

Laser Applications in Laryngology: Past, Present, and Future

Steven M. Zeitels, MD, FACS*,
James A. Burns, MD, FACS

*Center for Laryngeal Surgery and Voice Rehabilitation, Massachusetts General Hospital,
One Bowdoin Square, Boston, MA 02114, USA*

Endolaryngeal surgery has been a primary driver for the development of laryngology since its inception in the mid nineteenth century, and laser technology [1] has been a key element of that development over the past 30 years [2–5]. Endoscopic laryngeal surgery remained office-based despite the transition from indirect-mirror-guided interventions to direct-laryngoscopic (Kirstein 1895) procedures in the early twentieth century [6]. Kirstein [7,8] clearly envisioned the enhanced surgical precision provided by direct laryngoscopy and astutely foretold the changeover to direct endolaryngeal surgery. “Autoscopy is veritably a surgical method...I nevertheless believe that finally, in the course of years, autoscopy will be generally accepted as the standard method for endolaryngeal and endotracheal surgery” [8]. As is often the case, an advance in anesthesia (ie, topical cocaine) [9,10] allowed for surgical development. With the ability to administer effective local anesthesia with cocaine, Kirstein performed autoscopy (direct laryngoscopy) in his office with an assistant. Subsequently, Jackson [11] championed moving direct laryngoscopic surgery to the operating suite as illustrated in the first textbook of rigid endoscopy of the upper aerodigestive tract.

Throughout the twentieth century, seminal innovations such as the surgical microscope [12–15] and general endotracheal anesthesia greatly enhanced the precision and success of endolaryngeal surgery. This culminated in the introduction of the carbon dioxide (CO₂) laser to surgery in the 1970s by Polanyi [1], Jako [2], Strong [3,16], and Vaughan [5,17]. They coupled the CO₂ laser

The authors received the following instrumentation on loan: 585-nm pulsed-dye laser (Cynosure, Chelmsford, MA), 532-nm pulsed KTP (Laserscope), and the Thulium laser (LISA Laser Products OHG, Katlenburg-Lindau, Germany).

* Corresponding author.

E-mail address: zeitels.steven@mgh.harvard.edu (S.M. Zeitels).

to the surgical microscope, thereby creating a new means of precise hemostatic dissection. Clinically, the CO₂ laser is a fundamental tool for the endolaryngeal surgeon; however, its use has been limited to the operating room because the energy cannot be delivered through a fiber. Recently, the 585-nm pulsed-dye laser (PDL) [6,18–20] and the 532-nm potassium-titanyl-phosphate (KTP) laser [21–23] have become increasingly popular in endolaryngeal surgery. Unlike the CO₂ laser, both PDL and KTP lasers deliver energy through thin glass fibers. Therefore, the PDL and KTP lasers are well suited for use through the channel of a flexible laryngoscope in the office [6] as well as the speculum of a direct laryngoscope in the operating room. Most recently, a 2- μ m continuous wave laser has been introduced, which retains some of the key cutting and ablative characteristics of the CO₂ laser, but it is delivered through 0.2- to 0.6-mm glass fibers.

It is common for laryngologic investigators and clinicians to use terms such as laser treatment, laser therapy, and laser management. This terminology should be abandoned because it is imprecise and can lead to confusion. Various lasers have dramatically different tissue interactions and associated surgical capabilities. In this sense, they represent a spectrum of tools that assist in achieving different outcomes, depending on the clinical problem. Although the CO₂ laser has been the primary laser used in laryngeal surgery for decades, today the laser most used in the present authors' practice are the fiber-based photoangiolytic lasers. Furthermore, it is inevitable that there will be further development of new laser technology as most surgical disciplines become increasingly minimally invasive and office-based.

Carbon dioxide laser

After introducing the CO₂ laser to laryngology and surgery, Jako, Strong, and Vaughan explored its use with various benign and malignant disorders, including carcinoma, stenosis, papilloma, nodules, polyps, cysts, and amyloidosis [24–26]. The seminal nature of their contributions is envisaged by the number of subsequent investigations by generations of surgeons in and outside laryngeal surgery. This continues today as developments in the CO₂ laser [27] enhance its function, primarily resulting in broader application in endoscopic surgical oncology. However, improvements in cold instruments and techniques along with the development of photoangiolytic lasers have caused most surgeons to abandon the CO₂ laser in the treatment of benign nonepithelial lesions of the phonatory mucosa.

It is worthwhile to review key considerations for using the CO₂ laser in laryngeal surgery, but the reader is cautioned that there is a wide spectrum of opinion on this issue. Therefore, the present authors provide a specific philosophy of management that is based on (1) known physiological principles of laryngeal function during phonation and deglutition; (2) laser-tissue interactions that have been well studied; and (3) 2 decades of experience with a majority of laryngeal pathologies.

The CO₂ laser functions primarily as a hemostatic scalpel when the beam is focused. When the beam is defocused, the CO₂ laser can also be used effectively to ablate and cytoreduce epithelial disease such as diffuse papillomatosis. Carbon dioxide lasers deliver nonionizing electromagnetic radiation that is well absorbed by water, which is ubiquitous in the laryngeal soft tissues. Operating at a wavelength 10.6 μm in the infrared region, the CO₂ laser causes thermal injury to soft tissue. For this reason, this laser is relatively contraindicated for the treatment of lesions of the vibratory membranes of the musculomembranous vocal folds. The heat that develops can result in fibrosis of the delicate superficial lamina propria (SLP), which is the primary oscillator responsible for voice production. The associated fibrosis diminishes mucosal pliability, which is the key determinate of voice quality if glottal closure is maintained [28]. Given that the geographic position of many vocal-fold lesions is on the medial phonatory surface, heat absorption and subsequent fibrosis are further exacerbated by unavoidable tangential dissection. Furthermore, optimal subepithelial resection [28–30] of common vocal-fold lesions such as nodules, polyps, and cysts is impossible with a CO₂ laser because attempted dissection at the epithelial basement membrane would result in vaporization of the epithelium. It is reasonable to use the CO₂ on the vibratory membranes when (1) there is no functional SLP present as may be encountered in patients who have had previous surgery; and (2) cancer has already invaded and replaced the SLP.

It should be remembered that Jako introduced both “cold” microlaryngeal hand instruments [12] (1962) as well as the CO₂ laser (1972) [2]. In addition to its hemostatic properties, the CO₂ laser was extremely valuable in microlaryngeal surgery because most surgeons could not perform delicate cold-instrument dissection from a distance under high magnification, especially with their nondominant hand (M.S. Strong, personal communication, 1994). Because the delivery system took the form of a joystick and a foot pedal, a majority of surgeons were able to perform precise bimanual surgery. However, the enhanced manual dexterity of the joystick is offset by the vaporization and ablation of varied amounts of the layered microstructure (epithelium and superficial lamina propria), primary tissues necessary for optimal vocal-fold vibration.

Jako correctly intended that the CO₂ laser should be used synergistically with cold instruments, not alternatively. Unfortunately, since he introduced both approaches, there have been divergent efforts by different investigators to convince colleagues that they should make a choice as to their preferred vocal-fold dissection method: cold-instrument or laser. Those who espouse that an exclusive choice is necessary, not based on soft-tissue interactions and physiologic principles of function, tend to be invested either by habit, previous academic work, or by other motivations. Unfortunately, clinically based investigations performed to elucidate the clinical effects of using a CO₂ laser for benign vocal-fold lesions inevitably suffer from a number of design flaws such as (1) cases were not been randomized; (2) small subject

cohorts cases were not been stratified to account for differences in lesion type, size, and laryngoscopic exposure; (3) objective acoustic and aerodynamic measures were not obtained for conversation level and maximal range tasks; (4) those who assessed the results were not blinded to the treatment; (5) surgeons used different CO₂ lasers and had varied skill sets with different lasers and cold instrumentation; and (6) most importantly, the CO₂ laser resection was not compared with subepithelial resection, which is substantially more successful than cold-instrument amputation of most benign lesions (ie, nodules, polyps, and cysts) [28].

In summary, microspot CO₂ lasers are used optimally for epithelial lesions that require resection and whenever the preservation of superficial lamina propria is not necessary (ie, most supraglottic lesions), impossible (already lost from disease or prior surgery), or not appropriate (ie, when glottic cancer has invaded or replaced most of the SLP). The CO₂ laser is also valuable in treating selected posterior glottal disorders that require arytenoidectomy or dissection of subepithelial stenosis. The microspot CO₂ laser is ill suited to treat benign subepithelial masses of the phonatory vocal fold such as nodules, polyps, and cysts. These lesions are optimally resected by cold-instrument tangential dissection with maximal preservation of underlying SLP and complete preservation of overlying epithelium. Regardless of the dissection approach, it is valuable to use the subepithelial infusion technique [28,31–33], which is used to enhance the precise resection of these lesions.

Photoangiolytic 585-nm and 532-nm lasers

585-nm pulsed-dye laser

Anderson and colleagues [34–36] developed the concept of selective photothermolysis over 20 years ago for the treatment of dermatologic vascular malformations. This concept evolved into the 585-nm PDL because its wavelength is precisely selected to target an absorbance peak of oxyhemoglobin (approximately 571 nm) and to fully penetrate the intraluminal blood, thereby depositing heat uniformly into the vessel. The laser pulse width (0.5 ms) is precisely selected to contain the heat to the vessel without causing collateral damage to the extravascular soft tissue from heat conduction. After learning about vocal fold phonatory function, Anderson stated, “Treating vascular lesions in infants skin is similar to treating vocal folds, pliability must be maintained or restored.” (R. Rox Anderson, personal communication, 1996)

Pilot studies were performed using the 585-nm pulsed-dye laser for laryngeal papillomatosis by Bower and colleagues [37] and McMillan and colleagues [38]. Shortly thereafter, Zeitels and Anderson initiated large-scale investigations [6,18,19] into the treatment of a spectrum of laryngeal lesions, so that over 300 procedures have been carried out. They created new treatment paradigms for mucosal dysplasia [19], papillomatosis [6,18,20], early

glottic cancer [39], ectasias, varices, and hemorrhagic polyps [28]. Because these lesions are composed of aberrant or abundant microvasculature, a surgical angiolysis model of control is philosophically well suited. Similar to the dermatologic model, it was theorized that the microcirculation could be targeted to involute laryngeal lesions (dysplasia, cancer, papilloma, and varices) or facilitate cold-instrument resection (ectasias and polyps), while minimizing thermal trauma to the surrounding soft tissue, SLP, and epithelium. In theory, this would be ideal for maintaining the pliability of the vocal folds' layered microstructure (SLP and epithelium) and glottal sound production.

Early on, it became clear that the primary pathologies for which the PDL would provide the greatest advantage were papillomatosis and dysplasia. A PhotoGenica V 585-nm PDL (Cynosure Inc., Chelmsford, Ma), used primarily for cutaneous vascular lesions, was modified and used to photocoagulate the vocal-fold microvasculature (450-ms pulse width, 2.0 J/pulse max output, 2-Hz repetition rate, 0.6 mm fiber, approximately 1–2-mm spot size, 65–250 J/cm² fluence [energy delivery to the tissue]). The procedures were performed primarily through the Universal Modular Glottoscope (Endocraft LLC, Providence, RI) [40] or the Adjustable Bivalved Supraglottoscope (R. Wolf, Rosemont, IL) [41].

Initially, the PDL was used to enhance cold-instrument microflap epithelial resection without including any of the underlying SLP, the primary oscillator during vocal-fold vibration. However, it soon became clear that these lesions would involute without concurrent resection. Because the epithelium is not vaporized to expose the superficial lamina propria, bilateral treatment of disease was possible. Furthermore, if the epithelium was not completely removed during PDL irradiation, the internal surfaces of the anterior commissure could be treated simultaneously without fear of scarring, synechia, or webbing. Therefore, anterior commissure disease (internal aspect), which is usually treated with staged operations, can be treated simultaneously, thus minimizing the number of general anesthetic procedures with their attendant morbidity and cost. It is readily apparent that PDL treatment does offer relief of tumor burden without the long-term consequences of vocal fold scarring that results from repeated surgical procedures using the CO₂ laser or cold instruments.

The success with treating glottal keratosis with dysplasia by strict involution through photoangiolysis of the subepithelial microcirculation was somewhat unexpected. Understandably, erythroplastic lesions would be treated ideally with the PDL because of their vascularity. However, it was unclear how the PDL would enhance management of the substantially more common keratotic lesions. The present authors' prospective investigations revealed that the 585-nm pulsed-dye laser successfully involuted these lesions [19], and current experience reveals that 75% to 100% of the visible disease will involute, and the procedure can be repeated as necessary. Most commonly, this is now performed as an office-based procedure with topical anesthesia [6].

The PDL has been effective in treating papillomatosis and dysplasia without the associated clinically observed soft-tissue complications associated with the CO₂ laser (thermal damage, tissue necrosis, superficial lamina propria scarring, and anterior commissure web formation) [6,18,19]. The presumed mechanism of disease regression is the selective destruction of the subepithelial microvasculature and separation of the epithelium from the underlying SLP by denaturing the basement membrane zone-linking proteins [42]. This results in ischemia to the diseased mucosa, albeit not permanently. This microvascular “angiolysis” approach restricts survival and growth of neoplastic epithelium, while minimizing cytotoxicity to the delicate layered microstructure (SLP) of the vocal fold. Based on this experience, the present authors believe that pulsed angiolysis lasers are a platform technology that will likely serve as a driver for a variety of future innovations in the management of laryngeal diseases as well as other areas of the body in which superficial diseased mucosa is problematic (eg, Barrett’s esophagus, dysplasia of the cervix, and granulation in the nose and ear).

Disadvantages of pulsed-dye laser treatments

Despite the assets of pulsed-dye laser treatment, there are shortcomings to these technologies. The laser is expensive and is not likely to exist in most surgical suites. From the present authors’ investigations, it is apparent that PDL therapy is less efficient in the treatment of exophytic versus sessile lesions because of the superficial penetration (approximately 2 mm) of the laser energy. This may be an artifact of the relatively low power settings used in this study. The Photogenica V laser is capable of 5 J/pulse, and the typical power output in this study was generally 0.55 to 0.75 J/pulse. It is likely that exuberant exophytic lesions require an increase in power to reach the vasculature at the core of the papillomatous lesions.

Another disadvantage of PDL treatment is that it is difficult to accurately quantify the energy delivery and real-time tissue effects, despite the fact that this laser is unlikely to cause substantial soft-tissue injury to the vocal folds. Furthermore, given the extremely short pulse width (approximately 0.5 ms), it is not unusual for the vessel walls of the microcirculation to become breached, resulting in extravasation of blood into the surrounding tissue. In the skin this is seen as purpura. In laryngeal lesions such as papillomatosis, the extravasated blood diverts the laser energy in the form of a heat sink, which diminishes the effectiveness of laser. The bleeding also diminishes visualization of the pathology, leading to diminished precision.

Lesions perpendicular to the axis of the straight cleaved fiber are optimal for effective irradiation. Medial-surfaced lesions requiring significant retraction of the vocal fold and the inner aspect of the anterior commissure would be better treated with a side-firing tip. A delivery system that could be set to several angles (30°, 45°, and 90°) would help to ensure proper application of

energy to difficult areas such as the medial surfaces of the vocal folds or the subcordal anterior commissure region.

Office-based pulsed-dye laser treatment

Presently, a principle reason that the endolaryngeal treatment of glottal dysplasia and papilloma is performed primarily in the operating room is for the administration of general anesthesia. This approach allows for precise optimal management of the primary goals, which are diagnostic accuracy, regression of disease, and voice restoration and maintenance. However, there is an unavoidable morbidity associated with general anesthesia and a variety of costs associated with the preoperative evaluation and procedural intervention.

Consequently, a majority of patients with recurrent glottal dysplasia and papillomatosis are followed with known disease until the adverse effects of the lesions' growth justifies the morbidity and costs of the surgical intervention. All surgeons and patients acknowledge inherently the detractors associated with general anesthesia in microlaryngoscopic treatment because they are required to develop an individualized plan for repeated treatment. Essentially, readily observed disease is followed until one or a number of factors justify a decision to leave the watchful-waiting model to embark on surgical intervention. These factors include airway restriction, voice deterioration, and worrisome visual appearance on clinical laryngoscopy.

This current management approach in adult patients is based on pragmatic clinical factors that may not always align with optimal disease treatment. When these diseases occur in a more accessible region with less delicate function, such as the oral cavity or skin, they are often treated more frequently and by means of local anesthesia. There would be a lower threshold for intervention for laryngeal lesions if a safe and efficacious treatment modality existed that did not require general anesthesia. Given the success encountered with the 585-nm PDL in treating glottal papillomatosis [18] and dysplasia [19] with general anesthesia, the present authors redesigned the approach, using topical local anesthesia [6].

To date, the present authors' clinical office-based experience treating these lesions with the PDL exceeds 200 cases. The PhotoGenica V 585-nm PDL was engineered to accept a 0.6-mm core fiber used along with a Pentax model VNL-1530T flexible laryngoscope. Visual guidance was achieved by observing the PDL fiber through the distal working channel of the laryngoscope, which has a 2.0-mm internal diameter and a 5.1-mm outside diameter. Although the VNL-1530T still uses optical fibers for illumination, superior higher resolution imaging capability is provided through the placement of the charge-coupled device video chip in the distal end (examination tip) of the scope.

The initial prospective investigation of office-based procedures was performed on 51 patients in 82 cases of recurrent glottal papillomatosis

(30 patients) and dysplasia (52 patients) [6]. All individuals had previously undergone microlaryngoscopic management with histopathologic evaluation. Five cases could not be completed because of impaired exposure (2 patients), discomfort (3 patients). Of those patients who could be treated, there was $\geq 50\%$ disease involution in 68 of 77 (88%) cases and 25% to 50% disease regression in the remaining 9 of 77 (12%) patients. Patients' self-assessment of their voice revealed that 73 of 77 were improved or unchanged, 4 of 77 were slightly worse, and none was substantially worse. These data confirmed that diseased mucosa can normalize without resection or substantial loss of vocal function. The putative mechanisms, which vary based on the fluence (energy) delivered by the laser, are photoangiolytic of sublesional microcirculation, denaturing of epithelial basement membrane-linking proteins, and cellular destruction. This safe effective technique allowed the treatment of many patients (in a clinic setting), in which classical surgery-related morbidity would have often delayed intervention.

However, there is a surgical learning curve using the PDL because energy delivery to the tissue (fluence) is difficult to determine exactly. Therefore, it is suggested that a noncontact mode should be used until the surgeon is familiar with the laser. This reduces the primary potential morbidity, scarring of the superficial lamina propria, because the effective tissue penetration at this wavelength is approximately 2 mm. In a noncontact mode, the necessary level of manual precision is diminished with the PDL compared with effective microlaryngoscopic dissection with the CO₂ laser or cold instruments. One can envision the PDL fiber delivery of light similar in technique to airbrush shading of paint.

As stated earlier, quantifying the energy delivery of the PDL and the associated real-time tissue effects is difficult. This is the case regardless of anesthetic approach but is more pronounced without stereoscopic microlaryngoscopic visualization. These functional characteristics of the PDL contrast with the familiar properties of the carbon dioxide laser in which the mucosal surface is vaporized. In addition, the vocal fold is more difficult to treat in an awake patient with the flexible laryngoscope because the target tissue is moving. Finally, when using flexible fiber-optic laryngoscopes, there are unavoidable tangential vectors for visualization and laser delivery, which cannot be overcome by bimanual tissue retraction and facile fiber alignment. There are substantially greater degrees of freedom of fiber positioning using a malleable cannula through a rigid laryngoscope with general anesthesia.

Based on the shortcomings of the flexible laryngoscopic PDL treatment, the present authors believe that there are innovations achievable in the foreseeable future. A side-firing fiber tip would significantly enhance control over treating the medial vocalizing surface of the vocal fold. This would dramatically diminish the comparative advantage of bimanual dexterity with microlaryngoscopic surgery. Additionally, high-resolution (distal-chip camera) real-time stroboscopy would provide indirect assessment of acute

edema of the SLP, which is an indirect metric for energy delivery. Presently, one could remove the distal chip flexible laryngoscope and assess by telescopic stroboscopy; however, this approach is cumbersome and time consuming, considering the window of opportunity before more local anesthesia is required. Alternatively, stroboscopic capability is available with other flexible fiber-optic laryngoscopes; however, the optical resolution is suboptimal as compared with the distal-chip technology.

Despite the fact that PDL treatment of diseased glottal epithelium by flexible laryngoscopy with local anesthesia was less efficacious than by microlaryngoscopy with general anesthesia, there are considerable advantages to the former. The reduced morbidity associated with local anesthesia in the clinic considerably facilitates the treatment of older patients, particularly those with substantial cardiovascular and pulmonary disease. This scenario is not uncommon in aging societies with a predilection for tobacco use. In the younger and working populations, there is less lifestyle disruption if general anesthesia is avoided in the operating room.

There are a number of limitations with the flexible laryngoscopic approach. A specimen for histopathologic analysis is not obtained routinely as part of the decision-making process for treatment. This is considered to be acceptable for a number of reasons. Most importantly, all patients have previously undergone microlaryngoscopic biopsies, and the indication to obtain further post-PDL intraoperative biopsies or treatment remained unchanged, based on laryngoscopic appearance during the office examination. Therefore, if the post-treatment clinic examination improved so that transparent normal-appearing epithelium was observed, a biopsy was unnecessary. However, if there was insufficient resolution or response to treatment after 3 to 4 weeks, the intraoperative option remained available. It is highly unlikely that there would be a clinically unrecognized new malignancy given the previous non-cancerous biopsy results and even less likely that a delay of several weeks would have a deleterious effect on long-term outcome.

Another disadvantage of the local anesthesia approach is that this treatment pathway may lead ultimately to more procedures. This is mainly because the threshold for intervention is decreased commensurate with the diminished morbidity associated with local anesthetic treatment. In addition, individual office-based operations are generally less effective compared with operative procedures under general anesthesia. The surgeon is understandably less aggressive using the PDL with local anesthesia because of reduced visual precision and the fact that the vocal folds are moving. Hopefully, with greater experience in this new treatment pathway, we will be able to more closely simulate the treatment capabilities that we achieve using general anesthesia.

Involution and treatment of early glottic carcinoma with pulsed-dye laser

Based on the success of treating involuting vocal-fold dysplasia with the 585-nm pulsed-dye laser (PDL), a correlative treatment strategy was initiated

to involute or treat microinvasive early glottic cancer. This approach evolved as a consequence of Folkman's concepts of cancer growth resulting from tumor angiogenesis [43,44]. PDL treatment was carried out initially to involute limited areas of microinvasive vocal-fold carcinoma in a selected pilot group of six patients who presented with early bilateral glottic cancer in which staged endoscopic resection was planned. The vocal fold with a greater volume of cancer was treated conventionally and the contralateral side was treated with the PDL, without resecting the smaller volume of cancer.

It was believed that this approach did not pose a substantial risk to the patients because (1) the disease was of small volume; (2) early glottic cancer grows slowly and rarely metastasizes; (3) it is easy to follow patients closely during the postoperative healing period and to intervene immediately if clinically indicated; (4) the routine plan would have been to perform a microlaryngoscopic resection of the second vocal fold in a staged fashion to avoid airway stenosis; and (5) all conventional treatment options remained. Subsequently, PDL was used to treat a patient in whom disease recurred after two previous endolaryngeal resections. This is likely to be the first demonstration of using non-ionizing radiation without chemical enhancement to involute (without vaporization or resection) microinvasive vocal-fold cancer.

Despite treatment of bilateral disease, objective voice measures revealed overall improvements in postoperative vocal function as measured by aerodynamic efficiency, maximum phonatory ranges, and voice quality-related acoustic parameters. These results substantiated stroboscopic observations of postoperative improvements, which revealed normal epithelium and enhanced mucosal wave function of PDL-treated vocal folds.

The 585-nm pulsed-dye laser demonstrated the capacity to involute microinvasive vocal-fold cancer. This approach is conceptually attractive because it is repeatable and also enhances vocal function by improving mucosal pliability. These findings support the concept that the inhibition of neoplastic blood supply (antiangiogenesis and photoangiolysis) by means of nonionizing radiation results in tumor regression. These cases established the proof-of-concept that microinvasive cancer could be involuted by means of photoangiolysis and that mucosal function and pliability could be maintained or restored. No conclusions can be drawn about the long-term oncologic efficacy of this approach, but these observations warrant further investigation. It may be that at some point in the future, surgeons may adopt the approach of incremental treatment of cancer to diminish morbidity as espoused by radiation and medical oncology.

The yellow light emitted by the PDL does not penetrate deeply into soft tissues, and therefore the present authors are not suggesting that this specific technology should be transferred to other mucosal cancer models. Selective photothermolysis of the microvasculature extends approximately 2 to 3 mm deep in most soft tissues, depending on fluence. Therefore, in one or two treatments, the PDL would not be expected to adequately treat thicker and more deeply invasive tumors. The findings from this pilot group of

patients does support the fact that further research into developing laser technology that is capable of selectively ablating intralesional or sublesional tumor vascularity is a laudable goal. In fact, the elements of this approach were identified by almost 40 years ago [45]. Kleinsasser described the aberrant microcirculation associated with microinvasive vocal fold carcinoma, whereas Jako had already commenced investigations into the use of laser technology. "Experiments using laser beams for destruction of discrete areas of vocal cords are presently being conducted" [45].

Pulsed potassium-titanyl-phosphate laser

The potassium-titanyl-phosphate (KTP) laser is a green light laser with a wavelength of 532 nm, which coincides with one of the absorbance peaks of oxyhemoglobin (approximately 541 nm). Similar to the PDL, the light from this laser can be delivered through a thin glass fiber. It has been used in a variety of scenarios to treat vascular lesions within the larynx; however, all previous work was carried out with a continuous-wave mode. The investigators have reported success with subglottic hemangiomas [22] as well as vocal-fold ectasias and varices [21]. Based on Anderson's concept of selective photothermolysis and experience with the 585-nm pulsed-dye laser, the present authors sought to determine whether a 532-nm pulsed KTP laser would provide a clinical advantage over the PDL. An experimental pulsed KTP laser was designed to deliver a 15-ms pulse width to provide enhanced photoangiolysis and diminish extravascular blood extravasation, which had been experienced with the PDL. The pulsed nature of this new KTP laser takes advantage of the fact that the energy delivery time is less than the thermal relaxation time of the tissue. Consequently, there is minimal collateral extravascular thermal soft tissue trauma compared with using the same laser in a continuous mode. The experience thus far has been very favorable in treating over 40 cases of papilloma and dysplasia, including use in the clinic and the operating room. There has been less blood extravasation into the surrounding tissue, and the cytology of overlying diseased (papilloma and dysplasia) epithelium has been virtually unaltered by the subepithelial photoangiolysis. This newly configured pulsed KTP laser shows great promise for laryngeal use and is currently under investigation.

Two-micron continuous wave laser

Recently, a 2- μ m continuous wave laser was developed to simulate the cutting properties of the carbon dioxide laser. In a pilot study it has been reported to be efficacious for opening the tracheobronchial lumen for obstructing carcinoma [46]. The RevoLix laser (LISA Laser Products OHG, Katlenburg-Lindau, Germany) is a diode pumped solid state laser that has a thulium-doped yttrium-aluminum-garnet laser rod, which produces a continuous wave beam with a wavelength of 2013 nm. This wavelength has a target chromophore

of water. Because it is a continuous wave laser, there are no high peak power pulses (eg, the holmium laser) that create a rapidly expanding and contracting steam bubble each time a laser pulse is absorbed by tissue.

There are a number of distinct advantages of the thulium 2- μm continuous wave laser, primarily because it can be delivered on a glass fiber. Similar to a CO₂ laser, efficient absorption of this laser's radiation by water facilitates its cutting and dissection characteristics. However, unlike a CO₂ laser, the energy is delivered by means of a fiber, which allows for tangential endoscopic dissection. The present authors have used this laser to perform a number of endoscopic partial laryngectomy procedures in both the glottis and the supraglottis. The most remarkable observation was that the procedure was never halted to stop bleeding from laser dissection during any case. Although preliminary observations suggest that there is increased thermal damage on the soft tissues at the margin of the cancerous section compared with the CO₂ laser, it does not seem excessive. These authors are currently conducting a study to evaluate this observation. Furthermore, tangential dissection is more effective with the thulium laser because of the angulation of the fiber delivery system. In contrast, the mirror-based delivery of CO₂ laser energy cannot be angulated substantially. The present authors have also used the thulium laser through the flexible laryngoscope to perform ablation of diffuse recurrent respiratory papillomatosis and lesions of the larynx, apart from the phonatory membranes, which would be susceptible to the heat from this laser. Based on the favorable experience thus far, this laser is being prospectively investigated to determine its optimal applications in laryngeal surgery.

Summary

Since their introduction in laryngology over 30 years ago, lasers have facilitated critically important innovations. These advances have accommodated well to our specialty, which has led in designing minimally invasive surgical approaches since mirror-guided interventions in the nineteenth century. Lasers discussed in this article will provide new platform technologies that will likely lead to the enhanced treatment of a number of benign and malignant laryngeal disorders. There is an expanding group of centers in which fiber-based technologies have already caused many procedures to be performed by means of local anesthesia in the clinic or office, especially for chronic diseases such as papillomatosis and dysplasia. This approach is likely to expand significantly because of diminished patient morbidity along with socioeconomic pressures of health-care delivery.

One of the substantial roadblocks to the dissemination of these clinical advancements is the cost required to install the laser technology in institutions and surgeons' offices. Furthermore, the critical development of these new lasers is limited by the relatively small number of patients with laryngeal disorders, which discourages industry from investing substantial research and

development funding. To solve this problem, the present authors hope that laryngology will continue to serve as a model for high-performance minimally invasive surgery that can be translated to other mucosal diseases of the upper and lower aerodigestive tract, genitourinary organs, and the cervix. Broader use of these new lasers in other surgical disciplines should diminish costs for all surgeons and their associated institutions.

References

- [1] Polanyi T, Bredermeier HC, Davis TW Jr. CO₂ laser for surgical research. *Med Biol Eng Comput* 1970;8:548–58.
- [2] Jako GJ. Laser surgery of the vocal cords. *Cope* 1972;82:2204–15.
- [3] Strong MS. Laser excision of carcinoma of the larynx. *Laryngoscope* 1975;85:1286–9.
- [4] Strong MS, Vaughan CW, Cooperband SR, et al. Recurrent respiratory papillomatosis: management with the CO₂ laser. *Ann Otol Rhinol Laryngol* 1976;85:508–16.
- [5] Vaughan CW. Transoral laryngeal surgery using the CO₂ laser: laboratory experiments and clinical experience. *Laryngoscope* 1978;88:1399–420.
- [6] Zeitels SM, Franco RA, Dailey SH, et al. Office-based treatment of glottal dysplasia and papillomatosis with the 585-nm pulsed dye laser and local anesthesia. *Ann Otol Rhinol Laryngol* 2004;113(4):265–76.
- [7] Kirstein A. Autoskopie des Larynx und der Trachea (Laryngoscopia directa, Euthyskopie, Besichtigung ohne Spiegel) [Autoscopy of the larynx and trachea (direct examination without mirror)]. *Archiv für Laryngologie und Rhinologie* 1895;3:156–64.
- [8] Kirstein A. [Autoscopy of the larynx and trachea (direct examination without mirror)]. Philadelphia: F.A. Davis Co., 1897.
- [9] Jelinek E. Das Cocain als Anestheticum und Analgeticum für den Pharynx und Larynx. *Wien Med Wochenschr* 1884;34:1334–7; 1364–7.
- [10] Koller K. Ueber die Verwendung des Cocain zur Anesthesirung am Aug. *Wien Med Wochenschr* 1884;43:1276.
- [11] Jackson C. Tracheo-bronchoscopy, esophagoscopy and gastroscopy. St. Louis (MO): The Laryngoscope Co; 1907.
- [12] Jako GJ. Correspondence documents between Geza Jako and the Stuemar Instrument Company. 1962.
- [13] Jako GJ. Microscopic laryngoscopy. Presented at the New England Otolaryngological Society. 1964.
- [14] Kleinsasser O. Mikrochirurgie im Kehlkopf. *Arch für Ohren Nasen und Kehlkopfheilkunde* 1964;183:428–33.
- [15] Scalco AN, Shipman WF, Tabb HG. Microscopic suspension laryngoscopy. *Ann Otol Rhinol Laryngol* 1960;69:1134–8.
- [16] Strong MS, Jako GJ. Laser surgery of the larynx: early clinical experience with continuous CO₂ laser. *Ann Otol Rhinol Laryngol* 1972;81:791–8.
- [17] Vaughan CW, Strong MS, Jako GJ. Laryngeal carcinoma: transoral treatment using the CO₂ laser. *Am J Surg* 1978;136:490–3.
- [18] Franco RA, Zeitels SM, Farinelli WA, et al. 585-NM pulsed dye laser treatment of glottal papillomatosis. *Ann Otol Rhinol Laryngol* 2002;111:486–92.
- [19] Franco RA, Zeitels SM, Farinelli WA, et al. 585-nm pulsed dye laser treatment of glottal dysplasia. *Ann Otol Rhinol Laryngol* 2003;112(9 Pt 1):751–8.
- [20] Zeitels SM. Papillomatosis. In: Linville M, editor. *Atlas of phonomicrosurgery and other endolaryngeal procedures for benign and malignant disease*. San Diego (CA): Singular; 2001. p. 119–31.
- [21] Hsiung MW, Kang BH, Su WF, et al. Clearing microvascular lesions of the true vocal fold with the KTP/532 laser. *Ann Otol Rhinol Laryngol* 2003;112(6):534–9.

- [22] Kacker A, April M, Ward RF. Use of potassium titanyl phosphate (KTP) laser in management of subglottic hemangiomas. *Int J Pediatr Otorhinolaryngol* 2001;59(1):15–21.
- [23] Manolopoulos L, Stavroulaki P, Yiotakis J, et al. CO₂ and KTP-532 laser cordectomy for bilateral vocal fold paralysis. *J Laryngol Otol* 1999;113(7):637–41.
- [24] Strong MS, Healy GB, Vaughan CW, et al. Endoscopic management of laryngeal stenosis. *Otolaryngol Clin North Am* 1979;12(4):797–805.
- [25] Strong MS, Jako GJ, Polanyi T, et al. Laser surgery in the aerodigestive tract. *Am J Surg* 1973;126(4):529–33.
- [26] Strong MS, Jako GJ, Vaughan CW, et al. The use of CO₂ laser in otolaryngology: a progress report. *Trans Sect Otolaryngol Am Acad Ophthalmol Otolaryngol* 1976;82(5):595–602.
- [27] Remacle M, Hassan F, Cohen D, et al. New computer-guided scanner for improving CO₂ laser-assisted microincision. *Eur Arch Otorhinolaryngol* 2005;262(2):113–9.
- [28] Zeitels SM, Hillman RE, Desloge RB, et al. Phonomicrosurgery in singers and performing artists: treatment outcomes, management theories, & future directions. *Ann Otol Rhinol Laryngol* 2002;111(Suppl 190):S21–40.
- [29] Hochman II, Zeitels SM. Phonomicrosurgical management of vocal fold polyps: the subepithelial microflap resection technique. *J Voice* 2000;14:112–8.
- [30] Zeitels SM. Polyps. In: Linville M, editor. *Atlas of phonomicrosurgery and other endolaryngeal procedures for benign and malignant disease*. San Diego (CA): Singular; 2001. p. 37–56.
- [31] Kass ES, Hillman RE, Zeitels SM. The submucosal infusion technique in phonomicrosurgery. *Ann Otol Rhinol Laryngol* 1996;105:341–7.
- [32] Zeitels SM. Premalignant epithelium and microinvasive cancer of the vocal fold: The evolution of phonomicrosurgical management. *Laryngoscope* 1995;105(Suppl 67):S1–51.
- [33] Zeitels SM. Nodules. In: Linville M, editor. *Atlas of phonomicrosurgery and other endolaryngeal procedures for benign and malignant disease*. San Diego (CA): Singular; 2001. p. 57–68.
- [34] Anderson R, Parrish J. Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. *Science* 1983;220:524–7.
- [35] Anderson RR, Parrish JA. Microvasculature can be selectively damaged using lasers: a basic theory and experimental evidence in human skin. *Lasers Surg Med* 1981;1:263–76.
- [36] Anderson RR, Jaenicke KF, Parrish JA. Mechanisms of selective vascular changes caused by dye lasers. *Lasers Surg Med* 1983;3:211–5.
- [37] Bower CM, Flock S, Waner M. Flash pump dye laser treatment of laryngeal papillomas. *Ann Otol Rhinol Laryngol* 1998;107:1001–5.
- [38] McMillan K, Shapshay SM, McGilligan JA. A 585-nanometer pulsed dye laser treatment of laryngeal papillomas: preliminary report. *Laryngoscope* 1998;108:968–72.
- [39] Zeitels SM. 585nm Pulsed-dye laser treatment of glottal cancer: proof of concept and a possible harbinger of future treatment philosophy. Presented at the 84th annual meeting of the American Broncho-Esophagological Association. Phoenix, AZ. April 30–May 1, 2004.
- [40] Zeitels SM. Universal modular laryngoscope/glottiscope system. Endocraft LLC, April 13, 1999. US patent 5 893 830. 1999.
- [41] Zeitels SM. Adjustable supraglottiscope system. R. Wolf, March 3, 1992. US patent 5 092 314. 1992.
- [42] Gray S, Pignatari SSN, Harding P. Morphologic ultrastructure of anchoring fibers in normal vocal fold basement membrane zone. *J Voice* 1994;8:48–52.
- [43] Folkman J. Tumor angiogenesis: therapeutic implications. *N Engl J Med* 1971;285:1182–6.
- [44] Folkman J. Angiogenesis. In: Braunwald ASFE, Kasper DL, Hauser SL, et al, editors. *Harrison's textbook of internal medicine*. Columbus (OH): McGraw Hill. 2001. p. 517–30.
- [45] Jako GJ, Kleinsasser O. Endolaryngeal micro-diagnosis and microsurgery. Presented at the 120th annual meeting of the American Medical Association. New York, NY. 1966.
- [46] Stanzel F, Raasch P, Haessinger K. A new 2 micron laser in airway disobliteration: a feasibility and safety study. Presented at the 15th Annual Congress of the European Respiratory Society. Copenhagen, Denmark. September 17–21, 2005.