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## Theoretical analysis of transurethral laser-induced thermo-therapy for treatment of benign prostatic hyperplasia. Evaluation of a water-cooled applicator

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**Abstract.** A mathematical model for predicting the temperature rise in transurethral laser-induced thermo-therapy for benign prostatic hyperplasia was developed. In the model an optical line source emitting light from an Nd:YAG laser isotropically was placed in the urethra. Water cooling of the urethral epithelium was modelled using a two-tube system. The relationship between the difference in outlet and inlet water temperatures and the highest tissue temperature level reached was theoretically investigated. It was found that the water temperature difference was linearly dependent on the steady-state maximum tissue temperature. The theoretical calculations suggest that the water-cooled applicator can be used to measure the maximum tissue temperature. With temperature control, the prostatic tissue temperature can be prevented from exceeding the boiling point of water, excluding tissue carbonization. The model was also used to evaluate the influence of a number of different parameters on the damaged tissue volume. Increasing the urethral lumen radius by a factor of two by means of inserting different sized tubes was found to augment the tissue volume raised to therapeutic temperatures by up to 50%. The calculations showed that cooling of the urethral epithelium can result in an increase in the damaged volume by 80% as compared to not applying any cooling. The temperature of the cooling water was found to influence the tissue temperature only to a small extent.

### 1. Introduction

Benign prostatic hyperplasia (BPH) is a common condition affecting men past middle age (Berry *et al* 1984). Outlet bladder obstruction caused by BPH has most frequently been treated with transurethral resection of the prostate (TURP) (Blandy 1978). Despite a high efficacy, the intraoperative and postoperative morbidity associated with TURP, including failure to void, bleeding requiring blood transfusions and genito-urinary infections (Mebust *et al* 1989, Doll *et al* 1992) have led to investigations of alternative treatment modalities with fewer side-effects.

A number of medical treatment modalities for improving obstructive bladder outlet symptoms due to BPH are being clinically investigated (Petrovich *et al* 1993). The non-medical interventions under investigation include balloon dilatation (Wasserman *et al* 1990), urethral stenting (Nielsen *et al* 1990) and cryotherapy (Rigondet and Salé 1985) as well as thermo-therapy. Prostatic thermal coagulation and hyperthermia have been induced using microwaves (Strohmaier *et al* 1990, Devonec *et al* 1991, Homma and Aso 1993), focused ultrasound (Madersbacher *et al* 1994), radiofrequency heating (Schulman *et al* 1993) and laser irradiation.

Laser treatment of BPH has been performed relying primarily on either direct vaporization or photocoagulation of the adenomatous tissue. Transurethral vaporization

has been achieved using a 'hot tip' (Daughtry and Rodan 1993) or a contact free beam (Narayan *et al* 1994). For photocoagulation of the enlarged prostatic gland, different strategies have been employed such as transurethral coagulation using either side-firing fibres (Roth and Aretz 1991, Costello *et al* 1992, Kabalin 1993, Norris *et al* 1993) or diffusing fibres (Cromeens *et al* 1994, Suzuki *et al* 1994a, b). Using side-firing fibres, laser energy is applied to the enlarged prostatic lobes one at a time. The fibre is placed in up to eight different locations in order to coagulate a satisfactory amount of prostatic tissue. Simultaneous treatment of the prostatic lobes can be performed using a cylindrical diffuser. Transurethral coagulation eventually leads to sloughing of the necrotic tissue forming a cavitation followed by re-epithelization of the urethra (Cromeens *et al* 1994). However, the treatment does not result in an acute improvement in micturition, which leads to the requirement of inserting a suprapubic catheter. The catheter can in most cases be removed within 3 weeks (Schulze *et al* 1995). Another method of inducing prostatic photocoagulation involves interstitial application, which implicates that laser fibres are inserted into the prostate either percutaneously, transurethrally or transrectally (Muschter *et al* 1993, Amin *et al* 1993, McNicholas *et al* 1993, Orovan and Whelan 1994, Muschter and Hofstetter 1995). With this method, the urethral epithelium is spared. No tissue sloughing occurs; instead the coagulated tissue is replaced by fibrosis which reduces the prostate volume and relieves the pressure on the urethra (Johnson *et al* 1994). Using a power setting and an irradiation time of approximately 5 W and 10 min, respectively, coagulative necrosis of large volumes has been obtained. However, this mode of interstitial treatment requires up to 10 insertions at different locations in the prostatic gland, which makes the procedure time consuming. No laser method has so far been proved superior to the others or to TURP. Thus, each modality should be further investigated and the results should be compared to the results obtained using TURP.

The laser of choice for producing photocoagulation has been the Nd:YAG laser emitting light at 1064 nm, which is in the near-infrared region of the spectrum. Near-infrared light has a comparatively deep penetration depth in tissue enabling deep thermal coagulation (Svaasand *et al* 1985). Immediate coagulation occurs at a tissue temperature of about 60 °C (Thomsen 1991). However, the tissue damage depends on both temperature and time and can be described mathematically by a 'damage integral' based on an Arrhenius relationship (Henriques 1947). Raising the temperature to 100 °C will cause boiling of tissue water. The boiling process uses the laser energy as latent heat and the tissue becomes dehydrated. After dehydration prolonged irradiation inducing a subsequent temperature rise results in carbonization (LeCarpentier *et al* 1993). Carbonization of tissue during photocoagulation has in most cases been avoided due to the risk of damaging the laser applicators and by the fact that carbonized tissue absorbs laser light very strongly. This results in a diminished light penetration depth (Jacques 1993) which reduces the effectiveness of feedback temperature control (Tranberg *et al* 1995). However, by inducing carbonization, the damaged volume becomes greater for a given amount of deposited laser energy (Wyman *et al* 1994).

Mathematical modelling of thermo-therapy can be used for extensive and inexpensive simulations of different heating configurations in order to optimize the treatment. Thermal modelling of microwave prostatic hyperthermia has been performed by Martin *et al* (1992). They came to the conclusion that some kind of thermometry should be employed during treatment due to variability in tissue temperature depending on individual blood perfusion rates, exerting a tissue cooling mechanism. Thus, the concept of constant power setting should not be employed during a prolonged heat treatment. A number of mathematical models have been developed to predict the thermal response to laser irradiation (for a review see the article by McKenzie (1990)). A model simulating transurethral laser treatment of

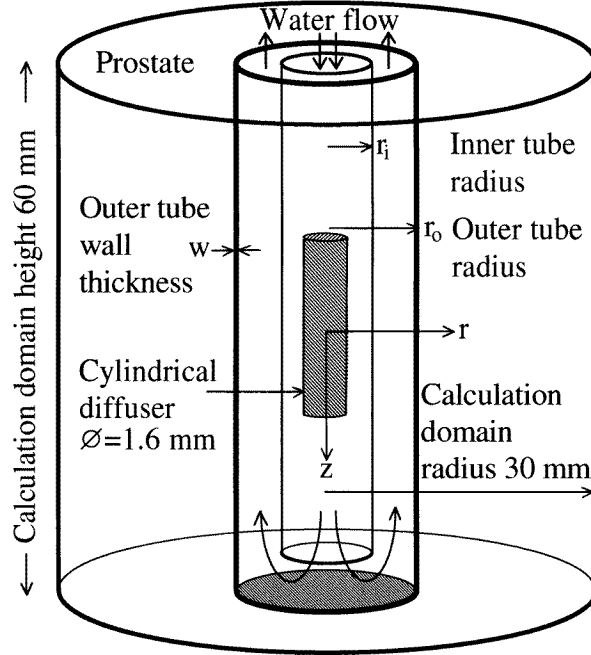
BPH using collimated light irradiating the inner wall of the urethra at a right angle has been elaborated by Anvari *et al* (1994). In that study, the theoretical results pointed to the diode laser at 810 nm being theoretically well suited for photocoagulation, although not as good as the Nd:YAG laser emitting at 1064 nm. Roggan and Müller (1995) have developed a model simulating the prostatic temperature rise during transurethral laser irradiation using cylindrical diffusers in conjunction with water cooling of the urethral epithelium. The temperature rises predicted in that study agreed closely with experimental measurements, which showed that cooling of the tissue surrounding the laser applicator can result in a significant increase in the coagulated volume.

The model presented in this paper was developed to thoroughly investigate the influence of a number of different parameters on the damaged volume in transurethral laser-induced thermo-therapy for BPH using cylindrical diffusers. This kind of laser treatment appears to be a promising therapeutic method (Cromeens *et al* 1994, Suzuki *et al* 1994a,b). The method is minimally invasive and simple to apply as it only requires the insertion of the diffuser into the prostatic urethra. The influence of cooling the urethral surface with circulating water was theoretically investigated. Cooling of the tissue surface during laser irradiation forces the maximum tissue temperature deep into the tissue (Svaasand *et al* 1985, Stureson and Andersson-Engels 1995b). Shifting the location of the maximum temperature from the surface of the applicator into the tissue will result in an increased volume of tissue damage, which is desirable in treatment of BPH. Critical areas such as the external sphincter can also be prevented from damage using a cooling system (Suzuki *et al* 1994b). The theoretical results are used to evaluate the effectiveness of a cooled applicator as compared to a non-cooled applicator in causing damage to the prostate.

Monitoring of the tissue temperature is critical if a temperature below the boiling point of water is to be maintained. By maintaining the tissue temperature below 100 °C tissue dehydration will be limited and carbonization will be prevented. Using the same laser power setting for different patients will result in uncontrolled tissue temperature due to interindividual variations in optical properties as well as blood perfusion rates. Temperature monitoring can be performed using invasive probes such as thermocouples or thermistors, or non-invasively using MRI (Jolesz *et al* 1988). However, if the laser applicator itself could provide information of the maximum tissue temperature, much is expected to be gained. In this study, the theoretical relationship between the maximum tissue temperature and the difference in outlet and inlet water temperature of the water-cooled applicator is investigated.

## 2. Mathematical model

Transurethral photocoagulation of the prostate in conjunction with surface cooling was modelled using the geometric representation as shown in figure 1. Because the laser irradiation emitted from a cylindrical diffuser can be described in cylindrical coordinates, this representation was chosen. The diffuser of variable length  $d$  with a circular cross section of radius  $r_d$  equal to 0.8 mm is assumed to be inserted into an open-ended inner tube of radius  $r_i$  with negligible wall thickness. The inner tube is concentrically placed in a closed outer tube of outer radius  $r_o$  and wall thickness  $w$ . The tube system is assumed to be inserted into the urethra. Water flows in the inner tube as illustrated in figure 1. The water flow is redirected at the bottom of the outer tube to flow in the opposite direction in the annulus between the outer and inner tubes. The inlet and outlet water temperature, that is, the water temperatures at  $z = -30$  mm, are denoted  $T_{in}$  and  $T_{out}$ , respectively. Prostatic tissue surrounds the outer tube.



**Figure 1.** A schematic representation of the model geometry showing the diffuser and the water-carrying inner and outer tubes. The two-tube system is assumed to be inserted into the prostatic urethra.

The water temperature will vary along the flow channels. Due to the relatively small temperature gradients in the direction of the flow, the conductive heat transport along the channels was neglected in the calculations. Also, the heat transfer between the water in the inner tube and the annulus between the inner and outer tubes was neglected because the water temperature difference is small. The temperature of the water in the inner tube can then be described by (Carslaw and Jaeger 1989)

$$A_i(z)\rho_w c_w \partial T_{w,i}(z, t) / \partial t = q_d(z) - V_w \rho_w c_w \partial T_{w,i}(z, t) / \partial z \quad (1)$$

where  $A_i(z)$  is the flow channel cross-sectional area of the inner tube ( $\text{m}^2$ ),  $\rho_w$  is the density of water equal to  $1.00 \times 10^3 \text{ kg m}^{-3}$  at  $5^\circ\text{C}$  and  $c_w$  is the specific heat of water equal to  $4.20 \times 10^3 \text{ J kg}^{-1} \text{ K}^{-1}$  at  $5^\circ\text{C}$  (Incropera and De Witt 1990),  $t$  and  $z$  represent the time (s) and axial coordinate (m), respectively, and  $V_w$  is the water flow rate ( $\text{m}^3 \text{ s}^{-1}$ ). The temperature of the water in the inner tube,  $T_{w,i}(z, t)$  (K), is taken as the average temperature over the cross-sectional area of the flow channel. The cylindrical diffuser is assumed to self-absorb a certain fraction,  $f$  (%), of the input laser power. This has been represented in equation (1) as a constant heat flux,  $q_d$  ( $\text{W m}^{-1}$ ), to the water in the inner tube. The flow channel area and the constant heat flux term have the following form:

$$\begin{aligned} A_i(z) &= \pi(r_i^2 - r_d^2) & q_d(z) &= \left( \frac{\text{laser power} \times f}{\text{diffuser length}} \right) & -d/2 < z < d/2 \\ A_i(z) &= \pi r_i^2 & q_d(z) &= 0 & \text{otherwise.} \end{aligned} \quad (2)$$

The temperature of the water in the annulus between the inner and outer tubes is described

by

$$\pi[(r_o - w)^2 - r_i^2]\rho_w c_w \partial T_{w,o}(z, t)/\partial t = [1/(R_t + R_{tw})][T_p(r = r_o, z, t) - T_{w,o}(z, t)] + V_w \rho_w c_w \partial T_{w,o}(z, t)/\partial z \quad (3)$$

where  $T_{w,o}(z, t)$  is the temperature of the water in the annulus (K),  $R_t$  is the thermal resistance of the outer tube wall ( $\text{m K W}^{-1}$ ) and  $R_{tw}$  is the thermal resistance between the water and the outer tube wall ( $\text{m K W}^{-1}$ ). In the above expression, the heat transfer between the water in the inner tube and the water in the annulus between the inner and outer tubes has been neglected. Also, the thermal resistance between the prostatic tissue and the outer tube was neglected assuming perfect thermal contact. The thermal resistances are expressed by (Rohsenow *et al* 1985)

$$R_t = (1/2\pi\lambda_t) \ln[r_o/(r_o - w)]$$

$$R_{tw} = (1/\pi\lambda_w \text{Nu}_o)(1 - r^*) \quad (4)$$

where  $\lambda_t$  is the thermal conductivity of the tube wall which was taken to be representative of glass equal to  $0.93 \text{ W m}^{-1} \text{ K}^{-1}$ ,  $\lambda_w$  is the thermal conductivity of water equal to  $0.57 \text{ W m}^{-1} \text{ K}^{-1}$  at  $5^\circ\text{C}$  (Incropera and De Witt 1990),  $\text{Nu}_o$  is the Nusselt number at the wall of the outer tube facing the water (dimensionless) and  $r^*$  is the ratio between the radii of the confining walls of the annulus formed between the inner and outer tubes, equal to  $r_i/(r_o - w)$ . The Nusselt number is defined as the ratio between actual heat transfer and conductive heat transfer. For laminar and fully developed flow in an annulus assuming constant temperature on one wall and the other insulated, the Nusselt number at the inner and outer tube walls can be found as a function of  $r^*$  in the book by Rohsenow *et al* (1985). The ratio  $r^*$  is in this study assumed to be 0.5 which gives a Nusselt number at the outer tube wall,  $\text{Nu}_o$ , of 4.43. Fully developed flow is obtained using tubes which are long in relation to the radii of the tubes. The assumption of laminar flow is unconditionally valid at a Reynolds number less than 1000 (Rohsenow *et al* 1985). The Reynolds number expresses the ratio between inertial and viscous forces in the fluid. In the present model, the Reynolds number will be greatest in the annulus between the diffuser and the inner tube. For this circular-tube annulus the Reynolds number can be expressed by (Hellström 1991)

$$\text{Re} = (2\rho_w/\pi\mu_w)V_w/(r_d + r_i) \quad (5)$$

where  $\text{Re}$  is the Reynolds number (dimensionless) and  $\mu_w$  is the dynamic viscosity of water, equal to  $1.52 \times 10^{-3} \text{ kg m}^{-1} \text{ s}^{-1}$  at  $5^\circ\text{C}$  (Incropera and De Witt 1990). By setting  $r_d$  to  $0.8 \times 10^{-3} \text{ m}$  and  $r_i$  to  $1.25 \times 10^{-3} \text{ m}$ , the maximum flow rate guaranteeing laminar flow becomes  $V_{w,\max} = 294 \text{ ml min}^{-1}$ . At the bottom of the tubes ( $z = 30 \text{ mm}$ ) the temperatures of the water in the inner tube and in the annulus were set equal.

The temperature of the prostate during laser treatment is governed by the following bio-heat equation:

$$\rho_p c_p \partial T_p(r, z, t)/\partial t = \lambda_p \Delta T_p(r, z, t) + Q_s(r, z) - \omega_p \rho_b c_b \rho_p [T_p(r, z, t) - T_b] \quad (6)$$

where  $T_p(r, z, t)$  is the tissue temperature (K),  $\rho_p$  is the tissue density ( $\text{kg m}^{-3}$ ),  $c_p$  is the specific heat of the tissue ( $\text{J kg}^{-1} \text{ K}^{-1}$ ),  $\lambda_p$  is the thermal conductivity of the tissue ( $\text{W m}^{-1} \text{ K}^{-1}$ ) and  $Q_s(r, z)$  is the laser heat-source term ( $\text{W m}^{-3}$ ). The third term on the right represents heat loss due to perfusion as modelled according to Pennes (1948), where  $\omega_p$  is the blood perfusion rate ( $\text{m}^3_{\text{blood}} \text{ s}^{-1} (\text{kg}_{\text{tissue}})^{-1}$ ),  $\rho_b$  and  $c_b$  are the density ( $\text{kg m}^{-3}$ ) and specific heat capacity of blood ( $\text{J kg}^{-1} \text{ K}^{-1}$ ), respectively, and  $T_b$  is the arterial blood temperature, in this study assumed to be  $37^\circ\text{C}$ . In the model, it was assumed that when the tissue temperature exceeded  $60^\circ\text{C}$  the blood perfusion was regionally interrupted due to

assumed shrinkage of coagulated capillaries caused by thermal denaturation and contraction of intracellular proteins (Thomsen 1991). The above expression for the perfusion neither accounts for the presence of major blood vessels nor deals with the directionality in the convective losses. However, it has been shown to give useful approximations of the general temperature distribution (Pennes 1948, Moros *et al* 1993) and is attractive due to the mathematical simplicity of the expression. For a survey of alternative models for perfusion, see the article by Arkin *et al* (1994). Because the metabolic heat generation is generally much smaller than the external heat deposited (Jain 1983), this term has been omitted from the above expression.

The heat flux at the boundary between the tissue and the outer tube is described by

$$-2\pi r_o \lambda_p \partial T_p(r = r_o, z, t) / \partial r = [1/(R_t + R_{tw})][T_p(r = r_o, z, t) - T_{w,o}(z, t)]. \quad (7)$$

The boundaries far from the laser source at  $z = \pm 30$  mm were assumed to be insulated. At the boundary at  $r = 30$  mm a constant temperature of  $37^\circ\text{C}$  was imposed.

The above equations were converted to finite-difference equations using the control volume formulation and solved numerically using a constant grid spacing of  $\Delta r = \Delta z = 0.25$  mm, where  $\Delta r$  and  $\Delta z$  are the radial and axial dimensions of the control volumes, respectively. The tissue control volumes next to the outer tube wall were modelled with half radial thickness.

The thermal properties of the tissue were given by the following relationships:  $c = 4.19(0.37 + 0.63W) \times 10^3 \text{ J kg}^{-1} \text{ K}^{-1}$  and  $\lambda = 4.19(0.133 + 1.36W) \times 10^{-1} \text{ W m}^{-1} \text{ K}^{-1}$ , where  $W$  is the water mass content of tissue (Welch 1984). By assuming a dry prostatic tissue density of  $1.3 \times 10^3 \text{ kg m}^{-3}$ , the prostatic tissue density was estimated from  $\rho = (1.3 - 0.3W) \times 10^3 \text{ kg m}^{-3}$  (Jacques and Prahl 1987). The water mass content of human prostate was assumed to be 80%. Using the above relationships, the thermal properties of prostate were found to be  $\rho_p = 1.06 \times 10^3 \text{ kg m}^{-3}$ ,  $\lambda_p = 0.51 \text{ W m}^{-1} \text{ K}^{-1}$  and  $c_p = 3.66 \times 10^3 \text{ J kg}^{-1} \text{ K}^{-1}$ . The heat capacity and density of blood were taken to be  $3.64 \times 10^3 \text{ J kg}^{-1} \text{ K}^{-1}$  and  $1.05 \times 10^3 \text{ kg m}^{-3}$ , respectively (Sekins and Emery 1982). As discussed above, the perfusion rate parameter,  $\omega_p$ , was irreversibly set to zero for the control volumes attaining a temperature of  $60^\circ\text{C}$  to account for capillary shrinkage. The initial temperature of the prostate was set to  $37^\circ\text{C}$ .

The laser light fluence distribution in the prostate was calculated using the Monte Carlo method (Wilson and Adam 1983). The Monte Carlo method implies the trace following of a great number of single photons in the tissue, resulting in the distribution of absorbed photons. For the Monte Carlo simulations a modified version of the Monte Carlo program written by Wang and Jacques (1992) was used. In the model an optical line source of variable length emitting light isotropically was inserted along the  $z$ -axis into a tube of radius  $r_o$  surrounded by prostatic tissue. The space between the  $z$ -axis and the tissue was assumed to have the same index of refraction as tissue and to be totally transparent without absorbing or scattering the photons. By defining the optical properties of the tissue,  $\mu_a$  ( $\text{m}^{-1}$ ),  $\mu_s$  ( $\text{m}^{-1}$ ) and  $g$  (dimensionless), assuming a Henyey–Greenstein distribution of the scattered photons, the Monte Carlo simulations give the light absorption distribution, that is, the number of absorbed photons per unit volume, in a two-dimensional, axially symmetric geometry. The light absorption probability ( $\text{m}^{-3}$ ) is then given by dividing the absorption distribution by the number of launched photons. The absorption probability multiplied by the total laser power then constituted the source term,  $Q_s$ , in equation (6). The optical properties used were those of coagulated human prostate which were taken to be  $\mu_a = 0.40 \text{ cm}^{-1}$ ,  $\mu_s = 180.0 \text{ cm}^{-1}$  and  $g = 0.95$  (Roggan *et al* 1995). In the Monte Carlo simulations a total number of  $2.5 \times 10^5$  photons were used for each simulation. Using  $5.0 \times 10^6$  photons the difference



in calculated tissue temperature after 600 s of irradiation was found to be less than 0.3% (results not shown).

The temperature of each control volume was repeatedly calculated after a small time-step  $\Delta t$ . The size of the time-step was chosen to ensure stability of the calculated temperature solution (Sturesson and Andersson-Engels 1995a). During the simulated laser irradiation, the tissue temperature was restricted so as not to exceed a certain pre-set level. In the model, this was done by switching off the laser during the time the highest allowed temperature was exceeded anywhere in the prostate. As to be discussed, the time-step used was in the range 0.5–50 ms, which enabled a very fast mode of controlling the maximum tissue temperature.

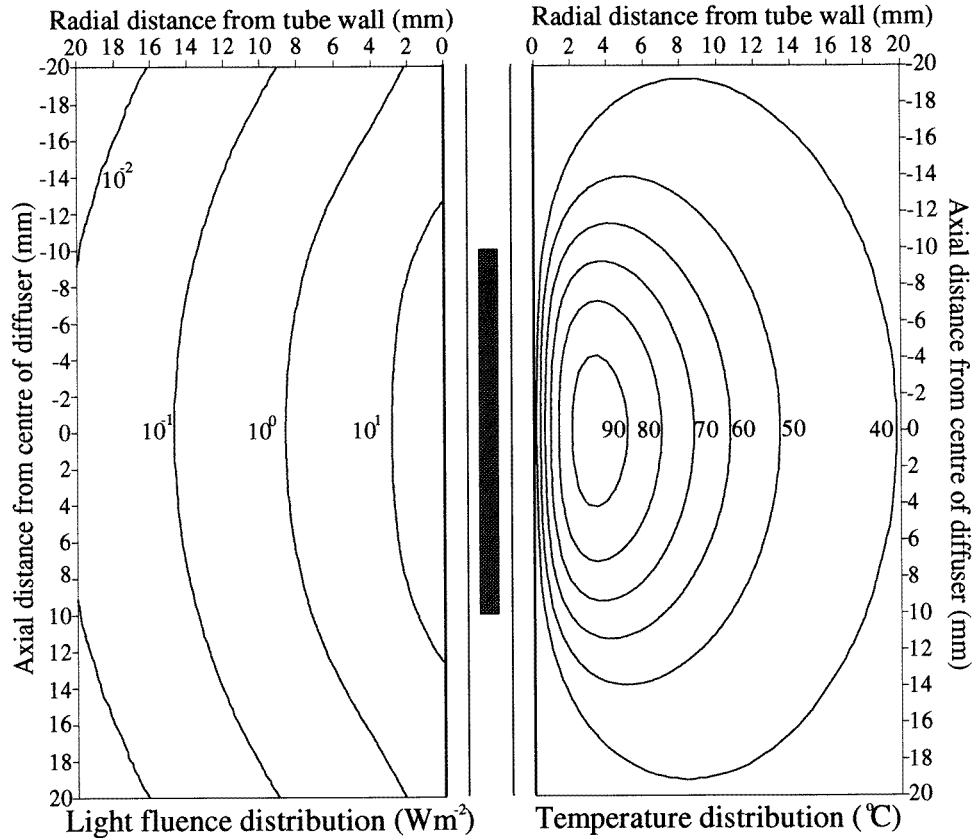
### 3. Results

In this section, the influence of diffuser length, outer tube radius, outer tube wall thickness, blood perfusion rate, cooling water temperature and highest tissue temperature level reached on the volume of coagulated tissue and the volume of tissue at hyperthermic temperature is investigated. The volume of coagulated tissue was evaluated as the tissue volume at a temperature greater than 55 °C at the end of a 600 s treatment, representing the necrotic volume immediately after the treatment. As the volume at hyperthermic temperature, the tissue volume at a temperature exceeding 45 °C at the end of the treatment is implied.

In the simulations, if not stated otherwise, the following parameters were used: a diffuser length,  $d$ , equal to 2 cm, a diffuser self-absorbing fraction,  $f$ , equal to 5%, an outer tube of radius,  $r_o$ , equal to 2.5 mm with negligible wall thickness ( $w = 0$ ), an inner tube radius,  $r_i$ , equal to  $(r_o - w)/2$ , a water flow rate,  $V_w$ , equal to 50 ml min<sup>-1</sup>, an inlet water temperature,  $T_{in}$ , equal to 5.0 °C, a maximum tissue temperature level equal to 95 °C and a homogeneous initial blood perfusion rate,  $\omega_p$ , equal to 17.7 ml min<sup>-1</sup> (100 g)<sup>-1</sup>. The value of the blood perfusion rate corresponds to the value of the average blood perfusion rate in BPH as reported by Inaba (1992).

Figure 2 shows the light fluence distribution using a total laser power of 35 W (left-hand side) and the temperature distribution after 600 s of irradiation (right-hand side). The highest allowed tissue temperature was maintained at 95 °C by means of temporarily switching off the laser whenever the tissue temperature exceeded 95 °C. The average laser power between 540 and 600 s was 20 W. After 600 s of irradiation the outlet water temperature was found to be 9.0 °C. When the temperature of a tissue region exceeded 60 °C, the perfusion rate of that region was irreversibly set to zero. As shown in figure 2, the temperature distribution is almost perfectly symmetric with respect to the plane  $z = 0$ , indicating that the influence on the tissue temperature of the non-uniform temperature of the water flowing between the inner and outer tubes is negligible. This observation made it possible to use only the region of positive  $z$  (figure 1) for the calculation of damaged volumes using a constant temperature of the water along the flow channels equal to  $T_{in}$ , which substantially reduced the computational time as the stability time-step increased from 0.5 ms to 50 ms. After 600 s of irradiation, using a blood perfusion rate of 17.7 ml min<sup>-1</sup> (100 g)<sup>-1</sup>, the coagulated and hyperthermic volumes were 96% of the values found after 1800 s of irradiation, indicating that the damaged volumes after 600 s are a good approximation of the steady-state volumes. An irradiation time of 600 s was used throughout the study. Extending the calculation domain in the radial direction from 30 to 60 mm resulted in an increase in temperature at  $r = 30$  mm of less than 0.4 °C. This enlargement of the calculation domain did not influence the predicted values of the damaged volumes.

The influence of varying the cooling water temperature,  $T_{in}$ , on the tissue temperature was investigated. Increasing the water temperature from 5 to 30 °C resulted in a small

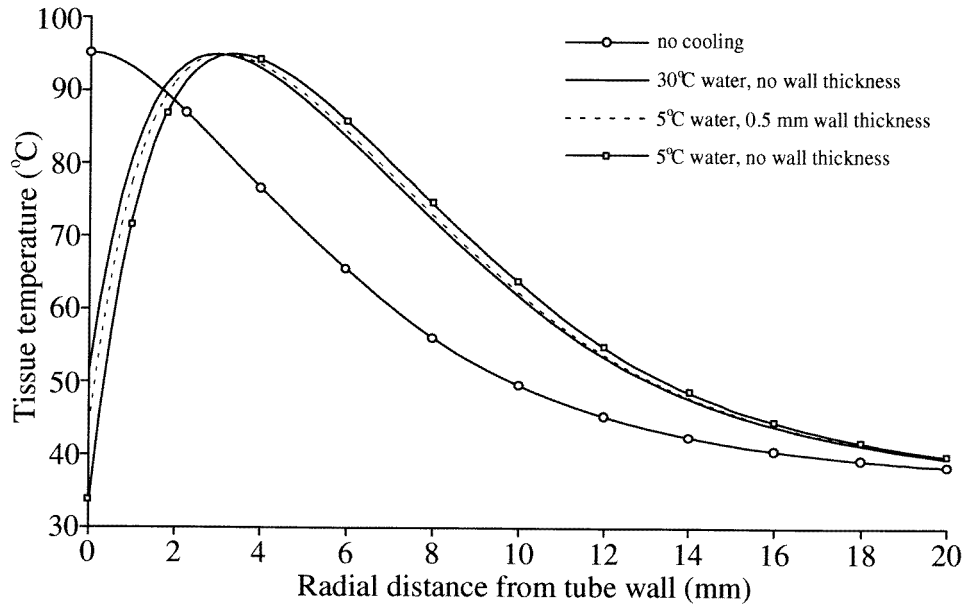


**Figure 2.** The light fluence distribution resulting from irradiation using a 2 cm diffuser with a total laser power of 35 W and an outer tube radius of 2.5 mm is shown on the left-hand side (logarithmic scale). The hatched area signifies the diffuser. On the right-hand side, the tissue temperature after 600 s of irradiation is shown. The maximum tissue temperature was restricted not to exceed 95 °C as regulated by switching the laser on and off. The prostatic blood perfusion rate was set to 17.7 ml min<sup>-1</sup> (100 g)<sup>-1</sup>. The inlet water temperature (at  $z = -30$  mm) was set to 5.0 °C and the steady-state outlet water temperature (at  $z = -30$  mm) was found to be 9.0 °C. Due to the cylindrical symmetry, only half of each distribution is shown.

change in tissue temperature, significant only at the tube wall as shown in figure 3. The coagulated and hyperthermic volumes were predicted to increase by less than 6% with increasing water temperature (results not shown). Figure 3 also shows the influence of introducing a finite wall thickness,  $w$ , of the outer tube equal to 0.5 mm with a thermal conductivity of the wall,  $\lambda_t$ , equal to 0.93 W m<sup>-1</sup> K<sup>-1</sup>. Included in the figure are also the simulation results obtained without cooling. To represent a situation without any cooling liquid, the thermal resistance of the outer tube wall  $R_t$  was assumed infinite.

The influence of varying the outer tube radius on the coagulated and hyperthermic volumes is shown in figure 4. With an outer tube radius of 5 mm, the coagulated volume with water cooling was predicted to be 18 cm<sup>3</sup>. The corresponding volume without cooling was predicted to be 12 cm<sup>3</sup>. By using an outer tube radius of 2.5 mm the coagulated volumes calculated with and without cooling were predicted to be 12 cm<sup>3</sup> and 7 cm<sup>3</sup>, respectively.

The influence of varying the diffuser length was also investigated. Figure 5 shows

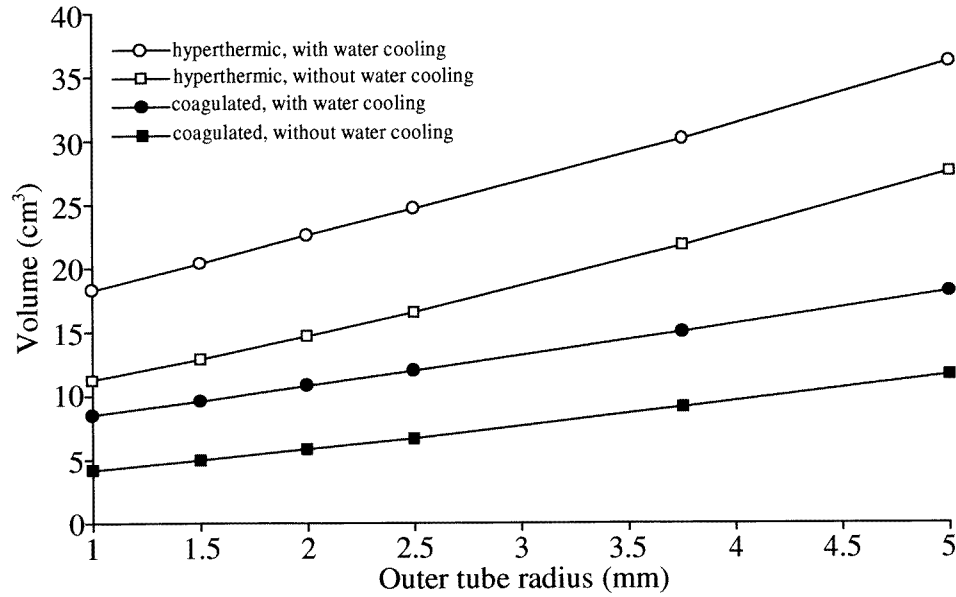


**Figure 3.** Temperature distributions at  $z = 0$  after 600 s of irradiation for different cooling conditions and different outer tube wall thicknesses. The highest allowed tissue temperature was set to 95 °C, the outer tube radius was chosen to be 2.5 mm, the diffuser length was taken to be 2 cm and the blood perfusion rate was set to 17.7 ml min<sup>-1</sup> (100 g)<sup>-1</sup>.

the calculated coagulated and hyperthermic volumes as a function of the diffuser length. As shown in figure 5, the calculations predict a linear relationship between the damaged volumes and the length of the diffuser. From the figure it can be concluded that for a diffuser of length 1 cm, the coagulated volume with cooling is predicted to be 70% greater than the coagulated volume without cooling, while the hyperthermic volume is 40% greater with, as compared to without, cooling. For the 3 cm diffuser, the corresponding percentages were 80 and 50%, respectively. The average laser power required to maintain a maximum tissue temperature of 95 °C was for the 3 cm diffuser with and without cooling predicted to be 24 and 7 W, respectively.

The reported values of prostatic blood perfusion rates in BPH are somewhat scattered (Inaba 1992). Therefore, the influence of blood perfusion on the damaged volumes was investigated in a parametric study. Figure 6 shows the coagulated and hyperthermic volumes, with and without water cooling, as a function of the blood perfusion rate. The average value of the perfusion rate as reported by Inaba (1992) was 17.7 ml min<sup>-1</sup> (100 g)<sup>-1</sup>. The minimum and maximum values in that study were 10.8 ml min<sup>-1</sup> (100 g)<sup>-1</sup> and 24.2 ml min<sup>-1</sup> (100 g)<sup>-1</sup>, respectively. In figure 6, it is shown that with a perfusion rate of 10 ml min<sup>-1</sup> (100 g)<sup>-1</sup> the coagulated volume with cooling was predicted to be 14 cm<sup>3</sup>. This value can be compared to the predicted coagulated volume using a perfusion rate of 25 ml min<sup>-1</sup> (100 g)<sup>-1</sup>, which was found to be 11 cm<sup>3</sup>.

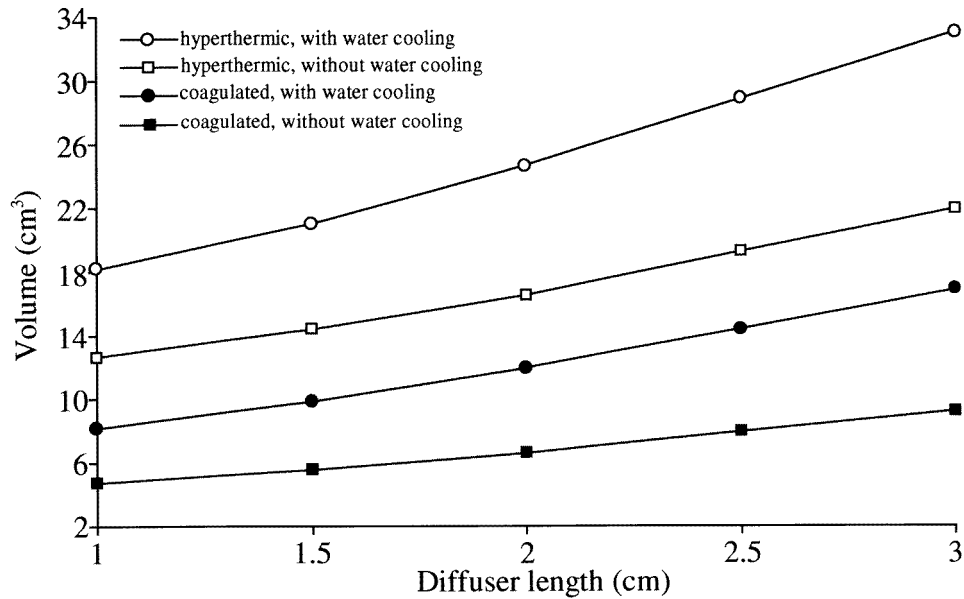
The damaged volume will depend on the temperature levels reached in the tissue. In order to obtain the largest possible damage the tissue temperature should be maximized. However, if carbonization is to be prevented the highest tissue temperature level reached should be below 100 °C. To investigate to what extent the highest allowed temperature



**Figure 4.** The effect of the outer tube radius on the damaged volumes after 600 s of irradiation. The highest allowed tissue temperature was set to 95 °C, the diffuser length was taken to be 2 cm, the blood perfusion rate was chosen to be 17.7 ml min<sup>-1</sup> (100 g)<sup>-1</sup> and the uniform water temperature was set to 5 °C. The outer tube wall thickness was assumed to be negligible.

influences the produced damaged volumes, simulations were performed. The influence of the highest allowed tissue temperature on the damaged volumes is shown in figure 7. The coagulated volume at a highest allowed tissue temperature of 95 °C was predicted to be more than twice the coagulated volume at a highest allowed temperature of 75 °C. This relationship applied to the two cases investigated: with and without cooling.

We also theoretically investigated whether the difference in outlet and inlet water temperature could be related to the highest tissue temperature level reached. The calculation domain now included the entire  $z$ -axis as shown in figure 1, that is,  $-30 \text{ mm} < z < 30 \text{ mm}$ . The water flow rate was assumed to be 50 ml min<sup>-1</sup> which resulted in a Reynolds number less than 1000, implying laminar flow. The water inlet temperature,  $T_{in}$ , was set to 5.0 °C and the temperature distributions of the tube water were evaluated after 600 s of irradiation. The tissue perfusion rate was set to 17.7 ml min<sup>-1</sup> (100 g)<sup>-1</sup>. In figure 8, the temperatures of the water in the inner and outer tubes for different values of the highest allowed prostatic temperature are shown. The temperature of the water in the inner tube is predicted to be almost identical for the different highest allowed tissue temperatures, although the laser powers were somewhat different. The outlet water temperature is shown to depend linearly on the highest temperature level reached. Figure 9 shows the linear relationship between the difference in outlet and inlet temperatures, and the maximum tissue temperature. A temperature difference of 0.1 °C in  $T_{out} - T_{in}$  corresponds to a difference of 3 °C in the maximum tissue temperature. To investigate the sensitivity of the water temperature difference  $T_{out} - T_{in}$  with respect to the optical properties of the prostate, the results of two simulations using different optical properties were compared. The optical properties utilized represented uncoagulated human prostatic tissue ( $\mu_a = 0.30 \text{ cm}^{-1}$ ,  $\mu_s = 80.0 \text{ cm}^{-1}$ ,  $g = 0.95$ ) and coagulated human prostatic tissue ( $\mu_a = 0.40 \text{ cm}^{-1}$ ,  $\mu_s = 180.0 \text{ cm}^{-1}$ ,



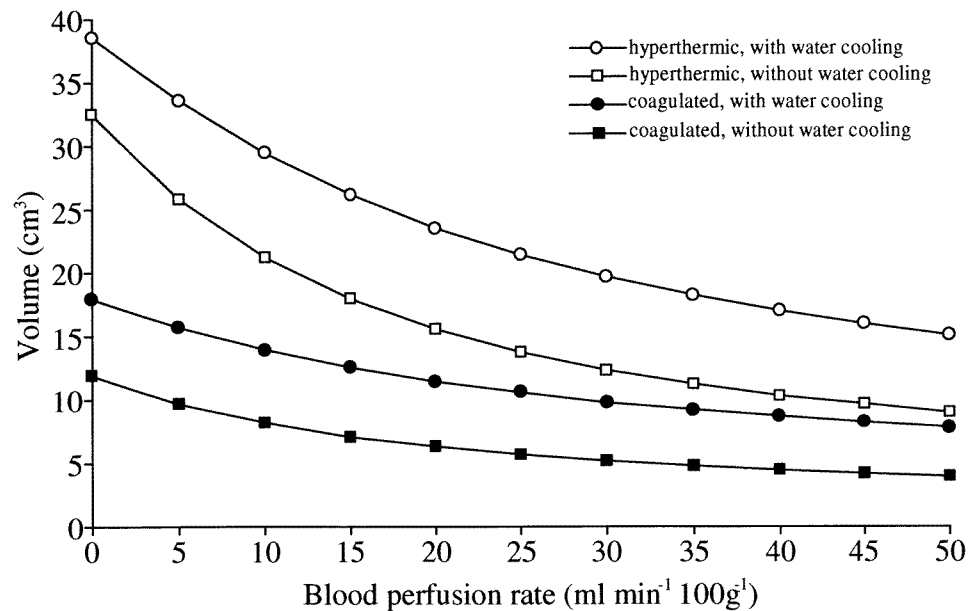
**Figure 5.** The effect of the diffuser length on the damaged volumes after 600 s of irradiation. The highest allowed tissue temperature was set to 95 °C, the outer tube radius was taken to be 2.5 mm, the outer tube wall thickness was assumed to be negligible, the blood perfusion rate was chosen to be 17.7 ml min<sup>-1</sup> (100 g)<sup>-1</sup> and the uniform water temperature was set to 5 °C.

$g = 0.95$ ), as taken from the work of Roggan *et al* (1995). The results of the simulations are shown in figure 9. The influence of the blood perfusion rate on the tube water temperature was also investigated. Two additional blood perfusion rates were considered: 10 ml min<sup>-1</sup> (100 g)<sup>-1</sup> and 25 ml min<sup>-1</sup> (100 g)<sup>-1</sup> using a highest allowed tissue temperature of 85 °C. The corresponding differences in water temperature,  $T_{out} - T_{in}$ , were found to be 3.54 °C and 3.64 °C, respectively, which can be compared with the value of 3.59 °C obtained using a blood perfusion rate of 17.7 ml min<sup>-1</sup> (100 g)<sup>-1</sup>. Assuming no blood perfusion resulted in a difference in water temperature of 3.43 °C.

#### 4. Discussion

In this study, we have theoretically investigated the amount of tissue damage produced in transurethral laser treatment of benign prostatic hyperplasia (BPH). The effect of changing a number of different parameters on the damaged volume was evaluated. A water-cooled applicator was modelled as a cylindrical diffuser inserted into an open-ended inner tube concentrically placed in a closed outer tube. The water was assumed to flow into the inner tube and be recollected in the annulus between the inner and outer tubes. The effectiveness of the water-cooled applicator in damaging tissue was compared with a non-cooled applicator. Also, the relationship between the steady-state maximum tissue temperature and the difference in outlet and inlet water temperature was investigated. The light absorption distribution within the irradiated prostatic tissue was modelled using Monte Carlo simulations and the subsequent temperature rise was calculated in cylindrical coordinates using finite differences.

In the present theoretical study, the highest temperature level reached in the prostatic

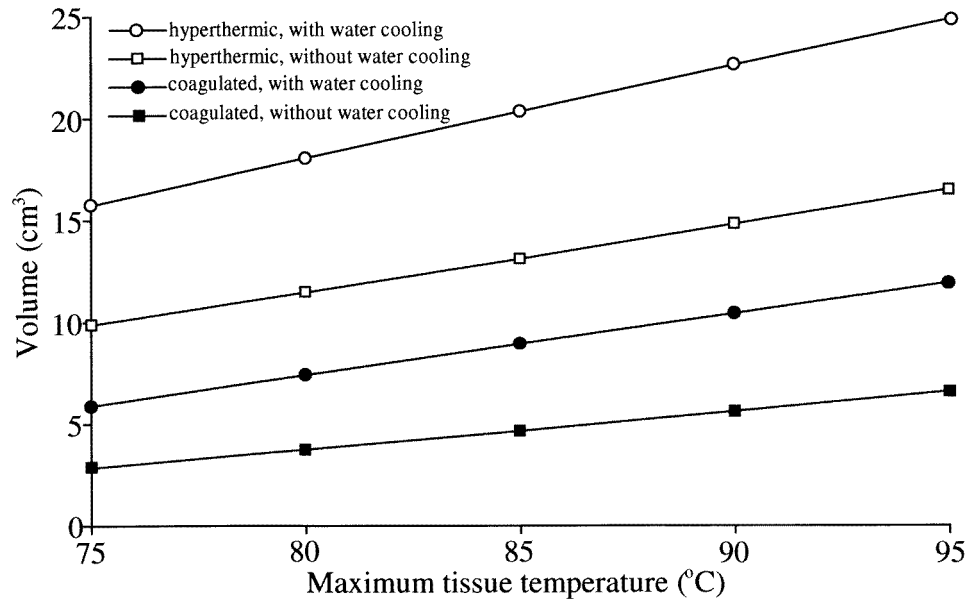


**Figure 6.** The effect of the blood perfusion rate on the damaged volumes after 600 s of irradiation. The highest allowed tissue temperature was set to 95 °C; the outer tube radius and the diffuser length were chosen to be 2.5 mm and 2 cm, respectively. The uniform water temperature was set to 5 °C and the outer tube wall thickness was assumed to be negligible.

tissue was restricted so as not to exceed a certain preset level below 100 °C. In this way, tissue carbonization was prevented. The maximum temperature was kept at the preset temperature level by regulating the laser power in an on–off cycle every 50 ms. Thereby, the damages produced using different treatment parameters could be compared.

The volume of coagulated tissue and the volume at hyperthermic temperatures were evaluated as the volumes attaining a temperature above 55 °C and 45 °C, respectively. The temperature was evaluated after 600 s of irradiation. After 600 s, steady-state conditions representing thermal equilibrium were obtained within a few per cent. The coagulated volume is an attempt to describe the volume of immediate cell death after a few minutes of irradiation (Thomsen 1991). The volume at hyperthermic temperatures represents the delayed necrotic volume obtained after a prolonged heat treatment (Dewey 1994). In transurethral laser treatment of the prostate, the necrotic tissue will eventually slough to form a cavity. In canine prostate, Suzuki *et al* (1994a) found that after 20 min of irradiation the cavity formation temperature threshold was 46 °C. Depending on the irradiation time, the true volume of irreversibly damaged tissue should then be somewhere in between the calculated coagulated and hyperthermic volumes. The time–temperature relationship of tissue damage during heat treatment can be mathematically described by an Arrhenius formalism providing a ‘damage integral’ (Henriques 1947). However, because the damage integral is tissue-type specific and, as yet, not has been evaluated for prostatic tissue, this approach was not used in this study.

In the modelling of the light distribution, the optical properties of coagulated human prostatic tissue were used (Roggan *et al* 1995). The influence of the coagulation process on the optical properties consists mainly of an increase in the scattering coefficient. The

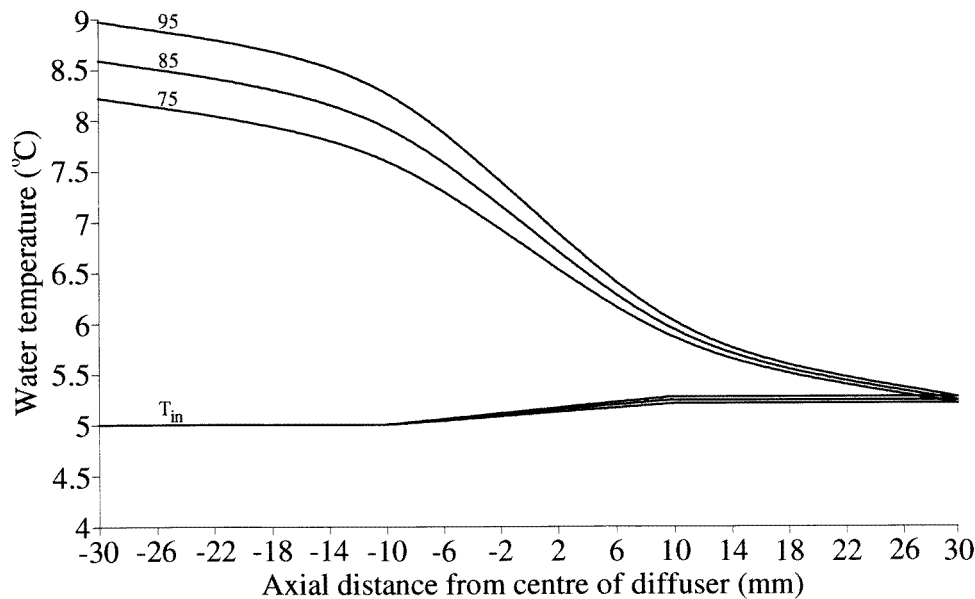


**Figure 7.** The effect of the highest allowed tissue temperature on the damaged volumes after 600 s of irradiation. The outer tube radius and the diffuser length were chosen to be 2.5 mm and 2 cm, respectively, and the blood perfusion rate was taken to be  $17.7 \text{ ml min}^{-1} (100 \text{ g})^{-1}$ . The uniform water temperature was set to  $5^\circ\text{C}$  and the outer tube wall thickness was assumed to be negligible.

fast rise in temperature of the tissue close to the tube wall (results not shown) leaving only a thin rim around the tube uncoagulated (figure 3) and the long irradiation time considered (600 s) justified the use of the optical properties of coagulated prostate during the entire treatment.

By using a water-cooled applicator much greater damaged volumes were predicted as compared with using a non-cooled applicator. The non-cooled applicator was modelled by setting the heat transfer from tissue to the outer tube to zero. With a length of the diffuser of 2 cm, an outer tube radius of 2.5 mm, a blood perfusion rate of  $17.7 \text{ ml min}^{-1} (100 \text{ g})^{-1}$  and a highest allowed tissue temperature of  $95^\circ\text{C}$ , the coagulated and hyperthermic volumes predicted using the cooled applicator were a factor of 1.8 and 1.5 greater, respectively, than the damaged volumes predicted with the non-cooled applicator (figure 4). Approximately the same relationship was seen in all the parametric investigations performed. Thus, using water cooling is predicted to substantially increase the damaged volume.

Using a large tube radius requires more laser power to maintain a maximum tissue temperature at a certain preset level as compared with using a small tube radius. The steady-state fluence rate at the wall of a large tube is however smaller than at the wall of a smaller tube (results not shown). The radial distance from the tube wall to the  $55^\circ\text{C}$  isotherm at the middle of the diffuser ( $z = 0$ ) was found to be approximately equal for all tube sizes (11 mm with  $r_o = 1 \text{ mm}$  and 12 mm with  $r_o = 5 \text{ mm}$ ). Figure 4 shows a linear increase in the damaged volumes with increasing tube radius. Doubling the tube radius will result in an increase in the damaged volumes by approximately 50% (figure 4). Therefore, it is advisable to use the largest tube possible in order to maximize the lesion. An alternative to using a tube would be to utilize an inflated balloon (Suzuki *et al* 1994a, b). When cooling the



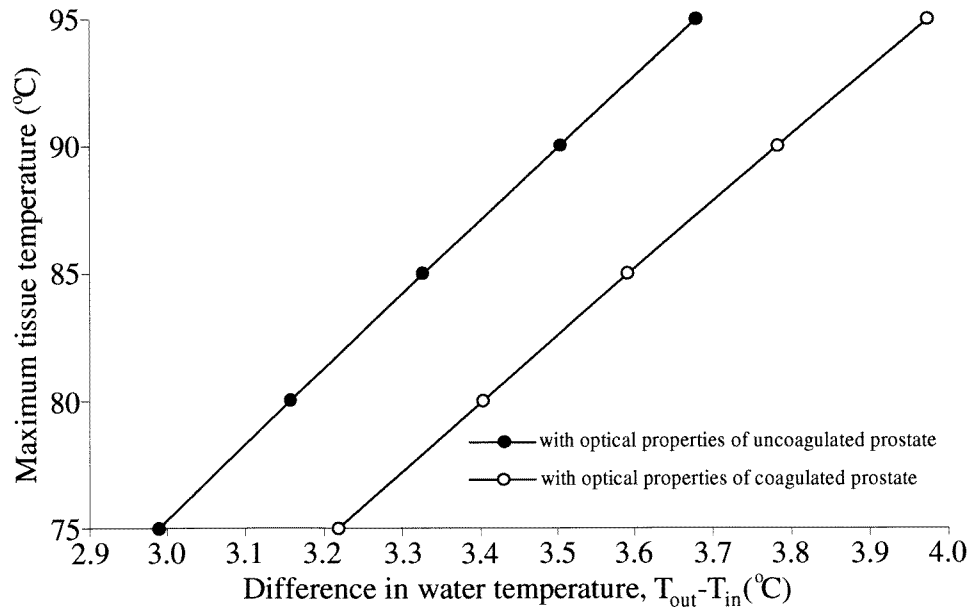
**Figure 8.** Tube water temperatures after 600 s of irradiation. The lower and upper curves represent the temperatures of the water in the inner tube and in the annulus between the inner and outer tubes, respectively. The values on the curves signify the maximum tissue temperature. The outer tube radius was taken to be 2.5 mm and the inner tube radius was half of the outer tube radius. The self-absorbing fraction of the input laser power by the diffuser was taken to be 5%, the diffuser length was set to 2 cm and the blood perfusion rate was chosen to be  $17.7 \text{ ml min}^{-1} (100 \text{ g})^{-1}$ . The water flow rate was set to  $50 \text{ ml min}^{-1}$ .

urethral epithelium with  $5^\circ\text{C}$  water, the maximum tissue temperature was predicted to occur approximately 3 mm from the urethral wall. Without cooling the maximum temperature was found at the border between the applicator and the prostatic tissue (figure 3). Indeed, with the set of parameters used in this study, cooling the urethral surface was predicted to result in approximately the same treatment outcome, that is, damaged volumes, as was found for the case without cooling when increasing the outer tube radius by 3 mm (figure 4).

It was found that increasing the cooling water temperature from  $5^\circ\text{C}$  to  $30^\circ\text{C}$  did not significantly alter the tissue temperature profile except close to the outer tube wall (figure 3). A water temperature of  $5^\circ\text{C}$  resulted in a temperature of less than  $37^\circ\text{C}$  of the urethral epithelium which would spare this structure from necrosis, an outcome also observed after *in vivo* canine prostatectomy performed by Cromeens *et al* (1994). In that study, prostatectomy was performed using a cylindrical diffuser inserted into the canine prostatic urethra. Irradiation was performed while the urethral mucosa was cooled by room-temperature saline fluid. Modelling a finite glass wall of the outer tube of thickness 0.5 mm and using a cooling water temperature of  $5^\circ\text{C}$  was found to be equivalent to the case of negligible wall thickness and a water temperature of  $20^\circ\text{C}$  (results not shown). Thus, if the urethral epithelium is to be spared, either a thin-walled outer tube or a lower-than- $95^\circ\text{C}$  highest allowed tissue temperature should be used. However, if sparing the urethral epithelium will be of any real benefit remains to be experimentally investigated as only a small portion of the urethral wall can be expected to survive due to the predicted large temperature gradients close to the tube wall (figure 3).

Increasing the diffuser length resulted in a linear increase in the damaged volumes. The





**Figure 9.** The calculated relationship between maximum tissue temperature and difference in outlet and inlet water temperatures of the cooled applicator. The two curves were calculated using the optical properties of coagulated and uncoagulated prostatic tissue. The inlet water temperature was set to 5.0 °C and the water flow rate was chosen to be 50 ml min<sup>-1</sup>. The outer tube radius was taken to be 2.5 mm and the inner tube radius was half of the outer tube radius. The self-absorbing fraction of the input laser power by the diffuser was taken to be 5%, the diffuser length was set to 2 cm and the blood perfusion rate was chosen to be 17.7 ml min<sup>-1</sup> (100 g)<sup>-1</sup>.

choice of length of the diffuser can be made from measurement of the length of the prostatic urethra, which is often longer than 3 cm (Petrovich *et al* 1993). As is shown in figure 2, the treated volume is predicted to extend a few millimetres above and below the proximal and distal margins of the diffuser. This effect should also be taken into consideration when choosing diffuser length in order not to unintentionally damage the bladder neck or the external sphincter.

Because the blood perfusion rate can be assumed to show variations, a parametric study investigating the influence of the blood perfusion on the damaged volumes was performed. By using the minimum and maximum values for the perfusion as reported by Inaba (1992), the damaged volumes decreased by 25% with increasing blood perfusion rate (figure 6). However, with the cooled applicator the maximum tissue temperature is predicted to occur approximately 3 mm from the tube wall independently of the blood perfusion rate (results not shown), which might be a useful observation if invasive temperature control based on the maximum tissue temperature is to be employed.

Temperature monitoring is important during prolonged laser treatment of BPH if carbonization is to be prevented and if the lesion size is to be maximized. Figure 7 shows that the damaged volume is highly dependent on the highest tissue temperature level reached. The use of invasive probes for temperature control complicates the procedure. Therefore, the possibility of using the difference in outlet and inlet water temperature of the cooled applicator for tissue temperature measurement was theoretically investigated. A

linear relationship between the difference in water temperature and the maximum tissue temperature was found (figure 9). The error in the measured maximum tissue temperature introduced by not knowing the blood perfusion rate beforehand was estimated by performing simulations with the maximum, average and minimum values of the blood perfusion rates as measured by Inaba (1992). By assuming the average perfusion rate value to be the true value while actually having one of the extreme perfusion rate values was predicted to influence the maximum tissue temperature measurement by less than 1.5 °C. The optical properties of prostatic tissue will influence the tissue temperature measurements if the difference in outlet and inlet water temperature is employed for this purpose. An attempt to estimate the error introduced due to interindividual variations in the optical properties was made by using the optical properties of uncoagulated prostatic tissue in the simulations. Using the relationship between the difference in water temperature and maximum tissue temperature obtained for coagulated tissue, as shown in figure 9, the introduction of the optical properties of uncoagulated tissue resulted in an underestimation of the maximum tissue temperature of less than 8 °C. The penetration depth in uncoagulated tissue is a factor of 1.7 greater than the penetration depth in coagulated tissue. It can be assumed that the variability in the optical properties after a few minutes of laser treatment is considerably smaller than a corresponding 170% change in the penetration depth. Thus, the investigated case of uncoagulated tissue can be assumed to overestimate the interindividual variations in the optical properties of coagulated prostatic tissue.

The water temperature rise in the inner tube due to a 5% self-absorbing fraction of the laser power by the diffuser was found to be almost independent of the highest allowed tissue temperature (figure 8), even though the steady-state laser power increased from 15 W at a highest allowed tissue temperature of 75 °C to 20 W at a highest allowed tissue temperature of 95 °C. However, the fraction of self-absorption was found to be an important parameter in calibrating the applicator. Having a self-absorption fraction of 5% and not accounting for this would result in an underestimation of the tissue temperature by approximately 5 °C (figures 8 and 9). Cylindrical diffusers that can withstand high powers are now available and commonly used (Cromeens *et al* 1994). In a study made by Eppert *et al* (1991) the temperature increase of air flowing through a tube with an inserted microwave antenna was predicted with good accuracy utilizing a set of equations similar to the ones used in the present study, further encouraging experimental evaluation of the theoretical predictions. In practice, water temperature measurements could be performed either by inserting small thermocouples into the tubes or, more practically, by measuring the water temperatures outside the patient's body. Using the latter approach, the theoretical relationship between the difference in outlet and inlet water temperatures and the maximum tissue temperature is found by extending the calculation domain in the  $-z$  direction (figure 1) and applying suitable boundary conditions. Although the theoretical calculations show that the described method for measuring the maximum tissue temperature is feasible, extensive experimental work is needed before the method can be used in the clinic.

## 5. Conclusions

The present study has given theoretical indications that a water-cooled applicator can be used to measure the highest tissue temperature level reached during laser treatment of BPH by measuring the difference between outlet and inlet water temperature. The fraction of self-absorption by the diffuser was found to be an important parameter for accurate calibration of the applicator. The error introduced in the maximum tissue temperature measurement by not knowing the tissue perfusion rate was estimated to be less than 1.5 °C. A probable

overestimation of the error in the measured tissue temperature due to variations in the prostatic optical properties was found to be less than 8 °C. By maintaining the highest allowed tissue temperature at 95 °C, the theoretical results showed that by using a cooled applicator an 80% increase in damaged tissue volume could be achieved as compared with using a non-cooled applicator. Linear relationships between the damaged volumes and the length of the diffuser as well as the outer tube radius were found. The temperature of the cooling water was found to influence the tissue temperature only to a small extent. The blood perfusion rate was found to significantly influence the damaged volumes. However, the location of the maximum tissue temperature was found to be independent of the perfusion rate and occurred approximately 3 mm from the outer tube wall.

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