fixed in 4% formalin. After embedding in paraffin, the blocks were frozen at −19 °C, sectioned and stained using haematoxylin and eosin (H&E) to measure the depth of the coagulation zone.

To further evaluate cellular viability and the depth of necrotic tissue zone, NADH staining was also applied on tissue frozen at −80 °C after fixation. The depth of coagulation and necrotic tissue zone induced by laser energy were determined by microscopy using a calibrated calliper. Specimen preparation and the assessment of the coagulation zone and necrotic zones were carried out by one examiner.

Statistical data are presented as the mean (sd); the statistical significance of differences was evaluated using the Mann–Whitney test, with P < 0.05 considered to indicate statistical significance.

### RESULTS

The tissue ablation rate at a power output of 70 W was 9.80 (3.03) g/10 min when using the 550 μm fibre. Increasing the fibre diameter to 800 μm lead to less tissue ablation, of 6.38 (1.08) g/10 min. The amount of released laser energy was comparable in both groups, at 42.01 (0.18) and 42.17 (0.06) kJ. Increasing the power output to 120 W increased the amount of ablated tissue to 16.41 (5.2) g/10 min with the 550 μm fibre and to 12.91 (2.8) g/10 min with the 800 μm fibre (P = 0.005). Again, the total amount of ablated tissue was less than with the 800 μm fibre than the 550 μm fibre. As before, the amount of delivered energy did not differ, at 72.25 (0.05) vs 72.44 (0.35) kJ. The bleeding rate was unaffected by increasing the energy output; using the 550 μm fibre the bleeding rate was 0.11 (0.03) g/min at 70 and 0.15 (0.09) g/min at 120 W (P = 0.413). Using the 800 μm fibre the bleeding rate was 0.17 (0.08) g/min at 70 and 0.14 (0.08) g/min at 120 W (P = 0.646). Likewise, there were no significant differences in bleeding rates between the 550 and the 800 μm fibres at settings of 70 (P = 0.289) or 120 W (P = 0.807).

Histological examination of the extent of coagulation and the necrotic tissue zone are shown in Table 1; there was a stable penetration depth with increasing power output and increased fibre diameter. NADH staining confirmed the depth of the coagulation zone as measured by H&E staining (Fig. 1). However, using NADH, an inner zone of necrotic tissue underlying the coagulation zone could be identified (Fig. 2).

### TABLE 1 The depth of coagulation zone and necrotic tissue layer

<table>
<thead>
<tr>
<th>Mean (sd) variable, mm; bare-ended fibre, μm</th>
<th>Tm-YAG laser</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>70 W</td>
</tr>
<tr>
<td>Coagulation zone (H&amp;E staining)</td>
<td></td>
</tr>
<tr>
<td>550</td>
<td>0.36 (0.02)</td>
</tr>
<tr>
<td>800</td>
<td>0.49 (0.07)</td>
</tr>
<tr>
<td>P†</td>
<td>0.240</td>
</tr>
<tr>
<td>Necrotic tissue layer, including coagulation zone (NADH)</td>
<td></td>
</tr>
<tr>
<td>550</td>
<td>1.09 (0.14)</td>
</tr>
<tr>
<td>800</td>
<td>1.09 (0.30)</td>
</tr>
<tr>
<td>P†</td>
<td>0.779</td>
</tr>
</tbody>
</table>

*Penetration depth with increasing power output; †Penetration depth with increasing fibre diameter.
EX-VIVO EVALUATION OF THULIUM : YAG LASER EFFICACY

DISCUSSION

Laser treatment for BPO is gaining widespread acceptance but currently several different laser systems are used for treating BPO. In addition to the holmium:YAG and potassium titanyl phosphate (KTP)/lithium triborate (LBO) laser prostatectomy, innovative laser systems like the Tm-YAG have been introduced and are producing promising clinical data [11]. The initial data are also available using diode laser systems [3]. Due to different physical properties, e.g. the mode of energy emission and possible power outputs, comparisons of different lasers systems in terms of coagulation and ablation capacity, and more so the penetration depth, remain difficult. Therefore, not only clinical but also ex-vivo evaluation of the introduced laser systems is essential to understand the clinical outcome and possible complications, and to keep the risk of unwanted side-effects as low as possible.

The Tm-YAG laser was introduced into the treatment of BPO with promising results [4], which have now been confirmed by others [12,13]. The first ex-vivo evaluation of the previously introduced 70-W Tm-YAG showed an ablative capacity greater than that of the KTP laser, with comparable low bleeding rates [6]. With the introduction of a high-power (120 W) Tm-YAG, a re-assessment of the ablative and haemostatic properties is obligatory. In particular, it needs to be clarified if the higher power could create a deeper zone of tissue coagulation and tissue penetration, which might lead to an increased risk of collateral damage.

Our results show that the amount of tissue ablation increased with increased power output. Tissue ablation was lower with the 800 μm fibre, as laser energy is distributed over a larger surface area, leading to a lower energy density. However, independently of the fibre diameter, tissue ablation with the Tm-YAG seemed to be more effective than that reported in other systems. Wendt-Nordahl et al. [7] reported their results of tissue vaporization with a 120-W, 980-nm diode laser. Within an interval of 15 min, 10.6 g of renal tissue was vaporized, using a 600-μm optical-core fibre. This leads to a mean tissue ablation rate of 0.71 g/min, compared to rates of 1.64 and 1.29 g/min in the present study using the 550- and 800-μm fibres, respectively, at 120 W. Wendt-Nordahl et al. [14] also reported their experience of tissue ablation using bipolar plasma-kinetic vaporization and photoselective vaporization comparing the 80 W KTP laser with the 120 W LBO device. In this report the mean tissue vaporization rate was 0.95 g/min using plasma-kinetic vaporization, compared to 0.70 g/min with the 120-W LBO laser and 0.39 g/min with the 80-W KTP device, again showing lower ablation rates than with the Tm-YAG. However, the highest tissue ablation rate was with TURP; with a constant drag speed of 1 cm/s, a mean of 16.5 g/min of tissue was removed [7].

The clinical advantages of the laser devices are mostly the underlying reduced bleeding rates. Therefore, the data on bleeding rate and tissue coagulation zone seem more appealing. The present results indicate that in Tm-YAG laser vaporization the bleeding rate remains stable with increasing power output. The bleeding rate using the 550 μm fibre at 70 W and 120 W was 0.11 (0.03) and 0.15 (0.09) g/min, respectively. This appears to be different from the KTP laser; as reported by Wendt-Nordahl et al. [14], the bleeding rate increased with higher power output, from 0.21 g/min in the 80 W KTP system to 0.65 g/min with the 120 W LBO device. Low bleeding rates are also reported in ex-vivo evaluations of different diode lasers, at 0.14–0.21 g/min [5,7]. Compared to TURP, the bleeding rate is definitely lower in all laser systems, promising reduced intraoperative bleeding in the treatment of BPO. Bleeding rates in TURP are as high as 20.14 g/min [7].

Whatever energy device is used to treat BPO, there is some thermal penetration of tissue, and coagulation artefacts and necrotic tissue layers are produced. Some of these artefacts are visible, as in surface carbonization or denaturation of haemoglobin, leading to a white surface [15]. More interestingly are the effects of energy in the deeper tissue layers, leading to a lower possibility of histological assessment, or even collateral damage if tissue penetration is high. Therefore, knowledge about this depth of tissue penetration is essential to estimate the risk of unintended collateral tissue damage. Using standard H&E staining, the coagulation zone extent with the 70-W Tm-YAG was as shallow as 0.36 mm with the 550-μm bare-ended fibre (0.49 mm/800 μm fibre), which is comparable to TURP (0.28 mm) and about half of that measured for the 80-W KTP laser (0.66 mm) [9], whereas data on the 120-W LBO device has yet to be reported.

Interestingly, the coagulation zone is much deeper in the evaluated diode laser systems. Seitz et al. [5,16] reported total tissue coagulation rims of 9.56 mm (940 nm) to 10.2 mm (980 nm), using power settings of 60 and 100 W, respectively, in a similar ex-vivo kidney model. If and to what degree this deep penetration of tissue has an effect on the outcome of treatment for BPO remains to be evaluated in clinical studies. However, the depth of tissue penetration is undoubtedly a crucial factor in laser therapy of the lower urinary tract, and might be responsible for significant complications. Recently the first clinical follow-up data were presented by Rieken et al. [17], showing high reoperation rates of 32% within 12 months. Almost 20% of the patients had to undergo repeat surgery due to obstructive necrotic tissue. The authors suspected that deep tissue penetration was responsible for the high rate of necrotic tissue.

The effect of heating does not end at the border of the coagulation zone. Due to the applied laser energy tissue is heated and vaporization occurs, and below this vaporization zone there is a coagulation layer. Furthermore, the tissue below this coagulation zone inevitable has some heat penetration, which might cause cellular damage. Seitz et al. [5] described these damage zones as an inner and outer layer of coagulated tissue. To further evaluate this effect, we used NADH staining to evaluate the histological effects of the Tm-YAG in the porcine kidney model; NADH staining is currently known to be the best means of determining cellular viability [18].

The present results confirm the findings of Seitz et al. [5] about the existence of an outer coagulation zone and an inner zone of tissue affected by laser energy (necrotic zone). NADH staining seems to have the potential to clearly identify these two layers of energy effects (Fig. 2). Due to the nature of this staining method, the measurement of the affected tissue area appears to be more investigator-independent. Nevertheless, in-vivo studies, especially on prostatic tissue, are needed to confirm these findings.

Limitations of the study were centred on the animal model used, which provides a tool for the systematic evaluation of ablative devices [8–10]. Although the specific variables like heat capacity, thermal conductivity and diffusivity, optical tissue absorption and
scattering in the renal and prostatic tissue are very similar, the blood-perfused kidney does not resemble human prostatic tissue in every aspect [19]. Furthermore, any comparison between different laser devices and different studies must be analysed with care, as different environmental conditions or investigator-related variations might alter the measured results, e.g., tissue ablation. Especially the distance to the treated surface and fibre speed have significant effects on ablation capacities and are at risk of being influenced by investigator bias, which can lead to favourable results for one device over the other. Therefore, the results for ablative and haemostatic properties, and the coagulation zone of the devices, might be different when lasers are used in vivo.

Assuming bias-free measurement in the different published studies, the present model offers comparable conditions for every measurement, power output and wavelength to achieve a valid comparison. Although the ex vivo results cannot be translated to a clinical effect without further investigation, the ex vivo evaluation provides relevant information on possible limitations and risks of the tested energy devices. In our study there was an effective ablation and shallow coagulation zone with increased energy output, leading to the conclusion that increased power of the Tm:YAG laser should not lead to unwanted energy-related complications in the clinical setting.

In conclusion, in an ex vivo setting, the increased energy output of the 2-μm continuous-wave Tm:YAG laser from 70 to 120 W leads to an increased rate of tissue ablation with no apparent increase in bleeding rate or tissue penetration. Although awaiting clinical verification of the 120-W device, these results promise high treatment efficacy with a considerably decreased risk of bleeding.

CONFLICT OF INTEREST

None declared.

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Abbreviations: BPO, benign prostatic obstruction; Tm–YAG, thulium:yttrium-aluminium-garnet; H&E, haematoxylin and eosin; KTP, potassium titanyl phosphate; LBO, lithium triborate.

EDITORIAL COMMENT

Ex vivo models to assess comparative tissue vaporization efficiencies of various laser technologies need to be examined with a clear caveat that bias in technique can interfere with the outcome, and be misleading. This can occur despite the best intentions of the investigators, as these models do not mimic conditions during real clinical scenarios.

The present model is particularly unsuited for comparing high power 532 nm, 980 nm, Nd/
YAG, holmium and thulium systems with each other, as the optimum parameters for each in this model might not reflect the optimum efficiencies obtained in the clinical setting. For example, the high-power 532 nm wavelength selectively uses oxyhaemoglobin as the main chromophore, with little absorption of power by the irrigating aqueous medium. This means that most of the power is absorbed in the target tissue, with potential local conductive heating if there is no local method to remove the heat, e.g. blood perfusion or cooling irrigating fluid. In the ex-vivo model, the deep coagulation necrosis is caused by the local high conductive heat that is produced from the effective and highly laser-absorbent resulting hot tissue that has been treated with the 532 nm laser light. There is deep coagulation necrosis despite the shallow optical penetration depth in the model. In the clinical setting, this is limited by quick sweeps, good aqueous irrigation cooling the tissue, and actual perfusion of the tissue by its blood supply, removing the heat. This important technical concept is termed ‘thermal confinement’, and it is important to maintain it during clinical practice, to limit the unwanted side-result of deep coagulation necrosis, resulting in prolonged dysuria, tissue sloughing, and oedema causing retention.

In this ex-vivo model, fixed parameters for one technology might not be optimized for another, and thus comparative evaluations are basically placed into question as to validity, and can be misleading. For example, if the same power, sweep speed and distance, irrigating and perfusion qualities are used with the high-power 532 nm laser vs the 980 nm laser, there would be less power absorbed into the tissue by the 980 nm laser because about half the energy is absorbed by the aqueous medium between the tissue and the laser fibre. Also, as the optical penetration depth is greater, the laser light would cause deep heating effects produced primarily by the laser light. In theory, given the same scenario and technique, deeper coagulation necrosis would result. As such, each laser system and wavelength requires a different technique to optimize their outcomes. Using the 532-nm technique with 980-nm lasers will not produce the same outcomes.

This particular study is excellent as it focuses only on one wavelength to compare and contrast with power as the main differentiator. The results are not surprising given the laser characteristic of the Tm:YAG laser for this model. However, as the primary chromophore is water with this laser, the primary mechanism of action is the hot vaporizing quasi-continuous bubbles produce by the laser on contact to near-contact. That being stated, it is impressive that such a mechanism of action is so efficient in ablating tissue. Hopefully, this will translate effectively in the clinical setting.

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