Interstitial laser coagulation for hepatic tumours

J. Heisterkamp, R. van Hillegersberg and J. N. M. IJzermans

Department of Surgery, Erasmus University and University Hospital Rotterdam ‘Dijkzigt’, Rotterdam, The Netherlands
Correspondence to: Dr J. Heisterkamp, PO Box 2040, NL-3000 CA, Rotterdam, The Netherlands

Background: The potential role of interstitial laser coagulation (ILC) for patients with irresectable hepatic tumours is currently being investigated. Since its introduction in 1983 it has evolved into an innovative minimally invasive technique.

Methods: On the basis of a Medline literature search and the authors’ experience, the principles, current state and prospects of ILC for hepatic tumours are reviewed.

Results: Animal studies and early clinical studies have shown the safety and feasibility of ILC. The site of interest can be approached at laparoscopy or percutaneously and treatment is easily repeatable. Recent advances include the use of fibres with a cylindrical diffusing light-emitting tip, the length of which is adaptable to tumour diameter, water-cooled fibre systems, simultaneous multiple fibre application, and hepatic inflow occlusion during laser treatment. ILC allows complete destruction of tumours up to 5 cm in diameter. Currently a limitation is the lack of reliable real-time monitoring of laser-induced effects but progress in magnetic resonance imaging techniques should allow accurate temperature measurements to be obtained rapidly during treatment. However, the actual benefit of ILC in terms of patient survival remains to be investigated.

Conclusion: In terms of tools and experience, ILC has now been developed sufficiently to study its effect on survival of patients with irresectable hepatic tumours.

Surgical resection of primary and secondary hepatic tumours leads to an improved 5-year survival rate of 20–40 per cent. The majority of patients with hepatic metastases of colorectal carcinoma, however, do not fulfill the criteria that justify partial hepatectomy. Resection of hepatocellular carcinoma (HCC) in cirrhotic liver is restricted even further by the high operative risk associated with the poor general status of the patient and/or the reduced functional hepatic capacity. In the past 10 years the introduction of screening programmes has resulted in a relative increase in the number of resectable cases; the absolute number of patients for whom no treatment is available has also increased.

Alternative therapies have been developed for the treatment of hepatic malignancies, aimed at local, regional or systemic treatment. As segmental and even subsegmental resections may yield results akin to those of larger partial hepatectomies, provided the resection margin is free from tumour cells, there is a rationale for local tumour destruction. Furthermore, on theoretical grounds, stimulation of dormant malignant cells may be less when using local approaches. In general, the various local techniques using physical means (cold, heat or dehydrating) lead to instant cell death. Cryosurgery, alcohol injection, radiofrequency coagulation and focused ultrasound are currently being investigated and have been reviewed in recent articles. Overall, their widespread clinical application has been hindered by ineffective or unpredictable tumour destruction or by hepatotoxicity.

Interstitial laser coagulation (ILC), introduced in 1983 by Brown, has matured in recent years. ILC is a thermal technique aimed at coagulation of solid tumours by local light delivery using thin flexible fibre(s) (Fig. I). Early experimental findings have been confirmed in preliminary clinical case series, as reported earlier in this journal. While the ILC procedure itself was judged feasible and tolerable, improvement in the technique was necessary for its successful application to tumours larger than 2.5 cm in diameter. In this review the background, recent progress and future perspectives of ILC are discussed with regard to the treatment of hepatic tumours.
Methods

A Medline search (OVID Technologies 3.0, New York, USA) was carried out for the period from 1983 to the present using the text words ‘laser’, ‘liver’ and ‘interstitial’. Furthermore, relevant papers were identified from the reference lists of the papers previously obtained through the Medline search together with abstracts from recent international meetings. Papers describing clinical studies were included only if (1) the tumour response rates were stated and (2) complications were described.

Laser-tissue interaction

ILC uses laser light at low power (3–15 W) with long exposure times (3–20 min), resulting in coagulation, noted as blanching of the tissue as in a boiled egg (Fig. 1). The treated area is left to undergo necrosis in situ with subsequent healing by regeneration and/or fibrosis. The volume of tissue destruction is a function of both fibre position(s) within the tumour, and the temperature gradients created by the amount of power and duration of exposure. The subsequent biological response to laser light depends on the interaction of the light with the tissue. On absorption of the laser light several thermal effects occur (Table I). Coagulation is defined as the irreversible thermal damage of tissue proteins at temperatures between 55 and 95°C.

The compromise between deep penetration of the laser light and sufficient absorption in the tissue determines the optimal wavelength for ILC. Neodymium yttrium–aluminium–garnet (Nd YAG) (wavelength 1064 nm) and diode light (890 nm) have been investigated. Both wavelengths are minimally absorbed by water and depend on tissue chromophores for their effect. Nd YAG light penetrates the tissue up to 10 mm from the light source.

As tumour and liver differ in colour, their optical characteristics might also differ. Van Hillegersberg et al. found no net difference in absorption coefficient between rat tumour and liver at 1064 nm; scattering was only slightly greater in tumour. More important are changes in optical characteristics in the process of coagulation (during

![Image](https://example.com/image1.png)

**Fig. 1** Coagulated lesion in **ex vivo** pig liver. After laser treatment (6 W during 6 min (2160 J) of neodymium yttrium–aluminium–garnet light) the liver was sectioned in the plane along the laser fibre which is in situ (0.9 mm in diameter with a cylindrical diffusing tip of 2 cm). The whitish region is the resulting area of coagulation (maximum length 36 mm, diameter 26 mm)

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Physical effect</th>
<th>Biological effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–45</td>
<td>Heating</td>
<td>Enzyme inactivation</td>
</tr>
<tr>
<td>60–140</td>
<td>Protein denaturation</td>
<td>Cell shrinkage, hyperchromasia, membrane rupture, pyknosis, hyalinization of collagen</td>
</tr>
<tr>
<td>100–300</td>
<td>Water vaporization</td>
<td>Extracellular steam vacuole and cell shrinkage</td>
</tr>
<tr>
<td>300–1000</td>
<td>Carbonization and ablation</td>
<td>Ablation vaporization and carbonization</td>
</tr>
</tbody>
</table>

From Thomsen, Hunter and Dixon and Welch et al.
laser treatment). Light measurements during laser treatment of a tumour implanted in rat liver showed that light uptake increased, suggesting that absorption in the coagulated area decreased and light penetration increased. This has recently been confirmed by determination of the optical characteristics of vital and coagulated tissue.

Both increasing power and increasing exposure time result in an increase in the area of coagulation; power is the most important factor. Eventually, lesion size is limited at a plateau owing to decreased light density and conducted heat at the tissue peripheral to the laser fibre.

Interstitial laser fibres

With the use of a conventional bare-tip fibre, where light emission is concentrated at the tip, carbonization occurs. The blackish tissue limits the penetration of light to the surrounding tissue resulting in local temperature accumulation. As a consequence, the temperature profile from a carbonized tip is different from that of any other type of hot tip; one might as well use a hot knitting needle. With cylindrical diffusing fibre tips homogeneous light emission is produced over the entire light-diffusing length, as seen in Fig. 1, allowing the emitted laser light to be distributed equally throughout the surrounding tissue. It was initially thought that carbonization was necessary to create a large lesion. However, at the optimal combination of exposure time and laser power, light-diffusing tips result in larger lesions with less interlesion variation. Recent years have seen major improvements in the quality of the diffusing tip fibres, resulting in better flexibility and thermoresistance. In addition, the length of the diffusing tip can be adapted to tumour diameter.

As the eventual coagulation size that can be produced with a single fibre is limited, simultaneous multiple fibre application has been used for lesions greater than 2 cm in diameter. Owing to a synergistic effect between the fibres, a fourfold to sixfold increase in lesion volume occurs, resulting in areas of coagulation 5 cm in diameter. Both reduced heat dissipation in the centre of the fibres and an additive effect at the borders of the individual lesions account for this effect. For this purpose several beam-splitting devices have been developed so that a single laser machine can feed multiple fibres. In studies in vivo porcine liver a discrete optimal mutual fibre distance (2 cm) for the maximal synergistic effect was found (lesions with a diameter of 5 cm). The importance of the mutual fibre distance is illustrated by the finding that smaller distances between the fibres resulted in smaller lesions with central carbonization, whereas larger distances resulted in multiple separate zones of coagulation.

The latest development is a closed catheter system, transparent to laser light, through which a diffusing tip is introduced into the tissue. The catheter is irrigated with water during laser treatment. This produces a temperature reduction at the surface of the catheter, allowing the exposure time and power to be increased without the risk of carbonization and fibre destruction. Lesions up to 5 cm in diameter can be created when used in combination with diffusing tips of 4 cm. The insertion of one fibre into a tumour is more precise than the positioning of four fibres at an equal depth and discrete mutual distance. However, as the closed catheter system is larger in diameter (1.6 versus 3 mm) flexibility is reduced and the risk of haemorrhage in the tract to the target may be increased.

Histopathological evidence of effect

Thermal protein denaturation results in macroscopic tissue whitening but this is not a good indicator of the exact outer boundary of the lethal tissue effect. Under light microscopy the borders of a coagulated lesion show a rim consisting of haemorrhage, hyperaemia and oedema. This haemorrhagic zone is a typical finding after laser coagulation in a variety of tissues and is explained by thermal intravascular erythrolysis. The cells of the zone are devitalized as shown by loss of mitochondrial enzymatic activity.

Morphological observations using light microscopy do not allow unambiguous conclusions about the cell viability in coagulated tissue immediately after treatment. Cells with a nucleus have been described in haematoxylin and eosin-stained biopsy specimens following ILC, which were found to be non-vital when studied with electron microscopy. With immunohistochemical methods the authors’ group and others have ruled out the presence of vital cells in animal models with and without tumour, using either localization of nicotinamide adenine dinucleotide metabolism directly after ILC treatment or by 5-bromo-2′-deoxyuridine incorporation 6–36 days after ILC (Fig. 2). Complete cell death has also been confirmed in laser-induced coagulation in the resection specimens of patients with hepatic metastases who underwent resection 2–3 days after ILC.

Notwithstanding the difficulties in defining coagulation damage, a rough outline can be given. In essence, no difference in reaction between tumour and normal tissue has been found. The acute lesion has a characteristic zonal architecture as described in detail in the literature.

Briefly, in a central zone surrounding the insertion of the laser probe the gross tissue structure is well preserved, whereas cellular build-up is characterized by acidophilic
hepatic tissue takes place between 3 and 12 months after laser treatment, as demonstrated in normal liver of rabbits, dogs and pigs.

**Studies in experimental animal models**

Studies in animal models have been performed using tumour-bearing rodents and rabbits, as well as in rodents, dogs, and pigs with normal livers. In the tumour models the cytotoxicity of ILC was studied; the normal-liver models allowed strategies to increase coagulation volume at human scale to be investigated.

The earliest documented work was by Matthewson et al. in rat liver using Nd YAG light. A 0.4-mm diameter fibre was inserted into the centre of a lobe of liver, exposed at laparotomy. Power settings of 0.5–2 W and exposure times of 50–2400 s were used to give well defined lesions of coagulative necrosis with sharp boundaries between normal and coagulated liver. The size of coagulation increased with increasing laser energy until a plateau was reached. Van Hillegersberg et al. studied ILC in a rat liver tumour model. Lesion size and liver enzymes increased with laser energy applied. Deterioration in liver function was not found. At optimal laser settings complete tumour eradication was obtained. In addition, several rodent models with subcutaneous implanted tumours showed the tumour cell killing potential of ILC. Recently an indication of reduced outgrowth of remnant tumour has been found after ILC compared with resection in liver tumours in rats.

In a second phase of animal experiments, modifications to enlarge the volume of coagulation were studied in large-animal models. Steger et al. used dogs to evaluate the use of a laser beam-splitting device to feed four fibres at a mutual distance of 1.5 cm which resulted in lesions of 3.5 cm maximum.

A second line of investigation was to evaluate the influence of hepatic blood flow on the magnitude of the coagulation. Computer simulations and mathematical modelling predicted a fourfold to fivefold increase in the area of coagulation in liver without blood flow. The relatively small size of previous animal models and the small volume of coagulation that could be produced had obscured such an effect. These predictions were confirmed independently by three research groups, using multiple and single fibre application in pigs. With physiological blood flow through the liver, the volume of coagulation is reduced to 10–20 per cent and tissue is preserved around large vessels. Germer et al. and Möller et al. investigated complete occlusion versus physiological flow, and the authors’ group also differen-
tiated between portal inflow occlusion only versus complete inflow occlusion (arterial and portal). It was found that portal inflow occlusion suffices to overcome the cooling effect of the blood flow. Although it is generally assumed that hepatic metastases are mainly supplied by the arterial tree, clamping of both hepatic artery and portal vein is unlikely to be needed in the clinical situation. The poorly organized vascular bed in the tumour will probably cause only minimal tissue cooling and thus minimal lesion reduction.

Furthermore, in the often ischaemic centre of the tumour, in particular, little extra effect can be expected from eliminating the arterial blood flow. However, the tumour is surrounded by well perfused liver parenchyma and it is here that the cooling effect is mainly exerted. Therefore, eliminating portal blood flow should enhance the destruction of the vital rim of the tumour and a margin of normal liver tissue. Also portal inflow occlusion alone, through a percutaneous transhepatic route, is less invasive than methods of achieving total arrest of blood flow. In a recent experimental study in pigs, the authors investigated the effects of ILC in the liver with portal inflow occlusion with a long-term follow-up. No adverse events occurred, even in the vicinity of large vessels situated centrally in the liver. For ILC of primary liver cancer, portal inflow occlusion may not be needed in a cirrhotic liver, as the portal flow is often negligible or even retrograde. In this situation the magnitude of the arterial flow should be considered as a potential cooling source.

**Treatment monitoring and evaluation**

Currently, ILC is limited by the lack of reliable real-time monitoring of laser-induced effects. Ideally, real-time monitoring of ILC should provide information about the extent of coagulation in relation to the anatomy of the liver during treatment. The intervention may then be prolonged to ensure complete coagulation of the entire tumour, or terminated to prevent damage to vital structures. Interstitially placed thermosensors and light detectors for precise measurements are of little use because of the limited number of sample points and the extra trauma associated with their placement. It is likely that real-time monitoring by a non-invasive imaging technique is the key to control ILC. Several such techniques have been investigated.

**Ultrasonography**

Ultrasonography enables accurate placement of catheters into the tumour. Real-time imaging of the treated area has also been investigated but the echogenic area that is observed during coagulation does not correlate with the coagulative damage. The image is caused by formation of bubbles from evaporated tissue water. Ultrasonography is also not helpful in evaluating lesions after treatment as the echogenic area becomes heterogeneous within minutes.

**Computed tomography**

For the diagnostic assessment before treatment, triphasic spiral computed tomography (CT) is indicated to define the number, location and dimensions of metastases before therapy. Contrast-enhanced CT after treatment shows the result of laser treatment very clearly as a well defined, non-enhanced area, easily distinguishable from the untreated, thus vascularized, enhancing tumour areas (Fig. 3). Contrast-enhanced triphasic CT after laser treatment should be considered as the evaluative ‘gold standard’. The optimal time to perform ILC after CT is between 1 and 4 days, which corresponds with the time at which experimentally induced coagulated lesions have their maximum diameter. Unfortunately, after longer intervals CT cannot differentiate between inflammatory change, regenerating liver or recurrent tumour. Because of the radiographic load and insensitivity to soft tissue changes, there is no role for real-time CT during ILC.

**Magnetic resonance imaging**

Magnetic resonance imaging (MRI) is not restricted solely to morphology; physiological parameters may also be measured. Initial experience in monitoring laser treatment in patients with hepatic metastases consisted of conventional T1-weighted imaging. These T1-weighted sequences are available on all clinical systems and do not require advanced computer-assisted image interpretation. The temperature dependence of T1 has been demonstrated in vitro for several biological systems. However, the relationship between T1 and temperature is not simple because of the multifactorial nature of T1; the temperature dependence of T1 also varies strongly for different types of tissue. Furthermore, precise measurements of the absolute value of T1 are difficult. Gewiese et al. visualized a laser heated region, in ex vivo tissue, as a bright area surrounded by a dark border which was found to correspond with an isotherm of 45°C (20°C increase from starting temperature). More subtle differences, however, were undetectable. Therefore the current status of T1-weighted monitoring of heat deposition in tissue does not represent adequate thermometry.

The change in the proton resonance frequency (PRF) represents an alternative temperature-dependent magnetic
Fig. 3 Contrast-enhanced computed tomogram a before, b 1 day after and c 7 months after laser treatment of a 4.5-cm large hepatocellular carcinoma in the anterior sector of segment four (arrow). Because of cirrhosis, portal flow was negligible during treatment (four fibres with diffusing tips of 5 cm). Through these fibres 12.5 W of neodymium yttrium-aluminium-garnet light per fibre was guided simultaneously over 6 min (4500 J per fibre). In b and c laser-induced avascularity is seen. In c a small enhancing rim (double arrow) indicates incomplete tumour destruction (a second laser treatment was scheduled).

Fig. 4 Magnetic resonance image showing a transverse slice of liver lobe (ex vivo) scanned in dynamic series during laser treatment with a single fibre (cylindrical diffusing tip of 2 cm) with 6 W over 6 min. Temperatures were calculated relative to the baseline proton resonance frequency in a reference scan before treatment. Colour overlays, over the baseline morphological image, represent temperature increases compared with those at the start of the experiment (32°C in this particular case): +8°C (blue), +18°C (yellow) and +28°C (red). Temperatures could be determined with an accuracy of ±3.5°C after 6 min of laser application (95% per cent confidence interval). Correlation between the dimensions of macroscopic coagulation and the largest diameters of the 60°C isotherm was 0.94. Bar indicates 1 cm.

resonance variable. The PRF method provides a direct estimate of temperature changes, and the feasibility and accuracy of this subtraction technique was demonstrated in 1995. In ex vivo and in vitro models the accuracy of phase-shift mapping was within ±4°C. Respiration-induced artefacts do not result in a decreased accuracy. Currently this technique is under investigation in preclinical models.

For MRI assessment after treatment both T1- and T2-weighted scans have been proposed. With sophisticated T1-weighted scans the area of coagulation at the end of treatment could be predicted very accurately. This was investigated in animal models and in surgical candidates who underwent resection 2–3 days after MRI-guided laser treatment (allowing correlation between MRI and histopathology). In a recent study these encouraging findings were compared with CT, considered as the gold standard, for validation. A good correlation was found between the MRI scan at the end of laser application and the CT scan at 24 h. Currently, space to access the patient is limited in high-field MRI machines; progress in this field...
and the development of magnetic resonance-compatible equipment promises future high-field MRI with the capacity for intervention from all sides.  

**Clinical experience**

The cumulative clinical experience is summarized in Table 2. The first clinical report came from Hashimoto et al. in 1985 who treated patients with liver metastases and HCC at laparotomy. A Nd YAG laser at a low power output of 5 W was used with a relatively long exposure time and a bare-tip fibre was employed. From this study it appeared that the technique could be performed without major complications. A drop in tumour marker levels was recorded, but the benefit to patients remained unclear. In later studies the technique was improved using various combinations of power output and exposure times, and adaptation of the fibre tip to avoid carbonization. Hahl et al. and Huang et al. actually used hyperthermia, instead of direct coagulation, which means that the temperature was held between 41 and 45°C over 10–30 min. A fatal complication was caused by air emboli as a result of interstitial air introduced for cooling of the fibre tip, a method of cooling that has been abandoned ever since.

The percutaneous procedure was introduced by Steger et al. and later adapted by Nolsoe et al. and Schroder et al. Total eradication of small tumours was described. Failures were noted mostly for lesions larger than 2–3 cm; this threshold for a complete response was also found in a larger series by Vogl et al. using single fibre application with a diffusing tip in a percutaneous procedure. In sequel

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Group characteristics*</th>
<th>Technique</th>
<th>Approach†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huang et al.</td>
<td>1991</td>
<td>7 HCC (2–4 cm)</td>
<td>Diffusing tip; 2–3 W, 20–30 min</td>
<td>Laparotomy (thermocouple)</td>
</tr>
<tr>
<td>Nolsoe et al.</td>
<td>1993</td>
<td>16 CRCs (1–4 cm)</td>
<td>Diffusing tip; 4–8 W, 5–45 min</td>
<td>Laparotomy 2 (thermocouple), percutaneous 9 (US)</td>
</tr>
<tr>
<td>Amin et al.</td>
<td>1993</td>
<td>34 CRCS, 21 secondaries of mixed origin (1–15 cm)</td>
<td>4 × bare tips simultaneously, 2 W, 7 min</td>
<td>Percutaneous (US)</td>
</tr>
<tr>
<td>Schroder et al.</td>
<td>1994</td>
<td>2 HCC (3–7 cm); 2 breast secondaries, 6 CRCs (0.5–7 cm)</td>
<td>Bare tip; 2–6 W, 8–15 min</td>
<td>Laparotomy (US)</td>
</tr>
<tr>
<td>Dowlatshahi et al.</td>
<td>1995</td>
<td>45 lesions in 20 patients; HCC and CRCs</td>
<td>Bare tip; 5–10 W, 7 min</td>
<td>Laparotomy (US)</td>
</tr>
<tr>
<td>Tranberg et al.</td>
<td>1996</td>
<td>3 HCC, 18 CRCS, 1 pancreatic secondary (1–10 cm)</td>
<td>Frosted sapphire tip; 6–10 W, 5 min with complete hepatic inflow occlusion</td>
<td>Laparotomy (US)</td>
</tr>
<tr>
<td>Gillsm et al.</td>
<td>1997</td>
<td>148 secondaries in 55 patients (1–6 cm)</td>
<td>2 × 4 bare tips simultaneously; 2 W per fibre, 7 min</td>
<td>Percutaneous (US and MRI)</td>
</tr>
<tr>
<td>Vogl et al.</td>
<td>1997</td>
<td>282 CRCS in 99 patients (&lt; 5 cm)</td>
<td>Diffusing tip; 10 W, 10–20 min</td>
<td>Percutaneous (MRI)</td>
</tr>
</tbody>
</table>

*Values in parentheses are tumour diameters. †Monitoring technique is shown in parentheses.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Tumour response at 6 months</th>
<th>Mean (range) no. of treatments</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huang et al.</td>
<td>1991</td>
<td>CT: 40% CR, 40% PD US: 75% CR (mean 2–4 cm), 25% SD (mean 3–4 cm)</td>
<td>11 (1–2)</td>
<td>Mild pain</td>
</tr>
<tr>
<td>Nolsoe et al.</td>
<td>1993</td>
<td>1 only Mild pain, temperature increase, pleural effusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amin et al.</td>
<td>1993</td>
<td>CT: 38% CR, 44% SD; failures at &gt; 4 cm in diameter</td>
<td>32 (1–8)</td>
<td>Severe pain, subcapsular haematoma, pleural effusion, temperature increase</td>
</tr>
<tr>
<td>Schroder et al.</td>
<td>1994</td>
<td>CT: 8% CR, 58% SD, 33% PD</td>
<td>18 (1–4)</td>
<td>Bilioma, vasovagal reaction, shoulder pain n.s.</td>
</tr>
<tr>
<td>Dowlatshahi et al.</td>
<td>1995</td>
<td>CT: 68% CR (&lt; 2.5 cm); 0% CR (&gt; 2.5 cm)</td>
<td>1 only</td>
<td>1 fatal multiple organ failure n.s.</td>
</tr>
<tr>
<td>Tranberg et al.</td>
<td>1996</td>
<td>CT: 16% CR, 38% PR, 46% SD/PD</td>
<td>1 only</td>
<td>Nausea, right subphrenic haemorrhage n.s.</td>
</tr>
<tr>
<td>Gillsm et al.</td>
<td>1997</td>
<td>CT: 15% CR, 38% PD</td>
<td>22 (1–12)</td>
<td></td>
</tr>
<tr>
<td>Vogl et al.</td>
<td>1997</td>
<td>MRI: cumulative 3-year survival rate 42%</td>
<td>8 (1–36)</td>
<td></td>
</tr>
</tbody>
</table>

HCC, hepatocellular carcinoma; CRCs, colorectal cancer secondaries; CT, computed tomography; US, ultrasonography; MRI, magnetic resonance imaging; CR, complete response; PD, progressive disease; SD, stable disease; PR, partial response; n.s., not stated.
to Steger’s study, Amin et al.76 used a method of bare-tip fibre application which required reinserterion and repulling of the fibres to cover the tumour completely. Tranberg et al.102 treated patients at laparotomy with complete hepatic inflow occlusion and from one to four fibres according to tumour size.

Complications

Minor complications such as pain at the fibre insertion site, pleural effusion, local (subcapsular) haematoma, and pain at the shoulder as a result of diaphragmatic irritation, occur in approximately 90, 10, 10 and 15 per cent of patients respectively. The subfebrile temperatures after treatment, reported in several series, may be due to the presence of necrotic tissue in the liver or a sterile peritonitis at the fibre insertion site. That the procedure is fairly easily tolerated is illustrated by the percutaneous protocols in which the patients are usually discharged 24 h after treatment with minimal requirement for analgesia.

Serious complications in the series without flow occlusion are seldom encountered; bilomas or haemorrhages requiring external drainage have not yet been reported. One case of fatal Budd-Chiari syndrome occurred on the day after laser treatment in a patient in London (S. G. Bown, personal communication), emphasizing the need for accurate monitoring of laser-induced effects near vital intrahepatic structures such as the hepatic veins. Tranberg et al.102 reported a death from multiple organ failure due to massive tumour necrosis after laser treatment of an 8-cm lesion. In their series complete occlusion of hepatic flow was applied. The situation may be compared with the ‘cryoshock phenomenon’ in which multiple organ failure ensued after treating large tumours with cryosurgery.108 There are no reports of injury to major vascular or biliary structures after ILC close to major portal pedicles with hepatic inflow occlusion, and so such siting is not considered as a contraindication to treatment. In the authors’ clinical experience, ILC with portal inflow occlusion of tumours up to 4.5 cm in diameter has always been safe and tolerable.

Outcome

As each study defines its own criteria of selection and evaluation, the outcomes in terms of tumour response and survival are difficult to compare (Table 2). In an updated series, Vogl et al.79 evaluated the effect on survival after percutaneous ILC in 99 patients with colorectal metastases of the liver. A 3-year survival rate of 42 per cent with a median survival of 36 months was reported (88 per cent at 1 year). This was at the expense of an average of 2.9 repeated treatments per tumour (range not stated), both for recurrence in treated tumours and for newly diagnosed tumours (not distinguished). In the cumulated London series mean survival was 18 months in 44 patients with an mean number of 2.2 repeated treatments; the 1-year survival rate was 87 per cent103. For patients treated at laparotomy, results were less favourable, possibly because of the larger diameters of the treated tumours (up to 10 cm)102. Median survival after treatment was 8.5 months and this was mainly influenced by recurrent disease at various extrahepatic sites (in 70 per cent of patients). Recently the first significant series of ILC in patients with HCC was reported; in 12 patients 17 lesions were treated and median survival was 34 months109. Currently, in the percutaneous protocols the number of tumours is limited to five and the diameter to 5 cm.

Procedural considerations

ILC can be performed percutaneously under intravenous sedation and analgesia, allowing a short hospital stay with 24-h observation after treatment. On the other hand, general anaesthesia with artificial ventilation results in better respiratory control for respiratory triggered real-time MRI scanning, prevents patient discomfort and movement during treatment, and renders portal inflow occlusion more tolerable. In the authors’ experience and as reported by others percutaneous transhepatic catheterization and balloon occlusion of the portal vein can be performed safely by an experienced interventional radiologist72,73,110. For lesions high in the hepatic dome, transthoracic and transdiaphragmatic fibre insertion may be necessary. For lesions located in the left hemiliver a subcostal route is feasible, whereas for right-sided tumours insertion in the intercostal space may be considered to avoid vital structures, especially when inserting multiple fibres. An advantage of percutaneous treatment is the feasibility of repeated treatment.

There are also advantages of an open or laparoscopic approach146,111. Fibre positioning under direct view may be more reliable, resulting in complete tumour destruction in a single treatment session. Intrapertoneal tumour deposits, making the laser treatment pointless, can be detected at laparotomy or laparoscopy. Needle tract haemorrhage is detected instantly and can be treated under direct vision. The liver can be mobilized allowing access to lesions located posteriorly112 and, finally, for deep-seated lesions more flexibility is created in choice of the insertion tract. In pigs, laparoscopic ILC has been combined with real-time MRI monitoring in an open interventional magnetic resonance scanner111. In this way
the precision of positioning under direct view is combined with reliable interstitial monitoring.

Conclusion

ILC is one of the modalities under current investigation for local control of hepatic malignancies. In this review the principles underlying ILC have been discussed. From the results of animal and clinical studies it may be concluded that ILC is safe and feasible using either a laparoscopic approach or percutaneous access. Recent advances are the use of fibres with a cylindrical diffusing light-emitting tip of which the length is adaptable to tumour diameter, water-cooled fibre systems, simultaneous multiple fibre application, and hepatic inflow occlusion during laser treatment. Complete destruction of tumours up to 5 cm in diameter can be realized. In the light of recent developments allowing accurate real-time monitoring with MRI, the authors are optimistic about the role of ILC in the management of hepatic malignancies. Although ILC for hepatic tumours should still be regarded as an experimental treatment, it is legitimate to evaluate its impact on the survival of patients with irresectable hepatic tumours. When the accuracy and efficacy of ILC has been established unequivocally, comparison with surgical resection in controlled clinical trials will be justified.

References


