*Laryngoscope Investigative Otolaryngology*


# Histologic Effect of the Potassium-Titanyl Phosphorous Laser on Laryngeal Papilloma

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**Objectives:** Tissue effects occurring with potassium-titanyl phosphorous (KTP) laser treatment are difficult to quantify due to the multiple variables that affect not only the fluence (energy delivered) but also the laser–tissue interaction. This histopathologic analysis of recurrent respiratory papilloma (RRP) removed after treatment with KTP laser therapy permits correlation of histologic effect with method of laser treatment.

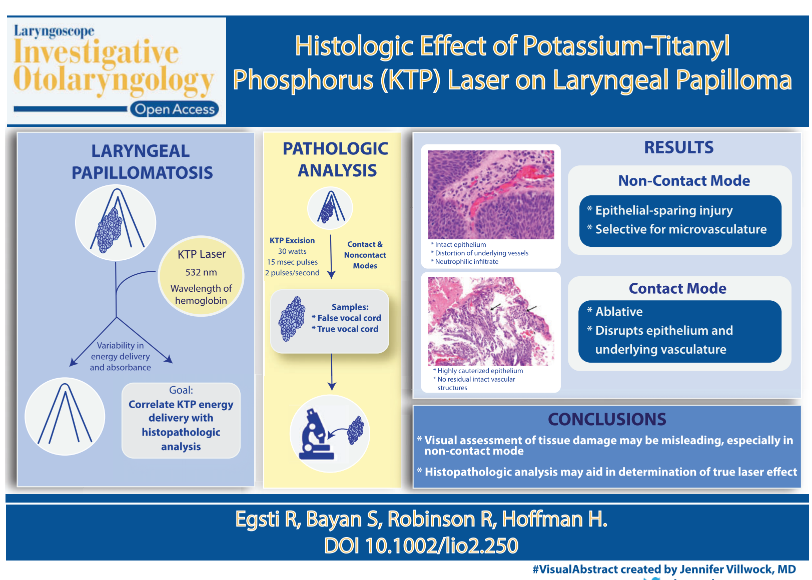
**Methods:** The histopathology of RRP resected specimens in a single patient was compared following treatment with KTP laser in contact and non-contact modes as documented with intraoperative photography and video imaging.

**Results:** Epithelial-sparing injury selective to the microvasculature was identified on histopathologic assessment of a specimen treated with noncontact angiolysis. Highly cauterized papillomatous epithelium without identifiable vascular structures was identified on tissue removed after treatment with the KTP laser in contact mode.

**Conclusion:** The histopathologic assessment of acute KTP laser effect on papilloma permits correlation between technique of application and tissue effect. Similar assessments may be helpful to modify dosimetry for individual patients requiring repeated treatment and may also assist in refining the development of existing KTP laser treatment classification systems.

**Key Words:** Potassium-titanyl phosphate (KTP), laser, recurrent respiratory papillomatosis, laryngoscopy, laryngology.
**Level of Evidence:** 4

**A Special Visual Abstract has been developed for this paper; watch the surgical video here. (Visual Abstract 1)**



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Editor's Note: This Manuscript was accepted for publication 10 December 2018.
Work conducted at the University of Iowa
**Conflict of Interest:** Henry T. Hoffman: a. COOK Medical: Research consultant and patent b. UpToDate: author c. IoataMotion: Research consultant with patent application Drs. Eigsti, Bayan, and Robinson have no conflict of interest.

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**DOI: 10.1002/lio2.250**

## INTRODUCTION

Potassium-titanyl-phosphorous (KTP) laser treatment of laryngeal epithelial disorders has become more common in the past decade. This laser treatment includes an angiolytic effect that results from the concentration of the laser energy in tumor microcirculation based on the similarity of the KTP 532-nm wavelength to that of hemoglobin.[1,2] There is emerging evidence that the KTP laser produces less thermal damage to normal tissue than the 10,600-nm wavelength CO2 laser.[3,4]

Reports have acknowledged the difficulty in quantifying degree of treatment with the KTP laser due to variability in energy delivery and absorbance with uncertainty in resulting tissue effect. A subjective grading system has been proposed that correlates method of delivery (contact or noncontact) with immediately observed tissue changes (Table I).[5] This grading system acknowledges the difficulty in correlating the amount of laser energy leaving the fiber tip with the energy impacting on the target. The energy delivered to the tissue (the fluence) is dependent on multiple factors including the power (watts), the pulse width (milliseconds), the spot size, and the distance from the target. This laser effect is then determined not only by the pulse frequency and total dose, but also by the targeted tissue characteristics including color, temperature, degree of hydration, vascularity, epithelial thickness, and light scattering properties.[1,6,7]

Animal studies of KTP laser–tissue interactions have offered histologic and biochemical analysis of effect on normal mucosa.[8,9] Although human study of KTP laser treatment has correlated the dose and method of delivery with clinical outcome, to our knowledge there has not yet been a histopathologic assessment of KTP laser effect as it correlates with dose to identify effect on the microvasculature in clinical practice.[7] We present histopathologic analysis of papilloma resected immediately after KTP laser treatment to correlate KTP type of energy delivery with histopathologic analysis of the microvasculature.

TABLE I.
Grading System for Laryngeal KTP Laser Effect.

| Treatment Classification KTP (Potassium titanyl phosphate) | Assessment of Immediate Tissue Effect |
|---|---|
| KTP V | Noncontact with angiolysis |
| KTP 1 | Noncontact mucosal blanching |
| KTP 2 | Noncontact minor epithelium disruption |
| KTP 3 | Contact or noncontact with epithelial ablation without tissue removal |
| KTP 4 | Contact with epithelial ablation with subsequent tissue removal |

Adapted from Mallur et al. 2014.[5]

TABLE II.
Histopathologic Findings Correlating With Laser Application.

| | |
|---|---|
| No lasing (Fig. 1) | Intact papillomatous epithelium with underlying vessels showing no abnormality. |
| KTP 1 (noncontact with epithelial blanching) (Fig. 2) | Intact papillomatous epithelium with distortion of underlying vessels showing endothelial cell prominence with surrounding neutrophilic infiltrates (exocytosis). |
| KTP 4 (contact mode with tissue removal) (Fig. 3) | Highly cauterized papillomatous epithelium. No residual vascular tissue can be discerned. |

## MATERIALS AND METHODS

Consultation with the University of Iowa Institution Review Board (IRB) identified this single case review was not subject to need for full board review.

Our practice in the management of laryngeal papillomatosis is to extensively photo-document procedures and to send biopsies for analysis in all cases treated with direct laryngoscopy under general anesthesia and in selected cases treated with transnasal laser ablation under local anesthesia.[10] Tissue removal before laser treatment is evaluated to establish the diagnosis on initial treatment and to identify potential progressive dysplastic change to carcinoma in situ or invasive cancer on treatment of recurrence. Tissue removed after laser treatment—both in-clinic and in the operating room—is done both for pathologic assessment and also to facilitate removal of papilloma that has uncertain potential for involution based on laser effect alone. Morselized papilloma removed employing the microdebrider is not subject to pathologic review.

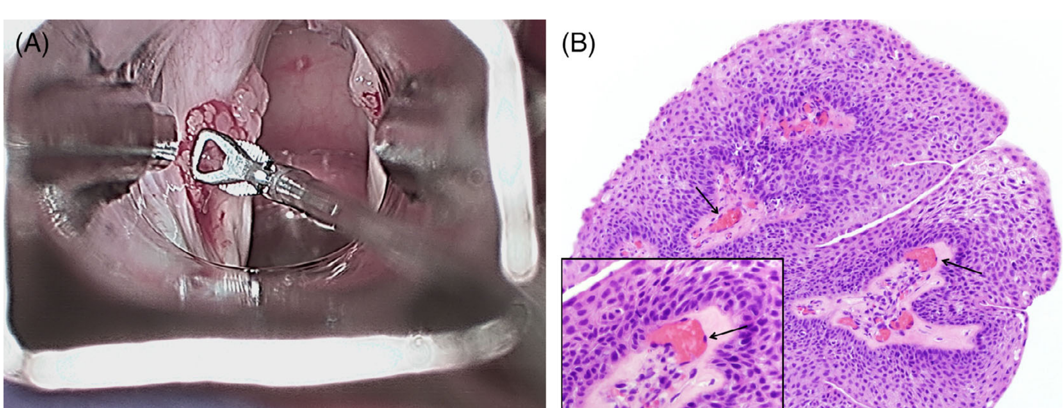


Fig. 1. A) Microdirect laryngoscopy showing untreated left false cord papilloma resected with forceps. B) Photomicrograph of the left false vocal cord papilloma biopsy with underlying vessels lined by unremarkable endothelial cells (arrows) showing no laser effect (200X, inset 400X).

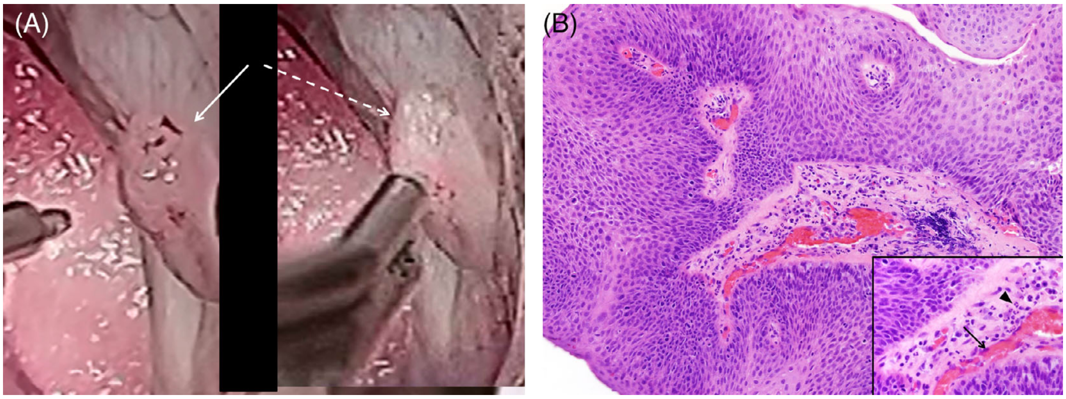


Fig. 2. A) Papilloma on the right false vocal cord before treatment (solid white arrow) and after treatment (dashed white arrow) to blanching without epithelial disruption with KTP laser (30 watts, 15 msec pulse, 2 pulses per second) in non-contact mode (KTP 1). (See also Video 1.) KTP = potassium-titanyl phosphorous. B) Photomicrograph of the right false vocal cord lesion resected after laser treatment revealing intact papillomatous epithelium with distortion of underlying vessels showing endothelial cell prominence (arrow) with surrounding neutrophilic infiltrates (arrow head) (200X, inset 400X).

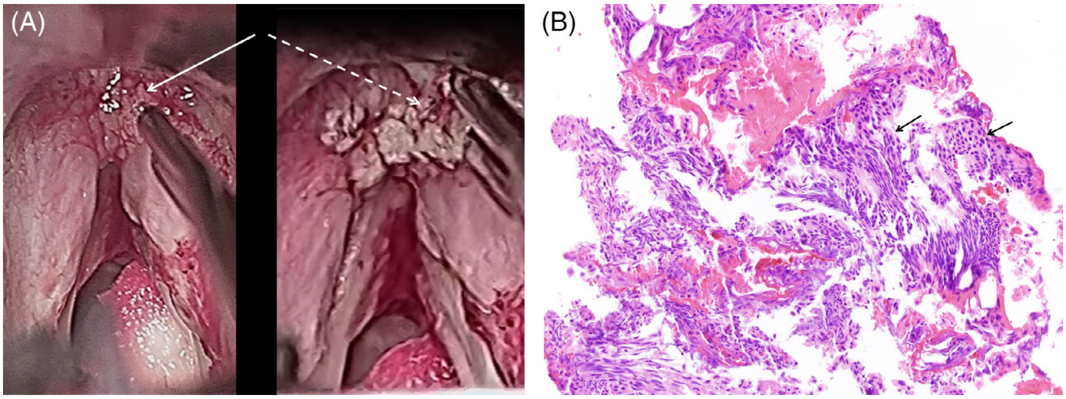


Fig. 3. A) Papilloma before treatment (solid white arrow) and in the course of KTP laser (30 watts, 15 msec pulse, 2 pulses per second) in contact mode (dashed white arrow) (KTP 4). (See also Video 2.) KTP = potassium-titanyl phosphorous. B) Photomicrograph reveals highly cauterized papillomatous epithelium (arrows). No residual intact vascular structures can be discerned (200X).

This practice permitted retrospective analysis of specimens removed in the care of a single patient with recurrent respiratory papillomatosis to correlate intraoperative photography and video imaging with re-review of histopathologic findings from separate sites in the supraglottic larynx. Exposure of the larynx with the Dedo laryngoscope (general anesthesia) permitted treatment of papilloma with the KTP laser in contact and noncontact modes at 30 watts with 15 millisecond (msec) pulses at two pulses per second (pps) employing laser-safe practice. Routine histopathology was performed on biopsies of the false and true vocal cords that were fixed in 10% formaldehyde and embedded in paraffin blocks. Four-micron sections were subsequently stained with hematoxylin and eosin.

## RESULTS

Comparison of laser treatment effect identified selective acute injury isolated to the vasculature for papilloma treated in the noncontact KTP1 mode (Table II).

Forceps removal of papilloma from the left false vocal cord before laser treatment showed papilloma with mild epithelial dysplasia and an intact fibro-vascular core (Fig. 1A, B).

The right mid-false vocal cord received 20 joules in the KTP1 noncontact mode (estimated 1 to 3 mm distance from laser tip) with blanching of intact epithelium demonstrating change from red and pink coloration to white blanching (Fig. 2A and also video 1). Histological assessment demonstrated intact epithelium with distortion of underlying vasculature (Fig. 2B).

The anterior right false vocal cord received 40 joules in a KTP4 contact mode with epithelial ablation and removal of tissue identifying highly cauterized papillomatous epithelium with no residual vascular tissue discerned (Fig. 3A, B, and also video 2).

## DISCUSSION

Selective coagulation of the subepithelial microvasculature of vocal cord lesions by laser treatment was initiated with use of the 585-nm pulsed dye laser (PDL)[6] in the 1990s[11] followed by application of the 532-nm KTP laser in 2006.[12]

Treatment with PDL—initially applied to manage cutaneous warts[13]—was subsequently adapted to address laryngeal papilloma by McMillan et al. as reported in 1994.[14] Further work by this research group introduced laser treatment in the clinic setting through flexible transnasal laryngoscopy. These investigators predicted that "This [technique] may change our approach in the way we manage this disease by providing early treatment for recurrences without waiting for the patients to become severely compromised by their symptoms."[15] These investigators additionally suggested that the capacity to selective address the vascular component of papilloma with preservation of the epithelium could reduce scarring or webbing at the anterior commissure.

Ayala et al. in 2005 offered histologic assessment of keratotic vocal fold lesions resected immediately after PDL laser treatment to the endpoint of "visible blanching and separation of the keratotic epithelial lesion."[16] They concluded that the PDL effects were specific due to selective absorption by oxyhemoglobin which helped to induce a cleavage plane beneath the epithelium to preserve the underlying basement membrane. This finding offers support for laser treatment before tissue removal to help define a resection plane in the effort to preserve underlying superficial lamina propria. However, these investigators also identified the potential for laser treatment to degrade histopathologic assessment and therefore performed a small biopsy before initiating laser treatment.

The PDL has been largely supplanted by the KTP laser for laryngeal surgery due in part to enhanced hemostasis with the KTP laser[17] and the capacity to vary the pulse width. The KTP laser has additionally been favored due to its solid-state energy medium that renders it less expensive and more reliable than the PDL—with the additional benefit of delivery through a smaller fiber.[18]

Growing support for use of the KTP laser both under general anesthesia and under local anesthesia in the clinic setting has developed for a variety of processes including papilloma, benign cysts, Reinke's edema, vocal process granuloma, leukoplakia, and cancer. Favorable results from clinical series have been reported but have left unanswered questions about dosimetry and method of application.

Uncertainty about the amount of KTP laser energy absorbed in the treatment of laryngeal processes both in the clinic and in the operating room remains problematic. Young et al. in 2015 studied KTP-laser effect on Reinke's edema and affirmed that the energy delivered to the tissue is dependent on the fiber-to-tissue distance as a variable that is not reliably controlled.[19] The subjective nature of the assessment of immediate clinical effect (KTP 1, 2, and 3) employed in their study added ambiguity to efforts to correlate fluence with tissue effect. The type of histologic assessment of KTP laser effect such as identified in our case report will hopefully improve assessment of laser effect for individual patients requiring repetitive treatment to direct future dosimetry through correlation of pathologically determined degree of damage with the dose administered. General application of this analysis correlating dose and method of application with histologic assessment may more broadly assist development of a more accurate treatment classification system by similar correlation of delivered does, grossly recorded tissue effect, and histologic assessment. The hemostasis provided by the angiolytic effect of the KTP laser was first reported in 1989 for management of sino-nasal disease.[20] This hemostatic laser effect was also identified to be useful in addressing laryngeal lesions by initial laser application followed by biopsy or debulking. The advantage of decreased bleeding from tissue removal following initial laser treatment has the disadvantage of disturbing the tissue for subsequent histologic assessment. Our practice has been to use the laser as a tool to supplement standard removal techniques to adapt to individual situations with laser treatment that may occur before or after tissue removal. This approach includes application of the concept developed by Zeitels et al of KTP photoangiolytic treatment of the underlying microcirculation after tumor debulking.[21,22] This single-case analysis supporting this concept of selective angiolysis through analysis of histologic effect is limited in scope, but will hopefully be amplified through reporting of subsequent experience.

## CONCLUSION

The immediate laryngeal tissue effect of energy delivered through KTP laser treatment is currently assessed visually but may benefit from correlative histopathologic assessment as identified in this report. This type of analysis may improve assessment of laser effect for individual patients to improve management for those requiring repetitive treatment. Similar analysis of a larger clinical series may assist in the development of a more accurate treatment classification system of KTP treatment effect than is currently available.

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