LASERS IN DIGESTIVE ENDOSCOPY

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(Paper JBO-111R received July 10, 1996; revised manuscript received Sep. 4, 1996; accepted for publication Sep. 9, 1996.)

ABSTRACT
Lasers were introduced in digestive endoscopy to stop active gastroduodenal hemorrhages. Their use spread progressively to the treatment of chronic hemorrhages from vascular malformations and sessile tumors. Lasers face competition from other endoscopic techniques such as electrocoagulation, injection techniques, dilation, stents, and brachytherapy. Many series have reported the efficacy of lasers in digestive endoscopy used for their thermal or photochemical effects. However, they were gradually abandoned for the treatment of hemorrhages because of competition from nonlaser techniques. Lasers are still used for ablation of sessile tumors, but their true impact is difficult to evaluate. Modern methods of technology assessment did not allow gastroenterologists to clearly define the place of lasers among surgery, radio-chemotherapy, and other endoscopic techniques, and data on the daily use of lasers are not available. Therefore, the conclusion can only be subjective. The best current application of thermal lasers appears to be in the treatment of rectosigmoid villous adenomas in elderly patients. Small superficial rectal cancers may also become a good subject due to the impact of endoscopic ultrasonography. Early lesions with multifocal or diffuse disease such as early esophageal cancers could be the most promising subject of application for photodynamic therapy in the future. © 1997 Society of Photo-Optical Instrumentation Engineers.

Keywords
digestive endoscopy; thermal lasers, photodynamic therapy; gastrointestinal endoscopy.

1 INTRODUCTION
After lasers were first introduced in 1975 in digestive endoscopy to stop active gastroduodenal hemorrhages, their use spread progressively to the treatment of chronic hemorrhages from vascular malformations and sessile tumors. Twenty years later, it is interesting to observe their current applications in digestive endoscopy and the extent of their daily use all over the world.

2 TECHNIQUES USED TO TREAT BLEEDING LESIONS OR SESSILE TUMORS
Lasers can be used in digestive endoscopy for their thermal or photochemical effects. While they face competition from other endoscopic techniques, there have been continuous technical improvements since 1975.

2.1 THERMAL LASERS

2.1.1 Optical Step: Absorption, Scattering, and Primary Heat Source
In a thermal laser, a heat source is created by converting the laser light into heat. The absorption of the laser light in tissues is a function of the coupling of its wavelength and the chromophore (Figure 1).

Most organic molecules strongly absorb ultraviolet light. Thus the depth of penetration of UV is extremely short (a few microns). In the case of visible light (blue, green, yellow), the absorption occurs mainly at the level of hemoglobin and melanin. Red and near infrared (0.6 to 1.2 \( \mu m \)) are poorly absorbed and penetrate deeply into tissues. However, their penetration is limited by optic scattering. In the middle and far infrared, water is the main chromophore. Absorption of the light results in a heat source that can be called the primary heat source.

2.1.2 Thermal Step: Heat Transfer and Secondary Heat Source
Heat transfer in tissues tends to increase the volume of the primary heat source. This transfer is ensured by thermal conduction because the effect of blood flow (transfer by convection) is negligible. The difference between the “primary” and the “secondary” heat sources depends mainly on the thermal characteristics of the tissue and the duration of the laser shot.

2.1.3 Biological Step: Tissue Denaturation
Heat can cause three types of responses in tissue depending on the quantity and the duration of heat. These responses include hyperthermia, coagulation, and volatilization. Table 1 gives the type of tissue damage as a function of temperature and time.

Hyperthermia is defined by a thermal increase of a few degrees during a long period (several tens of minutes). There is no immediate gross or histologic effect, and tissue necrosis is delayed. This absence
of immediate visible effect makes dosimetry very difficult; hyperthermia requires a long treatment time (several minutes to half an hour), which may not be well tolerated by the patient. Thus, hyperthermia is not currently used in digestive endoscopy.

Coagulation necrosis is obtained by a thermal increase of between 45 and 99°C during a period on the order of second. It induces desiccation of the tissue and denaturation of the proteins, especially collagen. The visual appearance of the tissue surface changes during the treatment. The surface becomes white, and the coagulated area sloughs off in the next few days. This is a very safe method for endoscopic treatment of sessile tumors, with a low risk of hemorrhage. However, several treatments may be required to eliminate large tumors totally.

Volatilization occurs when tissue is rapidly (0.1 s) heated to over 100 °C. The water inside the tissue boils, the proteins are denatured, and smoke is created. If the vaporization area is narrow, an incision effect is obtained. If the vaporization area is large, immediate ablation of a tumor can be obtained. Due to heat transmission, coagulation necrosis occurs at the edges of the vaporized area. The hemostatic effect depends on the degree of coagulation.

2.1.5 Practical Use of Thermal Lasers in Digestive Endoscopy

a. Different types of fibers. To obtain a well-demarcated light spot on tissue, the tip of the laser optic fiber has to be polished or cleaved. This tip is very fragile. If any contamination by blood or charred black particles occurs, the light is scattered from the tip and reproducible effects cannot be obtained. The best protection of the fiber tip is obtained by placing the fiber in a Teflon catheter with a metal nozzle at the tip. The protection of the sheathed fiber is reinforced by a permanent gas flow, generally nitrogen. During endoscopy, care must be taken to avoid overdistending the bowel with the gas, which is painful and reduces the thickness of the bowel wall, increasing the risk of perforation. In the rectum and colon, a cannula is introduced alongside the endoscope during treatment to evacuate the gas, and more proximal suctioning is done with the endoscope at the end of the treatment. The laser optic fibers can be maintained by nurses using a cleaving set.

A naked fiber also can be used. The fiber is inserted into the biopsy channel of the endoscope without the protection of a catheter or gas flow. Care must be taken to keep the tip clean. Even so, contamination occurs rapidly and the fiber tip has to be cleaved or polished more frequently than in the care of a sheathed fiber.
A naked fiber also can be used in direct contact with tissue. During treatment, the tip of the fiber burns like the wick of a candle and the fiber is replaced when it becomes too short. This technique has the advantage of avoiding the maintenance required by the fiber tip. However, the shape of the fiber tip is variable, and light scattering and absorption coefficients are unpredictable. The delayed tissue effects are difficult to predict from the endoscopic appearance of the tissue during treatment, and use of a naked fiber requires much expertise on the part of the endoscopist.

Contact sapphires were introduced to avoid the deterioration of the fiber tip in contact with the tissue. Sapphire is a much stronger material than the silica of the fiber. However, since sapphires can transmit only at low power (10 to 15 W) and it works very slowly, most endoscopists no longer use them.

b. Choice of the emission parameters of argon, 0.532 and 1.06 Nd:YAG lasers. Green lasers (argon and 0.532 Nd:YAG) and 1.06 Nd:YAG laser are mostly used with a continuous wave (CW) emission. The exposure time is preselected or monitored by the operator using a foot switch. These three lasers can induce coagulation and volatilization effects. Green lasers are rarely used for coagulation of tumors because their effect is too superficial. Regarding volatilization, the main difference between the two green and the 1.06 μm lasers is that the amount of coagulation necrosis is negligible with the green; with the 1.06 μm Nd:YAG laser, it is significant but difficult to predict from the macroscopic aspect during treatment. Therefore, the green lasers may be used for vaporization of superficial tumors until a flat surface is obtained. The 1.06 μm Nd:YAG laser is mainly used for coagulation (blanching) of large tumors. An interval of 2 to 3 days between two treatments allows the coagulated parts of the tumor to slough off. New Nd:YAG lasers that provide infrared or green options by pushing a button, without removing the fiber from the endoscope, are particularly well adapted to endoscopy. Table 2 lists the parameters commonly used at our institute for coagulation and volatilization with a sheathed fiber and gas flow.1

c. Choice of the endoscope. Video-endoscopes can be used with the 1.06 μm Nd:YAG laser if the manufacturer places an infrared filter between the lens and the video chip. All video-endoscopes now have this filter built in. However, with video-endoscopes using a color recombination system, the red light used as the aiming beam for the Nd:YAG laser is generally too intense and saturates the black and white video chip. With experience, treatment can be done without the red aiming beam.

The argon or 0.532 Nd:YAG lasers emit in the visible spectrum. A permanent filter would color the image in yellow and the design of a temporary filter at the tip of the video-endoscope requires extensive work by the endoscope manufacturers. Therefore, argon or 0.532 Nd:YAG lasers cannot be used with video-endoscopes at present.

d. Preparation of patient. The main disadvantage of laser ablation is the lack of material available for a total histologic study of the tumor. Therefore, an estimate of the lesion has to be done before treatment. The pretreatment evaluation is generally done by taking multiple biopsies from the tumor. For large tumors, a partial snare electroresection is performed when feasible. Snare resection provides larger specimens to the pathologist than biopsies, debulks the tumor, and decreases the laser treatment time. Invasion in the different layers of the digestive wall can be detected by endoscopic ultrasonography. However, endoscopic ultrasonography cannot determine whether a tumor is limited to the mucosa or is invading the submucosa. In both cases, the second hypoechoic layer of the digestive wall is broader, with an intact third hypoechoic layer. The infiltration of the muscularis propria is detected by the disruption of the third hyperechoic layer. Even with these limitations, endoscopic ultrasonography is helpful in preventing inappropriate treatment of tumors.2

With elderly patients, treatment should be adapted to provide minimal disruption in their life. At the Laser Center, most patients are prepared locally with a small enema just before the procedure. For 15% of the patients, good rectosigmoid preparation cannot be obtained by this method, and the usual preparation with polyethylene glycol is used instead. Laser treatment in itself is not painful and there is no special need for sedation, especially if the effects of the Nd:YAG laser are limited to pure coagulation.

e. Procedure. For bulky tumors, treatment consists of using the 1.06 Nd:YAG to coagulate as much of the tumor surface as can be reached by the laser beam. Smaller tumors are vaporized with the 0.532 Nd:YAG until a flat surface is obtained. During treatment, the parameters chosen on the laser (power and exposure time) are kept constant. The

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<th>Table 2 Effects induced by argon, 0.532 Nd:YAG, and 1.06 Nd:YAG lasers, as a function of exposure parameters.</th>
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distance between fiber and the tissue is continuously adjusted to maintain constant effect when the tumor moves or when the light absorption by the tumor changes. The laser technique is very safe and patients do not require special care after treatment. Thus, laser treatment is performed on ambulatory patients and the patients are in the clinic for a minimum period.

During initial treatment, they are treated once or twice a week until disappearance of the symptoms or complete intaluminal destruction of the tumor. During follow up, the patients are reendoscoped every month and eventually retreated. If the tumor seems to be completely destroyed, new biopsies are performed during follow-up examinations.

f. Complications and accidents. Complications can be defined as problems related to the treated zone (Table 3). The three main complications are hemorrhage, perforation, and stenosis. Hemorrhage and perforation are complications well known since the beginning of therapeutic endoscopy with diathermic resection. Hemorrhage and perforation can occur during treatment or in the next few days after treatment. Delayed stenosis is a new type of complication that is mainly reported after several Nd:YAG laser treatments and occurs several weeks or months after treatment. Its cause is not well established, but the endoscopic aspect is similar to that of ischemic colitis. Therefore, delayed stenosis is probably related to overheating of the submucosa and muscularis layer with a shrinkage of the small feeding vessels. Stenosis can be treated by endoscopic dilatation if it is diagnosed early after treatment.

Accidents can be defined as problems unrelated to the treated zone. They can occur in three main circumstances.

Eye hazards. The fiber bundle of a conventional endoscope transmits the green or infrared light of the lasers. Thus, the light reflected from the tissue has to be eliminated by a filter placed on the ocular end of the endoscope. Some laser safety officers are concerned about eye hazards for everyone in the treatment room if the fiber is withdrawn from the endoscope or broken between the laser and the endoscope. They recommend that laser safety goggles be worn by all the occupants of the laser treatment room. However, these goggles are uncomfortable. In our opinion, goggles are not needed if (1) the fiber is protected by a catheter, (2) a nurse stays close to the laser during the procedure and can put it in a stand-by position if the gastroenterologist withdraws the fiber from the endoscope, and (3) the appropriate filter is placed on the ocular end of the endoscope.

Plume hazards. Three potential hazards can be encountered with laser-generated plume during tissue volatilization: cancer graft from viable cells, a toxic respiratory effect from carbonized material, and transmission of viruses. These dangers should not be overestimated. Cancer graft and infectious transmission have not been clinically reported, and the toxicity of the plume is comparable to the toxicity of cigarette smoke. Nevertheless, the use of a special laser smoke evacuator with built-in filters is mandatory in a laser treatment room. However, smoke evacuators are not well adapted to endoscopic use. This is another argument for preferring coagulation (which does not generate smoke) to volatilization.

Explosion in the colon and rectum. Explosions during treatment in the colon and rectum with electric currents have been reported. High temperature may also occur with laser treatment and poses a risk. The risk is maximum when a naked fiber is used for tissue vaporization without neutral gas, at high power and in contact with the tissue. Accidents have been reported in these circumstances. The use of sheathed fibers with nitrogen gas flow is the best way to prevent this type of accident.

Prevention of complication and accidents. Endoscopic laser treatment is a rather new technique and only a small number of young gastroenterologists have been trained during their residency program. The best way of preventing complications and accidents is adequate training of the gastroenterologists through learning with an experienced person or by attending workshops. However, during treatment, the gastroenterologist is sometimes too busy to attend to all these safety precautions. Therefore, he should be assisted by a nurse trained in laser safety.

2.2 NONTHERMAL LASERS: PHOTODYNAMIC THERAPY (PDT)

Photodynamic therapy involves the interaction of a photosensitizer and light. The photosensitizer is

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<th>Complications</th>
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<td>Acute hemorrhage and perforation</td>
<td>Volatilization with green and 1.06 μm lasers</td>
<td>No 1.06 μm laser for volatilization. Large spot and long exposure time with green laser (see Table 2)</td>
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<td>Delayed stenosis</td>
<td>Volatilization or coagulation of circumferential tumor with a 1.06 μm laser</td>
<td>Limitation of the treatment to one third of the circumference during a session</td>
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chosen for two properties: selective retention by malignant tissue and its capability to generate singlet oxygen when excited by light. Singlet oxygen is very toxic and will kill all cells in the surrounding tissue. The most commonly used photosensitizer is a derivative of hematoporphyrin named Photofrin®. It is excited at 0.630 μm because it has an absorption peak at this wavelength and because red light penetrates deeply into the tissues. The 0.630 μm light is generally obtained from a dye laser pumped by argon or 0.532 nm Nd:YAG lasers.

Several hours after intravenous injection (24 to 78 h) of the photosensitizer, the patient is endoscoped and the tumor site is illuminated by red light. Distant fibers or interstitial fibers can be used. Irradiance has to be kept at a relatively low level in order to avoid thermal effects. Thus, treatment time is rather long and takes several tens of minutes. No visible effect is observed at the time of treatment. Several days later, a necrosis of the illuminated area can be seen, which is limited to malignant tissue if all the parameters (quantity of dye injected, delay between injection and treatment, and irradiance and exposure time) were properly chosen. However, the following problems remain to be solved.

2.2.1 Skin Sensitivity
Unfortunately, Photofrin is also retained by the skin. Therefore, patients have to avoid sunlight or even strong artificial light for several weeks after injection (4 to 6 weeks). Accidents of severe sunburn have been reported in patients who were exposed to the sun too early after treatment. New photosensitizers decrease the skin photosensitivity without completely eliminating it, but they are not approved for clinical use.

2.2.2 Dosimetry
All the parameters (quantity of dye injected, delay between injection and treatment, and irradiance and exposure time) have to be properly chosen. If the quantity of photosensitizer is too large or the time between injection and treatment too short, the concentration of dye in normal surrounding tissue will be too high, resulting in nonselective effects. On the other hand, a too low concentration of photosensitizer, a too long delay between injection and treatment, or a too low fluence will induce only a partial response and consequent treatment failure. The problem is that all these parameters are chosen rather empirically without enough scientific data.

2.3 COMPETING NONLASER TECHNIQUES

2.3.1 Electrocoagulation
High frequency electric currents can be applied through a catheter that has a monopolar or a bipolar electrode.

a. Monopolar electrode. The active electrode in this technique is a single electrical pole transmitting the electrical current into the tissue held in direct electrical contact. The current completes its electrical circuit by arriving at the distal neutral electrode. If the distal plate is large enough with a good electrical contact with the patient’s body, the current density is much higher at the monopolar active electrode. Both coagulation and cutting effects can be obtained with a monopolar electrode as a function of the voltage used. However, the heat diffusion and the depth of the effect are difficult to predict. There are several ways of using monopolar electric currents for sessile tumors: diathermic snare resection, hot biopsy forceps, and fulguration.

In snare resection, a wire loop acts as a monopolar electrode. This technique is extensively used for the treatment of pedunculated polyps. Snare resection can also be used for piecemeal polypectomy. It allows resection of fragments from large exophytic sessile tumors. Larger specimens than can be obtained with biopsy forceps will be available for histology. This also decreases the tumor volume and facilitates further treatment.

The hot biopsy forceps is used for small sessile polyps. It is insulated and conducts electric currents. The polyp is grasped between the jaw of the forceps and lifted away from the intestinal wall. Upon application of current, coagulation of the base of the polyps occurs and a white coagulated area can be seen. The specimen obtained from the forceps is suitable for histologic study. During fulguration, the probe is not in contact but close to tissue, and sparks are generated. Surface vaporization occurs with coagulation necrosis in the depth. This depth of necrosis is difficult to control. Therefore, this technique has been mainly used in the rectum, below the peritoneal reflection, where perforation of the digestive wall is without serious consequences.

b. Bipolar Electrode: BICAP® Probes. In this treatment, the distal neutral electrode is effectively brought up to an adjacent point of contact with the otherwise active monopolar electrode. Since the bipolar electrical fields that penetrate into the tissue are much more closely confined, the depth of tissue heating and resultant coagulation is much less than with the monopolar configuration.

The BICAP endoscopic coagulator consists of three pairs of bipolar electrodes spaced around and over the end of a cylindrical ceramic probe. Two types of BICAP probes are available: the “small” BICAP hemostatic probes which are 2 and 3.2 mm in diameter, and the “large” BICAP tumor probes, which are 6, 9, 12 and 15 mm in diameter. The tumor probes are rigid. Therefore, they are very helpful for palliation of circumferential esophageal cancers, but they are not well adapted to angulated lesions or obstructing cancers above the lower third of the rectum.

2.3.2 Nonelectrocoagulation Techniques

a. Heat Probe®. The tip of the heat probe consists of a metal tip covered by Teflon to avoid sticking, which
is heated by a computer-controlled coil to a temperature of 250°C. The heat probe is applied to a bleeding vessel or angioma and generates a coagulation necrosis.

b. Injection technique. To stop a hemorrhage, tiny catheters terminating in a small injection needle can be used through the endoscope to inject various drugs. Vasocclusion, desiccation, and sclerosis can be achieved by injecting, respectively, epinephrine, absolute ethanol, and various sclerosing agents.\(^7\) This effect can also be used for destruction of tumors.

c. Mechanical techniques. A stenosis can be mechanically dilated via rigid probes of increasing diameters such as “bougies” or “olives.” These are pushed over a guidewire that is previously inserted through the stenosis. This required axial force, and perforations were not uncommon. The balloon dilatation technique was therefore developed, which is safer because it induces only lateral forces. The benefit from dilatation is often only temporary and a prosthesis can be implanted after dilatation to maintain a patent lumen. The first types of prostheses were of nonexpandable plastic. They were not always well tolerated, and sometimes perforation of the digestive wall and migration of the prosthesis occurred. To overcome this disadvantage, self-expanding metal stents were developed.

d. Brachytherapy. Brachytherapy is a local radiation therapy with cesium 137 or iridium 192. The brachytherapy tube is first inserted and its position is checked by radiography. Then the radioisotope carrier is introduced via an afterloading unit, avoiding exposure of the staff. With this technique, deep treatment of the digestive wall can be obtained without irradiation of the surrounding organs.

3. CLINICAL RESULTS

3.1 HEMOSTASIS

3.1.1 Active Hemorrhages from Gastroduodenal Ulcers

Treatment of active hemorrhages from gastroduodenal ulcers were the first application of endoscopic lasers. The hemostatic effect is related to a laser-induced coagulation necrosis with two mechanisms: immediate shrinkage of the capillaries, which stops the blood flow, followed by the formation of a clot in the vessel lumen, which makes the hemostasis durable. To be efficient, the diameter of the coagulated zone has to be at least three times larger than the diameter of the bleeding vessel. This limits the hemostatic possibilities to arteries with a diameter less than 1 mm.

The first clinical results were published in 1975 by two German pioneers, P. Frühmorgen (argon laser),\(^8\) and P. Kiefhaber (Nd:YAG laser).\(^9\) The Nd:YAG laser was potentially more efficient than the argon laser due to its deeper penetration into the tissues, but it was difficult to demonstrate its superiority in clinical studies. For both lasers, the results were rather good, with a 70 to 94% success rate and a low complication rate (perforation and aggravation of the bleeding in less than 1% and 9 to 15% of the cases).\(^10\)

However, it rapidly became apparent that the main problem of this new treatment was not its ability to stop a hemorrhage, but the quantification of the benefit for the patient in terms of recurrence of the bleeding and mortality. The results of randomized controlled studies between laser and conventional treatment were in disagreement: some studies concluded that there was no benefit,\(^11,12\) others that only particular categories of patients benefited.\(^13,14\)

Finally, the use of endoscopic laser treatment for bleeding gastroduodenal ulcers was gradually abandoned for two reasons: the development of the antiulcerous drugs that rendered hemorrhagic complications less frequency, and the availability of endoscopic devices such as the BICAP, the Heat Probe, and injection techniques. These devices are less expensive, easier to use, and easier to bring to the patient’s bed in an intensive care unit.

3.1.2 Vascular Malformations

Vascular malformations (angiomas) are another cause of digestive hemorrhage. They can be responsible for severe chronic anemia and sometimes active hemorrhages. Both endoscopic argon\(^15,16\) and Nd:YAG\(^17\) lasers were effective in treating these lesions, but their use was progressively abandoned for the same reasons as for gastroduodenal ulcers. New drugs\(^18\) decreased the frequency of hemorrhagic accidents, and the BICAP and Heater Probe have replaced lasers.

3.2 ENDOSCOPIC TREATMENT OF SESSILE TUMORS

In the early 1980s, it appeared that thermal lasers had a great potential in the endoscopic treatment of sessile tumors,\(^19\) such as the palliative treatment of advanced esophageal and rectosigmoid cancers, and the curative treatment of benign rectosigmoid villous adenomas.

3.2.1 Palliation of Advanced Cancers

Palliation of the symptoms of advanced cancers aims at maintaining the highest quality of life in nonsurgical patients with limited life expectancy. Surgery is still considered the method of choice for palliation of advanced esophageal or rectosigmoid cancers. However, surgery is sometimes not feasible when the cancer is detected at a too advanced stage or when the patient is nonsurgical because of an associated disease. Under these circumstances, an endoscopic treatment can be proposed for palliation of the dysphagia from esophageal cancers, and palliation of the hemorrhagic and mucus discharges from the rectosigmoid cancers.
a. Thermal laser for palliation of advanced cancers. Numerous studies have been published on the palliative treatment of esophageal and rectosigmoid cancers by endoscopic thermal lasers. The treatment in general consist of an initial phase with repeated sessions every 3 to 4 days to obtain a maximal functional improvement. Then, a new treatment is performed every 4 to 6 weeks to maintain the functional result. In two series of 79 patients with esophageal cancer and 95 patients with rectosigmoid cancers, we reported in 1987 a 78 and 85% improvement rate respectively over a 5- and 10.2-month period, with a 5 and 2.5% complication rate, respectively. The results in esophageal cancers were slightly better than those obtained with the conventional dilation via rigid probes associated with non-expandable plastic prostheses. For the rectosigmoid cancers, it was a big improvement on the previous situation where no palliative technique was available. Comparable results have been presented by other authors with lasers alone or in association with radiation or chemotherapy.

In 1987, the BICAP tumor probe became available at our institute. Unlike in the case of gastrointestinal bleedings, it did not replace the lasers. The two techniques were proven to be complementary and the number of our patients referred for an advanced esophageal cancer reached its maximum in 1988 (Figure 2). In the early 1990s, advances in surgery, postoperative care, and radiochemotherapy made the number of nonsurgical patients much smaller than in the 1980s. In addition, the reduction of the use of thermal lasers came from the combined use of balloon dilation and expanding metal stents, which do not require repeated sessions to maintain functional improvement. As a consequence, the number of patients referred for palliation of esophageal cancer is now very small. In 1995 we had only 6 new patients, compared with 44 patients in 1988.

The number of patients referred to us for rectosigmoid cancers has also decreased to a maximum of 43 in 1986 to only 6 in 1995. This is not due to the advances in nonlaser endoscopic techniques but to advances in chemotherapy which have broadened the indications for resective surgery in patients with advanced lesions or preoperative metastasis.

b. Photodynamic therapy for palliation of advanced cancers. Several pilot studies have been published on the palliative treatment of esophageal, gastric, and colorectal cancers by PDT. They show a certain efficacy, without being exempt from complications such as skin photosensitivity, stenosis, and perforations. Comparative trials between Nd:YAG lasers and photodynamic therapy are underway, and some results are already available. For example, in a series of 42 patients with esophageal cancer, the duration of functional improvement after initial treatment was longer after PDT than after Nd:YAG laser treatment. However, authors only compare the effects of a single treatment and it is well known that Nd:YAG therapy requires retreatment every 4 to 6 weeks. In a multicenter randomized trial with 218 patients, PDT with Photofrin had an overall efficacy equal to Nd:YAG laser thermal ablation. Temporary skin photosensitivity was a limitation for PDT, which was associated with fewer acute perforations than Nd:YAG laser therapy.

3.2.2 Curative Treatment of Benign Tumors

Rectosigmoid villous adenomas are very distinct tumors. Patients suffer from mucus secretions that can lead to dehydration and malnutrition. The lesions are benign initially but can become malignant after a variable evolution period. Their implantation on the rectal wall can be very large, making transanal surgery difficult, especially in elderly patients. Figure 3 presents our results obtained with lasers over a period of 15 years.

We have been able to cure a large number of patients referred to us for a rectosigmoid villous adenoma. Total disappearance of the tumor was obtained in 93% of the 479 patients treated from 1980 to 1995. The main reason for the unsuccessful
cases was the detection of an invasive carcinoma in 6% of the patients on biopsy specimens obtained during laser treatment. The complication rate was less than 2%, allowing an ambulatory treatment mode. There are recurrences after all conservative treatment modalities. Our patients were followed up regularly and a recurrence was detected in 19% of them, which could be easily retreated in almost every case. Comparable results have been presented by other authors with endoscopic lasers. 37-40

Endoscopic laser treatment for rectosigmoid villous adenoma is an effective technique and progressively appeared to be an alternative to transanal surgery which was the established technique when we treated our first patient in 1980. It would have been very interesting to run comparative studies in order to determine when each technique was indicated. Unfortunately, it was not possible to design a protocol for such studies. At Lille, an agreement has been reached between endoscopists and surgeons that the ambulatory but repeated endoscopic laser treatment is safer for an elderly and fragile patient whereas a younger and healthier patient may prefer to be surgically treated in a single procedure. The inaccessibility of the villous adenoma to transanal surgery favors laser treatment because of the higher rate of complications for transacral or transabdominal surgery.

We started to treat patient with villous adenoma in 1980. The number of patients referred to us annually increased regularly, up to 59 in 1986. Since 1986, this number has remained at a rather high level, fluctuating between 25 and 40, with 32 annual patients in 1995 (Figure 3).

3.2.3 Curative Treatment of Small Cancers

Until recently, the definition of “small” cancers was purely endoscopic: “a tumor less than 2 cm in length, with a circumferential extent of the base that is less than one third of the circumference, without signs of infiltration, and purely exophytic configuration without ulceration.”21 This type of lesion generally, but not always, does not invade the muscular layer.

Now endoscopic ultrasonography is able to detect the T1N0 tumor.41,42 The T1N0 tumors are cancers in which the invasion is limited to the mucosa and submucosa, without invasion of the adjacent lymph nodes and, as a consequence, a very low risk of dissemination. Endoscopic ultrasonography provides a much more reliable staging of the tumor than an endoscopic description.

Small cancers of the rectum have been treated for a long time in a conservative manner, especially by radiation therapy.43 A complete local destruction was obtained with the Nd:YAG laser in all 19 patients we have treated. Two presented local recurrence that could be successfully retreated by laser, and neither is in danger of death from the cancer or from metastases. Endoscopic Nd:YAG laser treatment has several advantages over radiation therapy: it does not need anal dilation and it does not expose the patients to complications such as proctitis.

However, we have treated only a small number of patients over 15 years. We have limited our treatment to strictly inoperable patients because we did not have enough confidence in endoscopic description. Endoscopic ultrasonographic staging could modify this conservative attitude. However, if the endoscopic Nd:YAG treatment for T1N0 rectal cancers becomes accepted by oncologists, it will have to face competition from photodynamic therapy (PDT). Supporters of PDT see several advantages for their technique: among them are its selectivity and its deep penetration into the rectal wall. In our opinion, these potential advantages over the thermal lasers are not important once the extent of the cancer is known through endoscopic ultrasonography. The ease of using thermal lasers is in favor of this technique which requires no pretreatment injection, has a visual control during treatment, and no post-treatment complications.

Endoscopic ultrasonography is equally effective in the diagnosis of T1N0 esophageal cancers. However, the problem with this location is different from that of the rectum because the lymphatic vessels penetrate into the epidermoid mucosa. Lymphatic microinvasion may exist at an early stage of the cancer and will not be detected by endoscopic ultrasonography. In addition, the esophageal mucosa is abnormal over a much larger zone around the malignant lesion than in the rectum, and recurrence are frequent at some distance from lesions cured by conservative treatment. Nevertheless, interesting results have been obtained by Photodynamic Therapy,44 with fewer complications than brachytherapy, and this could be its best application in digestive endoscopy.

The stomach is the third main location for small cancers in the digestive tract. This disease is rare in western countries but frequent in Japan where Nd:YAG laser coagulation and PDT face competition from diathermic resection and absolute ethanol injection.

3.3 COST OF TREATMENT

The cost of any new treatment is a major problem all over the world, but little data are available. We found two studies in the literature evaluating the treatment cost of sessile tumors with lasers. One is from our group and concerns the treatment of rectosigmoid villous adenomas,36 and the second is by Mellow45 which deals with palliation of colorectal cancers.

3.3.1 Rectosigmoid Villous Adenomas

Each country has different cost accounting and health insurance systems, which makes comparisons of absolute costs difficult. Therefore, we preferred to estimate the relative cost of laser treatment.
as a percentage of the cost of surgery for a rectosigmoid villous adenoma of an identical size.36 We estimated the direct charges, including hospital costs, doctor’s fees, and ambulance transportation for a patient living in the Lille area and treated in our hospital, as a function of the circumference of the tumor base. As a comparison with the U.S. these costs were also estimated for a patient living in Los Angeles and treated at the UCLA Center for the Health Sciences (personal communication from Dennis A. Jensen). The results are given in Table 4.

This estimation is in favor of laser treatment for all the three types of tumors (C1 to C3) in both countries. If indirect costs were included (loss of time from work, disability, complications, etc.), laser treatment would probably look even better, especially for C1 which requires a small number of laser treatments.

### 3.3.2 Palliation of Colorectal Cancers

Mellow45 has analyzed the records of 56 patients treated during the same period for rectosigmoid cancer at the Presbyterian Hospital in Oklahoma City, of whom 35 had undergone surgical treatment and 21 endoscopic laser therapy. The total cost of hospitalization in which primary surgery was performed was $23,156±$2,321 (mean ±SEM). Mean costs for patients undergoing initial endoscopic laser therapy were $5,333±$391 for inpatients and $2,263±$367 for outpatients. Since surgery generally provides definitive therapy and endoscopic laser requires repeated treatment throughout the patient’s life, Mellow has calculated total lifetime charges for laser-treated patients. Patients with hepatic and/or pulmonary metastatic disease were compared. The mean survival in the 8 surgically treated patients was 28 weeks and surgical treatment costs were $22,900. The mean survival in the 10 endoscopically treated patients was 36 weeks and endoscopic treatment costs were $12,154 (p < 0.05 for treatment costs).

Definitive conclusion cannot be drawn from these two studies and we should not conclude that endoscopic laser treatment may be substituted for surgery for economic reasons! However, these studies have demonstrated that in two circumstances lasers were economically acceptable in comparison with the current surgical procedures.

### 4. DISCUSSION

The technical problems of using thermal lasers in digestive endoscopy have now been solved. The best system is the 1.06/0.532 Nd:YAG laser. It is indeed an expensive laser, but its multidisciplinary potential is so wide that it can be shared with other specialties such as pneumology; urology; ear, nose, and throat; dermatology; and gynecology.

Nevertheless, the true impact of thermal lasers in gastroenterology is difficult to evaluate: what are the good indicators for its use, and how often are thermal lasers used in gastroenterology all over the world?

Gastroenterologists have not reached a consensus on what constitutes a good indicator for the use of lasers. One could think that modern methods of technology assessment would allow us to clearly define the place of thermal lasers among surgery, radio-chemotherapy, and other endoscopic techniques. This has not been the case for three reasons:

1. Protocols are difficult to write and, in order to rapidly include a sufficient number of patients, it would be necessary to run multicenter studies. This requires much coordination of resources that are not always available.

2. The period when technology assessment can be useful is short. The technique has to be mature but its use should not be widespread, which would result in an irreversible situation.

3. Conclusions of randomized studies made by experts under optimal conditions are not always transferable to a daily practice.

As an example, randomized studies were carried out on thermal lasers for hemostasis of active gastroduodenal hemorrhages. The contradictory results were published when the lasers had practically become obsolete for this indication due to the availability of new drugs or new nonlaser endoscopic techniques. As a consequence, the impact of these randomized studies was very small.

Data on the daily use of thermal lasers in gastroenterology throughout the world are not available. The number of publications in the literature is not a good indicator. Once they have published a large series, authors may continue to use their laser without publishing new papers. The laser companies do not provide information on their sales. Even if these data were available, they would not be meaningful. Nd:YAG lasers are very durable machines that are not replaced frequently. On the other hand, lasers may be installed in a gastroenterology unit without being used.

Finally, we can only analyze the data from our...
own group. Figure 2 gives the annual number of new patients referred to the Lille Laser Center since 1980 and treated by laser and/or BICAP.

In addition to the technical reasons already mentioned, several other reasons can be proposed to explain the trend shown in Fig. 2. From 1980 to 1986, there was a period of high interest with a consistent increase in the number of patients for all four applications. The year 1986 marks the beginning of a drop in the numbers and corresponds to the acquisition of lasers by many gastroenterologists in the Lille area, who no longer referred patients to us. Despite this, the number of patients with esophageal cancer remained at a high level from 1987 to 1990. This was probably because we were alone in the North of France in proposing the combination of laser and BICAP treatment for this disease. In the most recent years, the number of patients referred to us for villous adenomas has reached a plateau, and this makes us confident that this is probably due to the effective application of thermal lasers in digestive endoscopy.

Therefore, our conclusion is mainly subjective, drawn from the analysis of our own experience. We think that the best current application for thermal lasers in digestive endoscopy is in the treatment of rectosigmoid villous adenomas in elderly patients. Small superficial rectal cancers may also become good subjects due to the impact of endoscopic ultrasonography. For photodynamic therapy, we see positive and negative points. Among the positive, the new diode lasers emitting in the red will be soon available. These systems will be much simpler to use than the current dye lasers, and cheaper to buy and maintain. Among the negative, PDT will remain a more difficult technique than thermal lasers. The operator cannot follow the visual aspect during treatment to monitor the laser parameters and will have to rely on the dosimetry calculated before treatment. The photosensitizer injected before treatment is considered a drug and must pass all the rigorous and expensive procedures of drug approval, which makes the release of new and better photosensitizers difficult. Therefore, the advantages of PDT over thermal lasers will need to be great enough to overcome these difficulties. This may not be the case for palliative treatments. Early lesions with multifocal or diffuse disease such as early esophageal cancers appear to be the most promising for application of PDT in the future.

Acknowledgments

We would like to thank François Guillemin, Centre Alexis Vautrin, Vandoeuvre les Nancy, France, for all the information he kindly provided to us on photodynamic therapy, and Mohan Nair, SPIE, for his editing of the manuscript.

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