Nd:YAG Laser Procedures in Tumor Treatment

CARSTEN M. PHILIPP, MD, EWA ROHDE, MD, and H.-PETER BERLIEN, MD
From the Department of Laser Medicine, University Clinic Benjamin Franklin, Berlin, Germany

Due to the wide variability of tissue interactions and the possibility of specific applications, the neodymium-yttrium-aluminum-garnet (Nd:YAG) laser is the most important surgical laser. With the adequate choice of application mode and relationship between interaction time and power density, it can be used for precise cutting in the contact mode with the bare fiber, with either a wide or small coagulation seam. With a handpiece a precise focal coagulation for preparation and hemostatic purposes is possible, as well as cutting with the focussed noncontact beam where additionally a wide coagulation seam is necessary. Endoscopically guided coagulation, vaporization, and cutting are possible with bare fibers which can be introduced through nearly all endoscopes. With increasing importance, the possibility for wide and homogeneous volume coagulation is used to destroy diseased tissues either by noncontact irradiation or interstitial placement of the fiber. Thus, the field of laser application in tumor therapy ranges from the treatment of superficial tumors to endoscopic tumor ablation, resection of neoplastic tissue in parenchymatous organs, and interstitial thermotherapy with coagulation of deep-seated primary and secondary malignancies. With its different application modes the laser can be used as a surgical instrument or as a central therapeutical method, whereby perfect control of tissue interactions is always possible by using either visual control for superficial and endoscopic procedures or magnetic resonance imaging and color-coded duplex sonography as a control for interstitial procedures. During 12 years of clinical work we have developed several application modes and have proved the Nd:YAG laser to be an effective instrument in tumor therapy.

KEY WORDS: tumor surgery, endoscopy, interstitial thermotherapy, bare fiber, contact surgery, noncontact surgery, color-coded duplex sonography

INTRODUCTION

With the development of modern medical lasers, laser therapy has gained an increasing role in the wide spectrum of treatment modalities. Also in oncology, laser techniques have become interesting alternatives in radical tumor resection and to palliative tumor treatment methods. Due to the great variability of induced tissue reactions from microsurgical precise coagulation and cutting to voluminous coagulation or tumor vaporization, the Nd:YAG laser (wavelength 1.064 nm) is the most important surgical laser. The possibility of transmitting its light through flexible fibers allows wide variation of applications and tissue effects. Even if this laser is mostly known for its ability of volume coagulation, which is due to its large optical penetration depth, it shows a reaction depth which can be varied in the widest range of all medical lasers by using the appropriate parameters.

The longest experience exists with all applications of...
voluminous coagulation for hemostasis and tumor destruction. Microsurgical preparation with the neodymium-yttrium-aluminum-garnet (Nd:YAG) laser became possible for the first time with the introduction of contact surgery with sapphire tips [1]. The great disadvantages of sapphire tips in practical use led us to introduce bare fiber contact surgery in 1983. Due to the easy handling and cheap method of bare fiber, this is at present our standard method for all contact applications, especially in endoscopic procedures [2]. Because light in the near-infrared range has the greatest penetration depth in tissue, it is also possible to produce homogeneous coagulation during direct irradiation of the diseased area by the fiber introduced percutaneously into the tissue to be treated. This method, called interstitial laser-induced thermotherapy (LITT), was first described by Bown [3] and Ascher in 1983 [4]. At the same time, interstitial laser therapy with bare fiber was introduced in our center. The first applications were for vascular malformations and hemangiomas [5]. In the following article, we extend the applications of Nd:YAG laser therapy to the treatment of benign and malignant tumors, chronic abscesses, and fistulas [6].

MATERIALS AND METHODS

Types of Nd:YAG Laser Application

One can distinguish—indeed, independent of medical specialties—between superficial application, open surgery, and intracorporal application (either with endoscopic or nonendoscopic approach) such as interstitial or intraluminal application. Especially in tumor therapy, it is sometimes necessary to combine these different methods to obtain the best result.

Four kinds of laser procedures, i.e., cutting/removal, LITT, photochemical reactions, and optical imaging, are possible in laser medicine. Currently, classical photovaporization and LITT have gained the most important role in laser tumor therapy.

Photovaporization. Due to the absorption of laser radiation by specific absorbers like water, chromophores, or proteins, heating of the tissue occurs, followed at 100°C by evaporation of water and, at temperatures between 150 and 350°C, by tissue dessication and carbonization. The carbonized surfaces will absorb most of the subsequent irradiation and also get vaporized. The typical interaction time of this process ranges from one-tenth of a second to several seconds. With longer exposure times, in addition to the penetration depth of the laser irradiation itself, heat conduction in the surrounding tissue occurs and causes thermal effects.

LLL. With this method an in situ coagulation of the tissue from heating of more than 60°C is possible. This is called laser-induced coagulation (LIC). Another process is the thermic dynamic reaction. In this case, after a short time of overheating, not an immediate coagulation occurs but an inflammatory reaction is induced. This inflammation is followed by an apoptosis with fibrotic repair and can change the structure of the tissue.

Practical Guidelines for Nd:YAG Laser Application

Independent of the specific disease or medical discipline it is possible to give general guidelines for the use of the Nd:YAG laser with different applicators (Fig. 1). With an appropriate choice of parameters it is possible to obtain a sufficient result with a low risk of side effects in very different situations. Undoubtedly, one has to adapt laser parameters to the specific surgical situation.

Focussing handpiece. By using a focussing handpiece, it is possible to induce a wide range of different tissue effects such as a small coagulation seam for preparation, a broad coagulation seam for excellent hemostasis, a subcutaneous coagulation without any damage of the overlaying tissue, or cutting/vaporization. For microsurgical preparation during the operation, a handpiece with a small focus diameter of 0.5 mm (which can be achieved with a f = 30 mm focussing handpiece) is used. With short exposure times between 0.1 and 0.5 seconds and a power setting of 30 W, one will achieve only small coagulation points for the preparation of tissue. If larger vessels are identified during this procedure, given parameters are not sufficient to perform a coagulation for the purpose of hemostasis. By defocussing the beam and with longer exposure times (approximately 1–2 seconds) large vessels can also be coagulated without any risk of vaporization or bleeding. Another possibility is to take the vessel between the forceps and irradiate the ends of the branches in noncontact with 30 W for 0.5 seconds or more to achieve an occlusion as with bipolar forceps.

To minimize the risk of large blood loss in the resection, especially from parenchymatous organs or highly perfused tumors such as sarcomas and embryonal tumors, one needs a higher power output. With a small focus of 0.5 mm and with a power setting of 60–100 W (depending on the quality of the focussing handpiece) in continuous wave irradiation, one can perform vaporization with a broad coagulation seam after starting the first carbonization point (Fig. 1b). By spreading the tissue, especially in partial resection of the liver, one can identify the hepatic veins and arteries and thus reduce the risk of unwanted and inappropriate vaporization and opening of these vessels. So the procedure is comparable to the ultrasound aspirator.
But in contrast to this, one has the additional advantage of a coagulated resection surface with a highly reduced risk of immediate or late bleeding or of forming a biliary fistula. In case of bleeding one has to remove the blood by rinsing with saline solution and suction. The water layer causes no absorption of the laser and one can irrigate with a defocussed beam during irrigation for the purpose of coagulation of the bleeding vessel.

For in situ coagulation, for example, of tumor rests, with a small coagulation seam either the 30 or 60 mm focussing handpiece can be used. At low power output of about 30 W but with a larger spot diameter, compared to microsurgical preparation, and at short exposure times of 0.2–0.5 seconds, a small coagulation seam will be achieved. If necessary, one can perform multiple exposures on the same area until blanching occurs. To avoid carbonization and for deep coagulation it is helpful to rinse the surface with saline solution. Since the coagulation seam depends mainly on the exposure time, for deeper coagulation longer exposure times should be used. For coagulation of major bleeding one has to use 60 W, a large spot diameter, and continuous rinsing with saline solution during irradiation. With this saline rinsing, all blood which would otherwise absorb most of the irradiation can be removed. In this way one can avoid carbonization and achieve a cooling effect on the surface as well as a deeper coagulation effect in the tissue.

A quite different technique is subcutaneous coagulation, which can be used, for example, in the treatment of Kaposi sarcoma and subcutaneous metastases of various malignancies. With a power setting of 35 W (cw), a spot size of 5 mm, and the additional use of sufficient surface cooling in the form of permanent ice cube cooling, one can coagulate subsurface tissue volumes through the surface and the ice cube. The penetration depth of the Nd:YAG laser radiation in tissue is approximately 5 mm while the cooling effect of the ice cube reaches only 1–1.5 mm into the tissue. Therefore, the tissue surface is cooled to less than 10°C and during the irradiation (through the ice cube) it does not exceed a temperature causing tissue damage. In deeper layers where the cooling is not sufficient, one can achieve temperatures of more than 60°C leading to coagulation. For this procedure, only ice cubes without air occlusions should be used and the ice cube must always be kept in good contact with the surface.

Contact/noncontact surgery with bare fiber in air. In a way comparable to the focussing handpiece one can also use a bare fiber in noncontact coagulation. For precise cutting or if only a small coagulation seam is desired, bare fiber in contact can be used. The main
application field is endoscopic surgery, but it can also be used in open surgery. The basic effect of bare fiber contact cutting is a boundary phenomenon. A carbonization layer which absorbs almost all of the Nd:YAG laser radiation is formed on the border between fiber end and tissue (Fig. 1a). Thus, in contrast to the typical Nd:YAG laser tissue coagulation, no efficient photon penetration into the tissue occurs, because most of the photons are absorbed by the carbonization layer. The depth of the coagulation seam depends strongly on the exposure time as it is induced by heat conduction in tissue.

For procedures where predominantly microsurgical contact vaporization is required, a fiber with the smallest available diameter should be used. If a wider coagulation seam is desired, it is preferable to use the 600 μm fiber. At a power setting of more than 30 W, especially when using the 200 or the 400 μm fiber, one needs additional cooling of the fiber with gas or saline to prevent destruction of the fiber end. The 600 μm fiber used with short exposure times (up to 0.3 seconds) of the single chopped pulses requires no cooling for an output of up to 35 W. Major bleeding requires continuous saline rinsing to remove the blood. In this case, one needs 50–60 W and exposure times between 0.3 seconds/pulse in noncontact and continuous wave irradiation. For exposure times longer than 0.5 seconds additional cooling of the fiber end is necessary also for 600 mm fibers.

Bare fiber offers the great advantage of alternating the use of contact mode for cutting or of noncontact mode for coagulation. For instant contact cutting the fiber has to be precarbonized. This can be done before the procedure on sterile cork or wooden spatula, or with some exposures in direct tissue contact. If additional noncontact coagulation is to be performed, for example, for the primary coagulation of larger vessels, one has to remove the fiber from the tissue. With the first chopped pulses in the noncontact method, the carbonization layer on the surface is removed by pyrolysis and most of the radiation is emitted from the fiber end again. So during a procedure it is not necessary to cut the fiber for a noncontact irradiation. The advantage of this combined instrument is, especially in endoscopic surgery, that with one instrument one has a precise cutting tool or an effective coagulation instrument only by changing the kind of application between contact and noncontact (Table I).

It is important to remember that bare fiber in contact surgery is not a mechanical scalpel, so it should not be pressed into the tissue; only the fiber end has to be kept in contact. Nor is the fiber a drill, and the fiber end must be visible at all times for control in the operation field.

### Table I. Parameters for Preparation of Bare Fiber for Instant Cutting Effect and for Pyrolysis of Carbonization at Fiber Tip for Precleaning Prior to Noncontact Coagulation

<table>
<thead>
<tr>
<th>Preparation of fiber</th>
<th>Preblackening for contact cutting</th>
<th>Preblackening for noncontact coagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>In air</td>
<td>Tissue contact or sterile cork</td>
<td>Freshly broken or noncontact</td>
</tr>
<tr>
<td></td>
<td>or wooden spatulas</td>
<td>Minimum 5 mm distance to the underlying tissue</td>
</tr>
<tr>
<td>Power: 30 W</td>
<td>Exposure time: 0.5 s</td>
<td>Power: 30 W</td>
</tr>
<tr>
<td></td>
<td>Single pulses, until blackening</td>
<td>Exposure time: 0.5 s</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Only one pulse, fiber flash up</td>
</tr>
<tr>
<td></td>
<td></td>
<td>shortly (pyrolysis)</td>
</tr>
</tbody>
</table>

**Contact/noncontact surgery with bare fiber in water.** The greatest advantage of laser application, especially in endoscopic surgery, over any kind of high-frequency application is that there are no limitations to working under saline solution. In principle, the application is like that in air, with two major differences. Due to the cooling effect of the surrounding water, noncontact vaporization is impossible and a higher power is required for contact vaporization. Another effect of the cooling is a smaller coagulation seam, so even more precise microsurgical vaporization than that in air is possible. For vaporization an appropriate power setting between 25 and 50 W can be chosen, depending on the fiber diameter and the desired effect. For coagulation either with a small or broad coagulation seam, slightly higher power settings are also necessary as compared to gas media.

On the other hand, one has no risk of surface carbonization. As in air or open surgery, one has the possibility of changing between contact cutting and noncontact coagulation. The cleaning procedure by pyrolysis is possible also in water, but it requires longer exposure times and higher power to start the pyrolysis. In open surgery or endoscopic procedures in gas media, one can imitate the effects of contact and noncontact bare fiber applications in water by extensive saline irrigation.

**Interstitial LITT.** Interstitial LITT, by which a bare fiber or a special LITT applicator is inserted through a needle or catheter into the tissue to be treated, enables the delivery of Nd:YAG laser light directly into the center of the diseased area. Due to photon absorption and heat conduction, both coagulative and hyperthermic effects can be obtained and thus immediate or delayed tissue destruction is caused. With adequate treatment parameters the effects of LITT can be limited to the diseased area without destruction of the surrounding tissue. Access to the tissue to be treated can be provided percutaneously, endoscopically, or during open surgery. In con-
Fig. 2. Different types of applicators for interstitial laser-induced thermotherapy (LITT): bare fiber, ring-mode applicator, and isotropic applicator (scattering dome applicator). With the anisotropic scattering and thermal diffusion in the tissue the coagulation becomes ball- or elliptically shaped, independently from the applicator. The differences in volume are related to the power (J/s, W) that can be delivered until carbonization occurs. Therefore the larger surface of the specially designed fibers allows a larger coagulation volume per single application. But the need for larger punctures and the limited flexibility limit their intraoperative use.

DISCUSSION OF CLINICAL APPLICATIONS

On account of the high penetration depth in tissue and the possibility of transmitting its radiation through optical fibers, the Nd:YAG laser can be applied universally. With either flexible or rigid endoscopes, one can use it for coagulation of hemorrhages and tumors and for recanalization of tumor stenoses. With either a handpiece or a bare fiber and corresponding high-energy densities the resection of tumors in parenchymatous organs with simultaneous hemostasis is possible. Especially with a bare fiber, which is cheap and easy to handle, it is possible to work alternating in noncontact for coagulation or in contact for cutting, even in endoscopic procedures. This results in effective laser therapy and short operation times [12].

The use of sapphire tips in contact laser surgery [13–15] is not recommended. Because of the reflection from the connecting surfaces between fiber and sapphire as well as high absorption within the sapphire tip
itself, an efficient cooling of the surfaces is required. Therefore, a relatively large diameter of the fiber connector is subsequently needed. Furthermore, there is a high risk of gas embolism due to the cooling gas, especially in endoscopic or interstitial application [15]. Because of the high absorption, the sapphire tip works more as a heater probe than as a cutting tool. At the beginning sculptured fibers permit a better cutting efficiency than bare fiber, but they change their quality during the procedure and switching between cutting in contact and coagulation in noncontact, such as with simple bare fiber, is not possible [16].

The range of applications of superficial laser therapy includes diseases as benign and malignant as vascular tumors, viral-induced tumors, anal carcinoma, basalioma as well as the skin metastases of Kaposi sarcoma, melanoma, and breast carcinoma [5,17]. Mostly the direct transcutaneous coagulation in the noncontact method was performed, either with a (de-)focussing handpiece or with the freshly broken, air-cooled bare fiber. For larger, exophytic growing tumors we used a tangential circumferential irradiation on the base of the tumor with a defocussed beam. The irradiation is stopped when the base is blanched. Usually rinsing is employed to avoid carbonization and to increase the coagulation depth. Smaller tumors with a diameter of up to 2 mm can be coagulated with the defocussed beam at a rectangular direction. In cases where the tumor is localized subcutaneously, an interstitial LITT application is used in addition or alone. The laser therapy can be performed with local anesthesia if the lesion is limited in size and number. Only in cases of larger tumors or multiple localizations is general anesthesia recommended.

For endoscopic surgery, the fiber-transmitted Nd:YAG laser is of major importance as an energy source. The indications for palliative recanalization treatment range from the laryngeal, bronchial, and esophageal tumors to colorectal carcinomas. The palliative ablation of tumor stenosis is mostly performed using a flexible bare fiber alternating for noncontact coagulation and cutting by contact vaporization. The resected tumor pieces can be removed with a forceps. On account of prior coagulation of the tumor, bleeding can be avoided and the recanalization can proceed rather continuously. Vaporization of tumor masses with a polished noncontact fiber is also possible, but due to a greater amount of plume production, sufficient plume suction and frequent cleaning of the optics are necessary. Also, the pronounced coagulation depth of noncontact vaporization makes this method less favorable in most cases. With the alternating method, healing is faster and the need for a second intervention for the removal of detritus is less frequent. The risk of creating a wrong pathway can be minimized by using guidewires or rendezvous endoscopy (i.e., if a gastrostomy was already necessary) with transillumination guidance or X-ray control. A subsequent afterloading therapy (brachytherapy) or stenting helps to prevent restenosis and increases the intervals between treatments. Also, occluded stents made from woven metal and without plastic coating can be recanalized in the contact method. Bronchoscopic therapy requires general anesthesia; shorter esophageal or colorectal stenosis can be recanalized under sedation.

For treatment of complications after conventional surgical therapy of carcinoma such as esophageal tracheal fistulas, we also use bare fiber for endoscopic fistula closure. During combined endoscopy of the trachea and esophagus with flexible instruments, the fiber is introduced into the fistula and under endoscopic control of both lumina, coagulation of the mucosa of the fistula is performed, followed by shrinking and occlusion [18]. In laparoscopy the multifunctional bare fiber is of increasing importance, but tumor surgery of malignancies requires an open approach in almost any case today. High-frequency electrocautery may be also used for cutting and coagulation but its penetration depth in tissue is limited [21]. In comparison to electrocautery, bare fiber contact surgery is a safer and more precise device for both cutting and coagulation.

The alternating bare fiber technique can be used in open surgery as well as in endoscopic surgery for preparation, coagulation, and removal/excision. With the use of short pulses, even adhesions close to the bowel can be removed and the preparation and mobilization of tumor tissue is eased. Tumors of the tongue were also removed with the bare fiber in contact. In any case, a good hemostasis could be achieved. For tumor resections from parenchymatous organs (e.g., resection of tumors of liver, lung, kidney, pancreas, and spleen), use of a focussing handpiece for cutting purposes is favorable, compared to the Cavitron UltraSound Aspirator (CUSA). As with the CUSA, the parenchyma of these parenchymatous organs is cut with the focussed laser beam while the larger vessels resist substantially longer (due to the intravascular flow and its cooling of the vessel) and can be ligated by clamping [19,20]. Unlike with the CUSA, the laser-sealed surfaces do not require fibrin glue for hemostasis and there is no risk of bleeding beneath the glue layer. While the CUSA is used for liver surgery and the removal of neurosurgical tumors, use of the Nd:YAG-laser with the focussing handpiece for cutting purposes can be extended to all parenchymatous organs, such as the kidney and pancreas, and is especially advantageous in lung surgery. With the sealing of the lung tissue and bronchioli a primary gas-sealed
surface can be achieved during the cut. In liver surgery the simultaneous sealing of the cut by the coagulation seam prevents blood loss and decreases the need for blood transfusions as well as the risk of complications such as biliary fistulas or secondary bleeding. In a comparison between a matched-pair analysis of patients with partial liver resections, the number of blood transfusions could be reduced by 55% in the laser group. Postoperatively these patients showed a significantly faster recovery from assisted ventilation and the length of stay in the intensive care unit was 1 day on average. The overall hospitalization time and the total costs per operation were also reduced [6,12,-22]. Thus, it is possible to carry out resection of tumors in parenchymatous organs and bloody tumors, even under difficult conditions. Exirpation of infiltrating malignant tumors in the thorax with protection of important structures can also be performed. Due to a bloodless and hermetically sealed resection field obtained during laser resection of intrapulmonary metastases, the danger of pneumothorax and hydrothorax can be reduced [12].

The advantages of the Nd:YAG laser application for tumor removal can be summarized as follows:

1. Hemostasis
2. High precision
3. Reduced instrumentation at the treatment site
4. Minimalization of the risk of infection
5. Minimal trauma of the surrounding tissue

Although radical tumor resection is sometimes impossible because of either tumor localization or gravity of illness, the patient may benefit from palliative treatment. Current treatment modalities such as chemotherapy or X-ray radiation have grave systemic side effects. Especially in the treatment of liver metastases, interstitial LIC can be performed with minimal discomfort for the patient. In comparison with other interstitial techniques, such as cryotherapy with its rigid application probes, or alcohol injection with its unpredictable alcohol distribution in tissue, this method is easier in application and the area of tissue destruction can be monitored online and precisely limited. Thus the entire tumor can be denaturated without destruction of the surrounding tissue. The advantage of bare fiber in comparison to specific ITT applicators is that its small diameter enables one to use ordinary puncture needles for approach and fiber introduction. Thus, multiple application and precise shaping of coagulation zone are possible.

One of the fields in our therapeutic program is interstitial LITT of benign vascular tumors. Since 1983 we have performed over 3,000 interstitial treatments of vascular disorders and since 1992, CCDS has been used for online control of this procedure. Since then, deep-seated primary and secondary liver tumors (in 3 patients) and subcutaneous metastases of breast carcinoma (in 10 patients) were also treated in this way [11,17]. After the sonographically guided fiber is positioned and irradiation started, the changes in the CCDS signal provide information about the intensity of tissue reaction and the course of coagulation. The coagulated volume becomes visible in the B-scan several minutes after laser exposition. General or local anesthesia was used in individual cases (Fig. 3).

Since 1992 we have also treated 26 patients with liver metastases of colorectal carcinoma with the MRI-controlled percutaneous interstitial LITT. For this purpose, an isotropic ITT applicator with a magnetite marker [23] was used with the power setting of 5 W at a minimum of every 10 minutes. After computed tomography (CT)-guided positioning of the applicator, the patients were moved to the MRI room. For process control, Turbo-Flash 2D sequences were used which showed temperature-dependent signal changes. The MRI control with contrast-enhanced sequences just after the procedure showed a loss of perfusion in the treated area. In all cases the procedure was performed under local anesthesia. Three months after the therapy signs of necrosis and/or fibrosis were visible in this area. At the present time we still note a decrease in tumor marker values in most patients after LITT, for up to 1.5 years after the treatment (Fig. 4).

For exact steering of the coagulation process, process control is needed. MRI enables the monitoring of temperature changes and its three-dimensional resolution is by far the best among all monitoring methods for interstitial laser therapy. Therefore, it is absolutely required in the stereotactic treatment of brain tumors. Disadvantages of this technique, such as the artefacts caused by movements of the patient, limited direct access to the patient, as well as the high costs of this method, reduce the use of MRI for online monitoring of interstitial LITT in other body regions. Furthermore, it cannot be used, either in open or in endoscopic surgery.

In contrast, CCDS is a reliable and simple technique which enables control and steering of tissue changes during interstitial laser therapy without great strain for the patient. This simple technique provides complete information, such as determination of the precise puncture route, control of fiber position, visualization of tissue changes during the procedure, as well as depiction of the reduction of tumor vascularization and coagulated volume. In combination with the techniques of endoscopic laser application, one has a wide range of techniques for minimal invasive surgery
Fig. 3. Color-coded duplex sonography imaging during interstitial laser-induced thermotherapy of subcutaneous metastasis of breast cancer.

Fig. 4. Magnetic resonance imaging during interstitial laser-induced thermotherapy of liver metastasis of colorectal carcinoma. The fiber is marked with a magnetite coating. The loss of signal intensity in the metastasis indicates a temperature sufficient for coagulation.
which can prevent a number of open surgical procedures, or can substantially benefit palliation.

REFERENCES