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Endoscopic Applications of the Nd: YAG Laser in Urology; Theory, Results, Dosimetry

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Summary. We present the results of experimental and theoretical investigations on the interaction of Nd:YAG laser light with biological tissue in general, and with the bladder in particular. A comparison is made between the thermal effects achieved with this laser and those of the argon and CO2 types. A therapeutically safe yet effective dosage for the endoscopic treatment of bladder tumours with the Nd:YAG laser is given. The operating techniques are described along with the first clinical results.

Key words: Laser types, Bladder tumours, Experimental and theoretical investigation of laser-tissue interactions, Dosimetry, Operating techniques, Clinical results.

INTRODUCTION

The Nd:YAG (an acronym for neodymium doped yttrium-aluminum garnet), a solid state laser emitting a continuous beam in the near infra-red region of the electromagnetic spectrum at a wavelength of 1.06 microns, has been successfully applied in clinical practice since 1976 for the local thermal destruction of solid and exophytic bladder tumours up to about the size of a pea or hazel nut (1, 2, 3). The principal characteristic of the Nd:YAG laser treatment is its ability to remain within the 60 to 90 degree range required for clinical use.

As necrosis can proceed to a considerable depth with only slight surface changes (blanching), it is of fundamental importance for the surgeon employing a laser of this type to know the exact relationships between irradiation dosage, observable surface change, and the extent of tissue damage achieved. In order to ensure that the irradiation dosage remains within safe limits and yet attains an effective clinical range, we have carried out investigations along four different lines:

1 laboratory measurements on human bladder specimens
2 animal experiments
3 theoretical investigations of the photo-thermal reaction of laser light with tissue
4 analysis of clinical observations.

MATERIALS AND METHODS

1. Laboratory Experiments

The outer fat tissue was removed from three total cystectomy specimens which were then preserved in a physiological salt solution until just before irradiation. About 10 different sites on each bladder specimen were irradiated. The total bladder wall thickness varied from 2 to 3 mm in the stretched condition. Since the temperature rise on the beam axis was of principal importance, a thermocamera (AGA 680) was centered alternately on the intersection of the beam axis with the front and rear walls, and the temperature rise there was recorded continuously as a function of time. For the determination of the backward- and forward-scattered power and its angular distribution, a combination thermocamera and wavelength-translator were used as described elsewhere (4).

Egg white coagulation experiments (5) were carried out to clarify our understanding of the scattering process and its effects on the penetration depth of Nd:YAG and CO2 laser light.

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2. Animal Experiments

To obtain a reliable indication of the severity of penetrating radiation, we irradiated the air-filled bladders of live rabbits, the outer surfaces of which were brought into immediate contact with an intestinal loop. Twenty lesions were in the 1.5 mm thick bladder walls by 4 s irradiation with a 40 watt Nd:YAG beam 2 mm in diameter, and the resulting damage to the intestine was examined.

3. Theoretical Investigations

In a parallel approach to the better understanding of the interaction of laser light with biological tissue, a theoretical model was developed in order to calculate the temperature rise produced when a tissue slice of a given thickness was irradiated at one surface with a laser beam (4). The temperature at any point in the tissue after a given period of time was calculated for an arbitrary laser, making the assumption that the physical constants (thermal conductivity, heat capacity and thermo-optical properties including absorptivity and scattering) were constant throughout the specimen and time independent. A review of the data reported in the literature in the light of our theory provided an estimate of the scattering coefficient for the calculations.

The effects of multiple scattering were taken into account by a further refinement (6). In the previous model, they had been approximately accounted for by suppressing the damping of the first scattered radiation.

4. Operative Techniques

The Nd:YAG laser has been used endoscopically since 1976 at the Urological Clinic of the University of Munich for the destruction of small solitary or multiple bladder tumours or for the irradiation of the tumour bed after a resection. Prior to irradiation, biopsies from the crown and base of the tumour and from its immediate surroundings were taken. A Charr. 21 cystoscope (into which the laser insert was later introduced) was used for the biopsy. The end of a flexible light guide was fastened in a movable mounting, the manipulation of which permitted a deflection of the light guide, and thus the laser beam could be directed to almost all points on the bladder wall so that a working distance of 1 to 4 mm from tumour surface to the tip of the light guide was maintained (7, 8).

For the coagulation of papillary or solid tumours, single shots of 35-40 watts over a maximal period of 2 s were applied. For surface irradiation, after a transurethral resection of the tumour, for example, the radiation could be applied continuously, taking care after the onset of noticeable blanching and tissue shrinking to guide the beam slowly in a back and forth motion.

In our early treatments the bladder was filled with air so that a gas flow (CO_2) along the optical window of the light fibre channel of the cystoscope was required to maintain vision, but in all recent Nd:YAG treatments, the bladder was filled with a (0.9%) physiological NaCl solution (7, 8).

RESULTS

1. Laboratory Experiments

The temperature rise at the front surface of the bladder during and after irradiation periods of 1, 2, 3 and 4 s with a 30 watt beam of 3 mm diameter is plotted in Fig. 1a. As the sample was initially at room temperature (23°C), the coagulation point was attained after a temperature rise of 37°C. In actual treatment where the bladder would have an initial temperature of 37°C, coagulation would occur after a rise of about 23°C. The break at 25°C appearing in about 50% of our curves can be explained by the change in thermal and optical constants described later. The temperature rise at the rear wall is shown in Fig. 1b.

In temperature increased at the rear wall in a water filled bladder are shown in Fig. 1c; temperature measurement at the front wall is not possible with the thermocamera in water filled bladders so that comparison with the curve from the front wall of an air filled bladder with the same irradiation cannot be made. The maximum temperature reached is 50% lower than with air filled bladders, but the temperature peak and thus the achieved necrosis are broader. For a temperature rise of 10°C, a total energy of 120 joules (30 watts x 4 s) was required; for the rise of 20 to 30°C needed for coagulation, we estimate the energy required to be between 200 and 300 joules typically three 2 s pulses of 40 watts each for total necrosis. Pauses of several seconds between the pulses are recommended to allow for thermal equilibrium within the tissue. Fig. 2 shows the general characteristics of the scattered light leaving a specimen of 2 mm thickness; quantitatively, the forward scattered power amounts to 25 to 30% and the back scattered power 30 to 40% of the total incoming power, depending on the constitution of the tissue in the target area (blood content, etc.).

2. Animal Experiments

A fistula was observed in the intestinal mucosa of about 20% of the cases after two weeks. The lesion begins at the inner wall due to the higher ab-

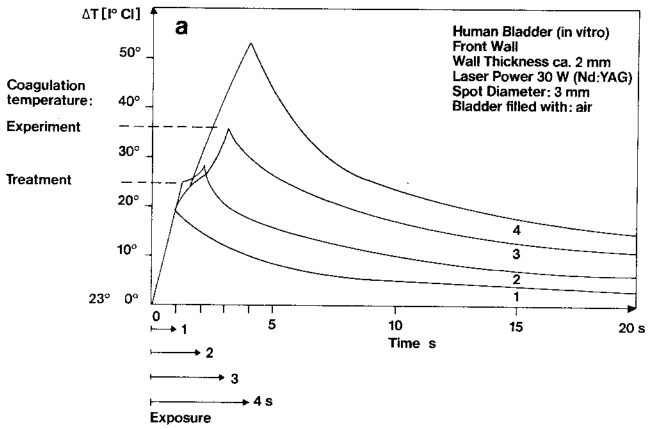

Fig. 1a. Temperature changes on the beam axis as a function of time during and after irradiation (front wall)

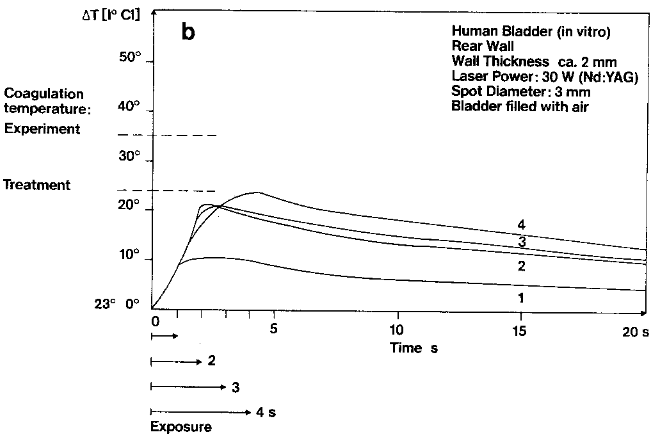

Fig. 1b. Temperature changes on the beam axis as a function of time during and after irradiation (rear wall)

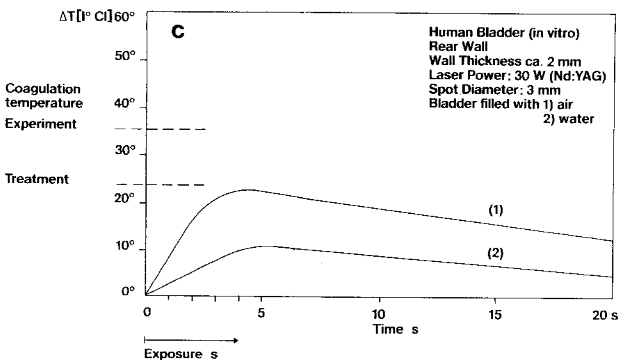

Fig. 1c. Comparison of on-axis temperature rises at the rear wall for air and water filled bladders

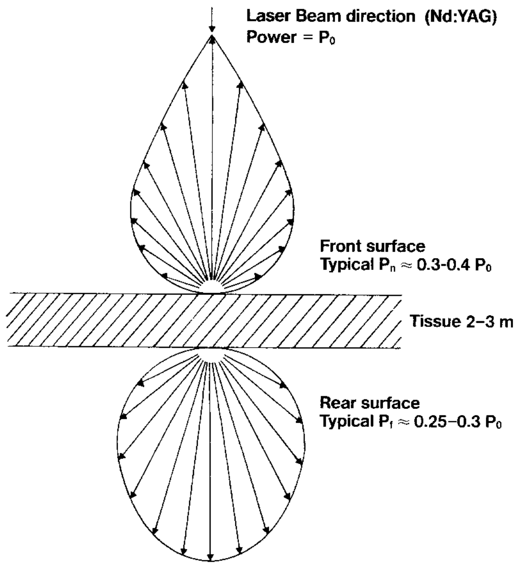

Fig. 2. The pattern of forward and backward scattered Nd:YAG radiation from a slice of bladder tissue

sorption of the blood-rich mucosa. With a reduced exposure time of 2 s no fistulae were produced although necrosis of the type shown in Fig. 3 was occasionally observed at the inner wall of the intestine.

3. Theoretical Investigations

In addition to theoretical estimates of the backward- and forward-scattered power to within 10% of the measured values, a surprisingly good fit of the temperature measured at the intersection of the beam axis with the front and rear walls of a 2 mm slice of human bladder in vitro was obtained. In Fig. 4, the temperature values are plotted as a function of time, the measured curves being represented by solid lines and the curves calculated from our model by broken lines. Fig. 5 compares the front and rear heating curves of a 40 watt Nd:YAG and a 1/2 watt CO_2 laser (again the tissue slice is 2 mm thick and the beam diameter 3 mm), clearly demonstrating the fundamental difference in their heating effects. The CO_2 laser with a moderate power output of 1/2 watt induces a rapid temperature rise at the front surface of the tissue in the short space of 4 seconds leaving the rear face relatively unaffected, whereas the Nd:YAG, operating at 80 times the power output, heats much more slowly and uniformly over the entire depth of the tissue with the broadly distributed direct heating of the penetrating radiation being superimposed on the equalizing tendency of the heat flow from front to rear surface. In

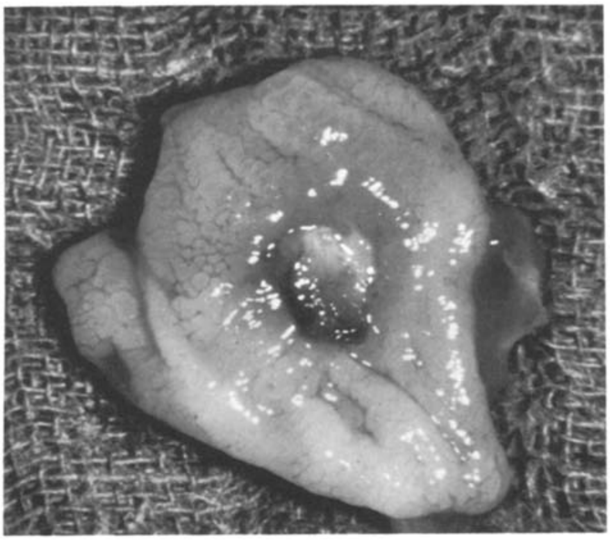

Fig. 3. Example of necrosis produced at the inner wall of a rabbit intestine in vivo as a result of bladder irradiation

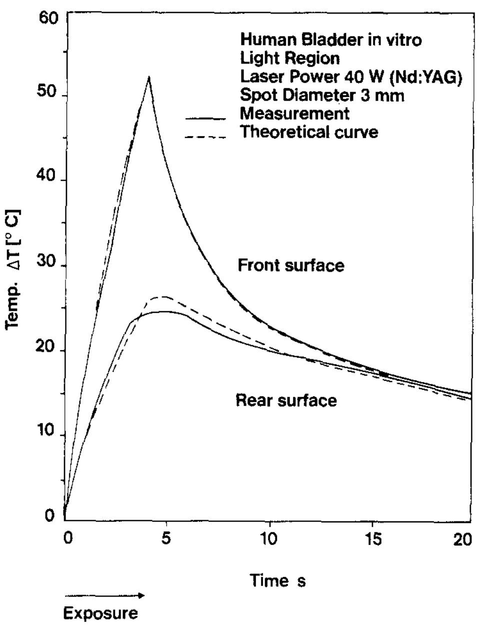

Fig. 4. The on-axis temperature rises at the front and rear walls of a 2 mm thick slice of bladder tissue: measured and calculated from our model

contrast to the CO2 laser, coagulation can be produced at the rear walls without drastic overheating of the irradiated surface.

An interesting theoretical result known as the decrepitation or popcorn effect (6) was obtained and subsequently verified in the laboratory and corroborated with the results of clinical practice. The theorem states essentially

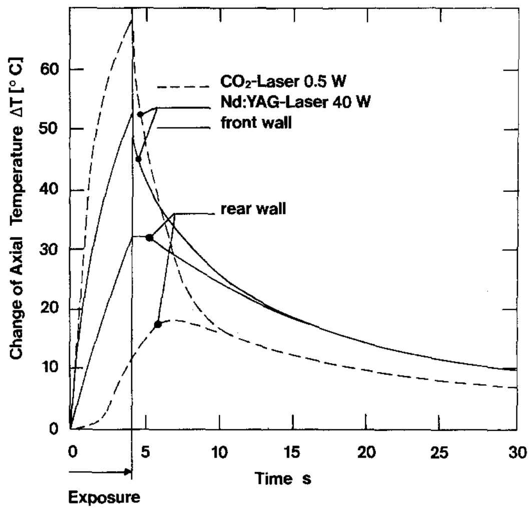

Fig. 5. Comparison of CO2 and Nd:YAG laser heating of a 1.75 mm thick slice of membrane tissue

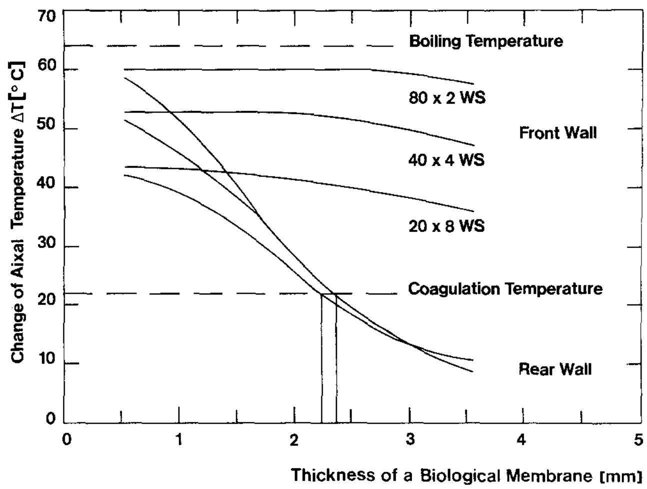

Fig. 6. Irradiation of a membrane with a Nd:YAG laser distributing the constant dosage of 8000 watt s/cm2 over different exposure times

that the light intensity distribution inside a medium with scattering does not have the simple, customary exponential fall-off as in an homogeneous material, but is internally magnified by the scattering in such a way that it attains its maximum at a depth below the surface which can be in the order of 1/2 mm. This subcutaneous overheating was observed in the egg white coagulation experiments (5) in the form of an explosion of the coagulated bud, and can explain the decrepitation craters often observed in practice without resorting to an ad hoc internal focusing hypothesis or the postulation of a subcutaneous rise in the absorption coefficient.

Fig. 6 shows the maximum temperature attained at the front and rear walls calculated for the Nd:YAG irradiation of a slice of variable thickness for three different combinations of power output and exposure time, all delivering the same total energy to the specimen.

CLINICAL RESULTS

In the 69 patients with 110 tumours up to hazel nut size treated since 1976, 15 recurrences were observed, 10 of which however were certainly due to insufficiently developed endoscopic irradiation techniques. Since the irradiation technique was improved only 2 local recurrences were observed in 24 patients.

DISCUSSION

The main advantage of photocoagulation, or the heating of tissue by absorption of light, with the Nd:YAG laser over electrocauterization or irradiation with lasers of other types, such as argon or CO2, lies in the greater depth to which the tissue is heated allowing safe and thorough destruction of tumour cell clusters deeply imbedded in the bladder wall. This effect occurs because of the combination of extremely low tissue absorptivity at the Nd:YAG wavelength and the scattering phenomenon discussed below, which has the effect of spreading the radiation of the narrow incoming beam relatively evenly over a broad and deep region centred at the irradiation site, permitting relatively slow homogeneous heating of a large tissue volume without surface ablation. This effect has been described in detail (10, 11) and calculated (4, 6). For necrosis, a temperature of 60°C must be induced over a period of several seconds. This corresponds, in clinical practice, to a power output of up to 40 W in separate pulses of 1 to 3 s duration, at which dose necrosis penetrating to a depth of 2 to 4 mm is easily achieved.

Other lasers frequently used in medicine are the CO2 laser, a molecular gas laser emitting in the middle infrared at a wavelength of 10.6 microns, which has been successfully applied in neuro- and microsurgery; and the argon laser, an ion gas laser emitting visible green light between 0.458 and 0.514 microns, which has been successfully used for producing shallow lesions in the retina. The necrosis they produce is always superficial because of the higher absorption by blood and, in the case of the CO2 laser, water at their operating wavelengths. In our opinion, this will severely restrict their application in the field of urology. Because of the surface concentration of their heating effects, the temperature rise they produce, even at low operating powers, is very rapid as in electrocautery, and they produce intense ablation at the radiation site accompanied by a high perforation risk to the bladder wall without achieving the desired depth of penetration for thermal destruction.

Fig. 7 is a schematic drawing of the optical and mechanical surface effects induced in the bladder by lasers and electrocautery arranged in order of increasing temperature. During heating to a temperature of 60°C there is no tissue damage and no mechanical or optical change. Between 60 and 65°C, protein denaturation and irreversible tissue damage set in, accompanied by a whitening of the originally reddish tissue. The denaturation proceeds up to a temperature of about 100°C, the boiling point of the cell water. As considerable latent heat is absorbed on vapourization of the cell water, the temperature remains constant for a while until most has escaped. The temperature begins rising again until at several hundred °C the tissue carbonizes, increasing the surface absorption. This in turn produces an ablation due to outgasing; smoking and burning begin. As these processes are heat consuming as well, they allow only a slight subsurface temperature rise. From this scheme we can evaluate the therapeutic ranges of various lasers as well as electrocautery.

Another aspect of the Nd:YAG treatment, important in selecting the proper irradiation dosage, is the considerable radiation loss due to scattering of the input beam backwards out of the irra-

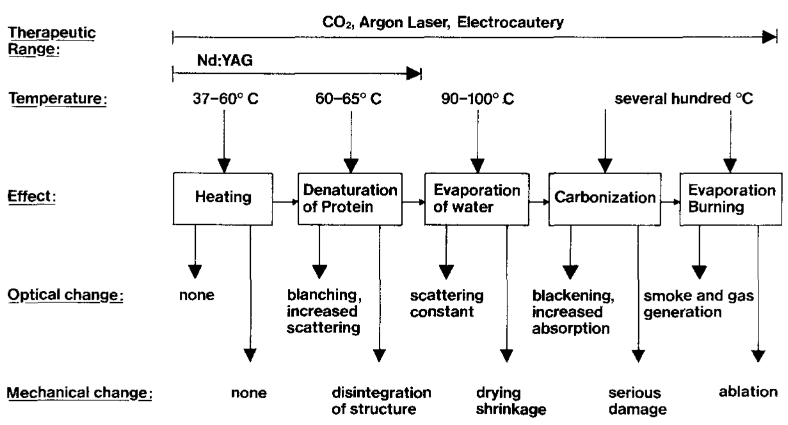

Fig. 7. Thermal interaction of laser radiation with biological tissue

diated area and forwards through the bladder wall. The forward scattered light will be absorbed by adjacent organs on the opposite side of the bladder wall, but since the radiation is extremely diffuse, it is normally distributed over a relatively large area of the neighbouring organs, and thus its heating effect will not be very great. Thermal damage might possibly occur in cases where the neighbouring organ is dark (highly absorbent) such as an intestinal loop, and in immediate contact with the bladder at the irradiation site.

1. Laboratory Experiments

The experiments described here measured the distribution of optical energy and the resulting heating effect in specimens of human bladder tissue. Due to the lower blood content and the absence of the cooling effect of circulating blood as well as thermal contact with other organs, the penetration depth and indepth heating are greatest in in vitro experiments; they can thus be considered as a sort of "worst case" situation. Important for treatment is the relatively slow cooling of the rear wall, showing that the coagulation temperature can easily be attained by a series of several 40 watt pulses spaced several seconds apart.

The radiation leaving in the forward direction will heat adjacent organs, but because it is very diffuse, it fans out over a larger area without causing intense damage. An important characteristic of this radiation is that its magnitude depends on the extent of the heating damage in the tissue. Fig. 8 shows schematically the forward- and back-scattered power we measured during a continuous exposure of the tissue to a beam of constant input power. As necrosis proceeds, the back-scattered power slowly increases while the forward-scattered power decreases at a similar rate. That this effect is due to an increase in the scattering caused by the finer structure of the

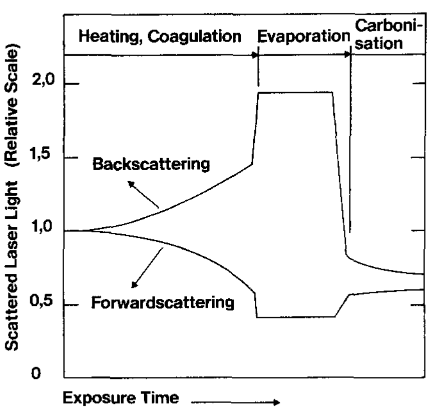

Fig. 8. Intensity changes of backward and forward scattered light during Nd:YAG laser irradiation of membrane tissue (human bladder in vitro)

coagulated phase is indicated by the blanching observed. This is an illustration of an automatic "self defense" mechanism in the tissue against damage by Nd:YAG irradiation. At the boiling point of the cell water, the back-scattered light suddenly increases discontinuously and the forward power drops correspondingly. During the evaporation of water or drying of the tissue, the scattering remains relatively constant until the onset of carbonization. At this point, there is a sudden drop in the back-scattered power because of the darkening (increased absorption) followed by a slow increase in the forward power due to the reduction in wall thickness (ablation). The consequences of this investigation as regards the safety aspects are very important. It shows that as necrosis proceeds, the incident radiation is automatically more strongly rejected by the tissue, and that the absorption is at its minimum prior to mechanical injury of the surface.

2. Animal Experiments

As the total thickness of the human bladder is much greater than that of the rabbit, we consider the 40 watt - 4 s dosage sufficiently mild to insure against possible damage to adjacent organs. An additional safety factor is provided by operating in a water filled bladder as discussed below.

3. Theoretical Investigations

The model is based on a beam damping arising from direct absorption as well as scattering or redirecting of the beam energy, which for want for any theoretical or experimental indications to the contrary, is taken to be spherically symmetric, rebroadcasting the radiation uniformly in all directions. The close agreement between the predictions of our model and the actual measured curves strengthens our confidence in the basic validity of our model as well as its applicability to simulation of the heating characteristics of other lasers. The thermal parameters (conductivity, specific heat, etc.) as well as the direct absorption coefficient used in the numerical computations are those of water, the principal constituent of the cells, justifying the assumption that these parameters remain constant during the Nd:YAG irradiation. The scattering coefficient being a function of the structure, it will remain constant up to temperatures just above the coagulation point (60^{o}C), at which it increases due to the finer structure induced. For radiation directly absorbed at the surface, as is the case with the CO2 laser, the role of the scattering will be negligible, and validity is expected up to the boiling point.

From the curves in Fig. 6, it is seen that although high power pulses of short duration are effective in near axis subsurface heating up to a depth of about 1 mm, their advantage disappears at thicknesses (depths) upwards of 2 mm. A low power irradiation over a longer period of time, on the other hand, uses more advantageously the heat conduction in raising the penetration depth; i.e. higher temperatures at greater depths can be attained while maintaining a subcritical surface temperature.

4. Operative Techniques

A water-filled bladder is advantageous because of the cooling effect around the irradiation site (see (9)). A further safeguard is provided by the effect known as "thermal blooming" in the water. Due to the absorption of the laser light in the water layer between the tip of the light fibre and the tissue surface, the water is heated and begins to disperse the incident beam. As a result, the beam is widened on its way to the tissue surface, the spot size is enlarged, and the power density drops, the energy being distributed over a larger area. Since this effect increases with the laser power employed, it acts as a sort of safety valve, preventing excessive irradiation density at the tissue surface where too high a power is accidentally applied. At the typical working distance of several millimeters, the spot diameter enlargement is 50 - 100% and the total transmission loss in the water is 5 - 10%.

The bladder should be filled without unnecessary stretching of the wall; it is sufficient that the field of operation be unfolded and accessible. A bladder volume of 100 ml should in general be sufficient. Overstretching of the bladder wall leads to a considerable reduction in its thickness, which entails the danger of simultaneous irradiation and coagulation of neighbouring organs - above all intestinal loops – as has been observed in one case, in which an output power of 70 watts was inadvertently applied in an air filled bladder (12).

FUTURE PROSPECTS

After three years of clinical use, we are of the opinion that the endoscopic application of the Nd: YAG laser for irradiation of small or previously resected bladder tumours represents a valuable extension of the currently available transurethral resection procedure, since it has been proved experimentally that the penetration of this laser is far superior to that of electrocautery or the CO2 or argon lasers. Preliminary clinical results in a relatively small number of cases appear to substantiate the assumption that endoscopic laser irradiation is also capable of completely destroying even intramural tumour cell nests. We hope to be able to further improve the long-term survival rate in cases of bladder carcinomas. The indications for total cystectomy, especially in younger patients, should, however, not be changed until a larger number of cases have been treated.

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