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Interstitial Laser Photocoagulation with Four Cylindrical Diffusing Fibre Tips: Importance of Mutual Fibre Distance

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Abstract. Simultaneous application of multiple fibres could increase the volume of coagulation produced with interstitial laser photocoagulation (ILP) for solid tumours. To take full advantage of the presumed synergistic thermal effect between the fibres, the optimal combination of laser power and distance between the fibres was investigated. Four fibres with a cylindrical diffusing tip of 2 cm length were used, coupled to an optical beamsplitter for Nd:YAG light (four channels, maximal variation 9.5%, transmission >85%). The distance between the fibres was 1, 1.5, 2, 2.5 , 3 or 4 cm with a power output of either 4, 5, 6 or 7 W/fibre; energy per fibre was constant at 1800 J by adjusting exposure time. After laser application, dimensions of the coagulated lesions were measured.

The optimal mutual fibre distance was 2 cm ($p<0.01$) at all power levels. This resulted in lesions with a mean (SD) volume of 44.5 (2.1) cm^3 and a largest diameter of 5.1 (0.4) cm at 7 W/fibre. Smaller distances between the fibres resulted in smaller lesions with central carbonisation, whereas larger distances resulted in four separate zones of coagulation. It was concluded that simultaneous application of four interstitial fibres may result in a considerable increase of volume of coagulation. Fibre position and mutual fibre distance determines whether synergism of the coagulative effect occurs.

Keywords: Beamsplitter; Liver; Metastases; Nd:YAG; Tumour

INTRODUCTION

Ever since the introduction of interstitial laser photocoagulation (ILP) efforts have been made to increase the volume of coagulation produced by this technique [1–5]. Recent clinical series show that small hepatic metastases (1.6–2.6 cm) can be destroyed effectively [6–8]. However, in tumours larger than 2.6 cm, lesions with variable dimensions are induced often resulting in incomplete destruction. We recently showed that by using a single optical fibre with a heat-resistant cylindrical diffusing tip it is possible to produce spherical lesions of 3.5 cm in diameter [9]. Most irresectable hepatic metastases originating from colorectal cancer, however, are 4–5 cm in diameter at diagnosis [10]. It is, therefore, evident that improvements in the technique are a prerequisite for effective clinical application. Tranberg et al. [7] and Amin et al. [1] described the techniques of multiple puncturing and redrawing of the laser fibre during application to increase the volume of coagulation. This has two disadvantages: firstly destruction is inaccurate and secondly the technique is time-consuming.

Simultaneous multiple fibre application, using four fibres introduced in a square fashion into the tissue, has been proposed as an alternative strategy. Not only will an overlap occur between the lesions produced by the four fibres, but also a synergistic thermal effect between the fibres will be induced. This has been shown in a mathematical model [11]. A reduced heat dissipation in the centre of the fibres together with an additive effect at the borders of the individual lesions account for this effect [12]. The phenomenon of a synergistic thermal effect between multiple heat applicators is not unique to ILP and has also been described for radiofrequency coagulation [13,14].

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When using simultaneous multiple fibre application, the distance at which the fibres are positioned determines whether the synergistic thermal effect between the fibres occurs [15,16]. To determine the optimal combination of laser power and mutual fibre distance the effects of simultaneous multiple fibre application were studied in ex vivo porcine liver.

MATERIALS AND METHODS

Experimental Design

Four fibres were used simultaneously, implanted in ex vivo porcine liver. Output power per fibre was varied in the range 4–7 W (CW) (2–3.5 W/cm diffuser length, 20–35 W output from the laser). By adjusting exposure time (258–450 s (4, 5, 6 and 7 min, respectively)), energy per fibre was constant at 1800 J. For each power setting, distances between the four fibres were varied from 1 to 4 cm. Each combination of power and fibre distance was replicated five times.

Porcine livers were preserved at −20°C and gradually defrosted overnight. Lobes were then separately warmed, using warm water mattresses, to approximately 28°C (range 26–29°C) and then used for one or two laser applications. Liver core temperature was recorded with a Ni(Cr)-NiK thermocouple (Thermodig N800, AIS, France). The temperature used is considered a compromise between a simple practical model and a complex, expensive set-up more closely simulating physiological conditions. Small-bore cannulas (Adsyte 14G, Becton Dickinson, Spain) were positioned at the corners of a square, the side being the experimental distance, using a custom built template. After inserting the fibres the cannulas were withdrawn.

After laser application, the liver lobe was dissected with a long-bladed knife orthogonal to the insertion of the four fibres in slices of 0.5 cm. Coagulated volume was estimated as the macroscopically detectable whitish colour change compared to normal-coloured liver parenchyma. Height (h) of the lesion and diameter of the largest coagulated plane (w) were measured with callipers. Volume was approximated using the volume of a rotational ellipsoid: $V = h \times w^2 \times \pi/6$ [17]. When no confluence of coagulated zones had occurred, the total coagulated volume was calculated by summing the volumes of the four zones. Each lesion was checked for carbonisation.

Light Delivery

Fibres with a cylindrical diffusing tip of 2 cm length, outer diameter 1.65 mm and core diameter 600 μm were used (Lightstic™, Rare Earth Medical, West Yarmouth, Ma, USA). The four fibres were fed by a custom-built optical 1 × 4 beamsplitter (Lightstic 4X™, Rare Earth Medical), coupled by standard SMA-905 connectors. The beamsplitter consisted of three semi-transparent (50/50) dielectric coated mirrors, splitting the laser output into four approximately equal beam trains. Nd:YAG light of 1064 nm (KTP/YAG 814, Laserscope, San José (CA), USA) was guided to the beamsplitter using a coated 600 μm connecting cable. Power from the connecting fibre from the laser and output directly from the four ports was measured with a calibrated power meter (Labmaster E Thermopile, Coherent, Santa Clara, CA, USA). Transmission efficiency of the beamsplitter was always above 85% (88.3% (1.3) mean (standard deviation)). Variation in output between the four output channels was always below 10% (8.0% (0.51), Table 1). Overheating of the beamsplitting device or breakdown of the diffusing fibres never occurred; also no signs of carbonisation were detected macroscopically at the diffusing tips.

Statistical Methods

Values are expressed as mean ± standard deviation (SD). Two-way analysis of variance (ANOVA) was used for two independent explanatory variables: distance (six levels) and power output (four levels) and one response variable: coagulated volume [18]. Differences between the regression lines for the respective mutual fibre distances type were tested using students' t-test on the calculated regression coefficient. Values were considered statistically significant at $p<0.05$.

RESULTS

Three typical lesions, produced with 7 W per fibre (3.5 W/cm diffuser length) with the fibres at three different mutual fibre distances, are shown in Fig. 1. At distances of 2.5, 3 or 4 cm between the fibres confluence of the four zones

Table 1. Power output from the four channels of the beamsplitter for several laser input power levels

P input (W)	Output port 1 (W)	Output port 2 (W)	Output port 3 (W)	Output port 4 (W)	Mean output port 1–4 (W)	Variation output[a] port 1–4 (%)	Transmission[b] (%)
5.3	1.2	1.2	1.1	1.1	1.2	7.0	87
10.3	2.4	2.3	2.0	2.1	2.2	7.5	85
19.1	4.7	4.6	4.0	4.0	4.3	8.0	90
23.6	5.8	5.5	4.8	4.9	5.3	9.5	89
27.1	6.7	6.5	5.6	5.7	6.1	8.9	90
32.3	7.5	7.6	6.8	6.9	7.2	9.0	89

[a]Variation of the power between output channels was calculated relative to the total output power.
[b]Power from the four channels was summed and divided by the original input power to obtain the net transmission percentage.

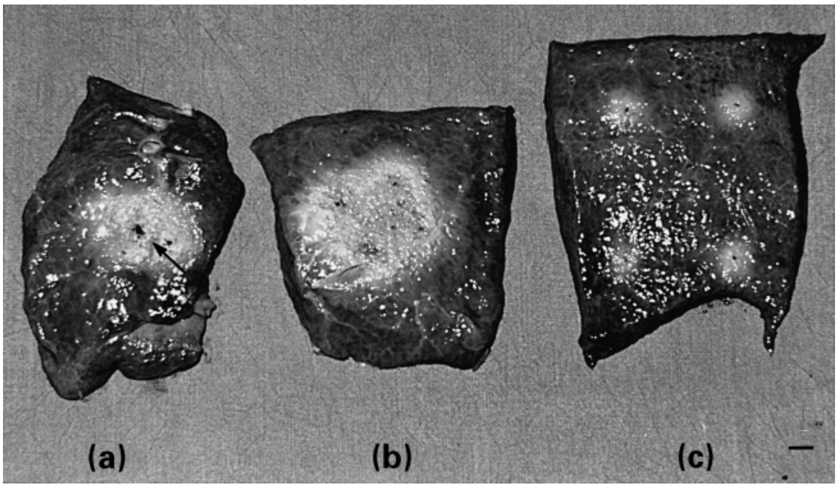

Fig. 1. Typical lesions produced by simultaneous multiple application of four interstitial fibres with 7 W/fibre (1800 J) in ex vivo porcine liver. Mutual fibre distance (*d*) is respectively 1 cm (a), 2 cm (b) and 4 cm (c). With d=1 cm, carbonisation in the centre between the four fibres was always found (*arrow*). Bar=1 cm. Mean total volumes (SD) are respectively 16 (0.6), 44 (2.1) and 15.4 (0.7) cm^3 (n=5 for each combination).

of coagulation never occurred. Thus comparable volumes of coagulation were found for these three distances at each respective power level. At distances of 1, 1.5 and 2 cm between the fibres, confluence of the four zones always occurred. With 1 cm between the fibres, carbonisation was found in the centre of the square. The largest volume of coagulation, 44.5 (2.1) cm^3 (lesion diameter of 5.1 (0.4) cm), was produced with 7 W and 2 cm mutual fibre distance, whereas with 7 W and 4 cm fibre distance mean volume was only 15.1 (0.2) cm^3 (four lesions with a diameter of 1.7 (0.2) cm each) (Fig. 2). Thus a threefold increase of coagulation (44.5/15.1) is created by the synergistic effect. Both distance and power were independent factors for coagulated volume ($p<0.001$ and $p>0.0001$, respectively) indicating that the various levels of power and distance resulted in significantly different coagulated volumes. Interaction of both factors was found also ($p<0.001$) indicating synergism between duration and magnitude of the exposition. Residuals were examined and it was found that the model fitted the data.

DISCUSSION

In this study we assessed the optimal combination of laser power and distance for four interstitial laser fibres, applied simultaneously with a custom-built high-power beamsplitter. In this ex vivo porcine liver model, an optimal synergistic effect was found at 7 W for 258 s (1800 J/fibre) with 2 cm between the fibres (coagulation of 5.1 cm in diameter). The synergistic effect of simultaneous application results in 3 fold enlargement of the volume of coagulation.

High-power beamsplitters are a prerequisite when using fibres with a cylindrical diffusing tip to maintain adequate power over the entire diffusing length. Until now, however, beamsplitting devices have been used which were either inefficient [11, Bown, personal communication] or showed a large output variation

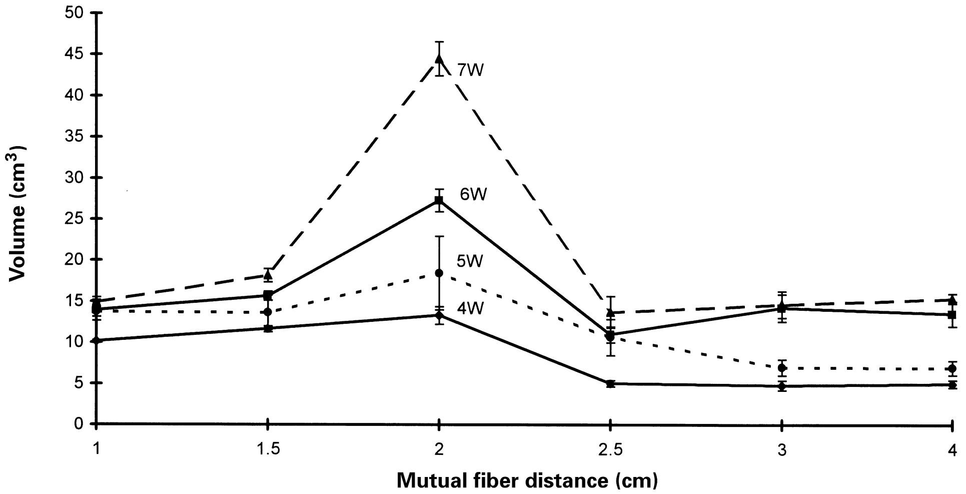

Fig. 2. Volumes of coagulation produced with simultaneous application of four interstitial fibres in ex vivo porcine liver. Laser power was varied between 4 W (◆), 5 W (●), 6 W (■) and 7 W (▲). By varying exposure time, energy was constant at 1800 J/fibre. Points and bars represent the mean and SD of five experimental results.

between the channels [19]. In the present study a beamsplitter with a net transmission percentage above 85% was used. No cooling was necessary with this beamsplitter.

Results of ex vivo experiments are of value only if they can be extrapolated to the in vivo situation. By performing our ex vivo experiments at 28°C, the optimal distance between the fibres might have been slightly underestimated. It should also be noted that the optical properties of normal liver tissue are not identical to human liver metastases as shown by Germer et al. [20]. Preliminary results of experiments with interstitial laser coagulation in human hepatic metastases show areas of coagulation of tumour and surrounding liver tissue similar to those found in this study (unpublished data). In addition, blood perfusion of the target tissue influences the magnitude of the destructive effect by cooling [12,21]. As has been demonstrated in pigs, occlusion of the portal inflow during laser application increases the volume of coagulation fivefold [22]. For this reason we, and others [7,23,24] occlude the portal inflow during clinical ILP application. As the hepatic inflow is then limited to the artery, which is irrelevant to perfusion of the hepatic parenchyma no cooling effect is exerted. Therefore, we do not expect to have to adapt the findings, presented here, for the effects of blood perfusion in vivo.

The optimal mutual fibre distance determines the size of coagulation in the plane perpendicular to the fibres. The size of coagulation in the plane parallel to the fibre is mainly determined by the length of the cylindrical diffusing tip. In this study, fibres with a diffusing tip of 2 cm length were used. Larger or smaller lesions can be produced by adjusting the length of the fibre tip. Likewise lesion shape can be adapted to tumour geometry.

Two beamsplitters for Nd:YAG light have been described in more detail with regard to the used mutual fibre distance. In a study in dogs Steger et al. [15] differentiated between 1 cm and 1.5 cm mutual fibre distance between four bare-tip fibres illuminated simultaneously with Nd:YAG light. The largest lesions were produced at 1.5 cm. A direct comparison, however, between their study and the present results is hampered by the different conditions and the difference in applied laser power. Steger et al. were limited to 1.5 W/fibre due to high energy losses in the beamsplitter used. Ivarsson et al. [19] studied the use of simultaneous application of four sapphire spherical distributing fibres in ex vivo bovine liver with diode laser light (805 nm). The mutual distance between the fibres of 2 cm was chosen on the basis of pilot experiments and not varied in the described experiments. Another important feature of their study was the use of a thermometry system with microprocessor-controlled feedback to the laser. The duration of the diode light up to 1.8 W was 40 min compared to 7 W for a maximum of 4 min in the present study. The difference in the laser parameters used is reflected in the largest volumes produced in both studies. In Ivarsson et al.'s study maximal volume of coagulation was 2.7 cm^3 compared to 44.5 cm^3 in our experiments.

CONCLUSIONS

In conclusion, we showed that by using a 1×4 beamsplitting device the maximum volume of coagulation produced with ILP can be substantially increased. For the optimum effect of simultaneous multiple fibre application the optimal combination of power and distance between the fibres needs to be assessed. By using a newly developed beamsplitter with high transmission efficiency for high power Nd:YAG light and minimal variation between the outgoing beams, lesions with a largest diameter of 5 cm were produced in this model. This diameter is sufficient to treat patients with large solid lesions, such as intrahepatic tumours.

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