Recommendations for Potassium-Titanyl-Phosphate Laser in the Treatment of Cholesteatoma

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Potassium-titanyl-phosphate (KTP) lasers possess many characteristics suitable for otologic surgery. The objective of this report is to provide recommendations on the use of KTP laser for cholesteatoma surgery based on a narrative review of currently available evidence. PubMed and the Cochrane Review of randomized control trials were searched for relevant publications on efficacy and adverse effects and relevant articles appraised by the authors using Oxford Centre for Evidence-based Medicine criteria for recommendations. The potential benefits of KTP laser in cholesteatoma surgery include reduced rates of residual cholesteatoma and improved hearing outcomes. Cholesteatoma may be more effectively removed using KTP laser than using mechanical dissection alone. Reduced rates of residual cholesteatoma have been reported with KTP laser with level 2 evidence. In addition, KTP laser may facilitate the removal of cholesteatoma without the risk of mechanical trauma. This potentially allows for improved postoperative hearing outcomes through a) minimizing cochlear trauma and reducing sensorineural hearing loss and b) reducing the need for disruption of an intact ossicular chain. Currently, level 4 evidence exists to support improved postoperative hearing outcomes with the use of KTP laser. KTP laser use appears to be safe in otologic surgery if appropriate guidelines are followed. Current evidence is sufficient to strongly recommend KTP laser use for the prevention of residual cholesteatoma (Grade B recommendation) and an option for KTP laser use for optimizing hearing outcomes (Grade C recommendation).

KEYWORDS: Cholesteatoma, laser, hearing, residual disease

INTRODUCTION
Laser devices emit a narrow beam of electromagnetic radiation that is monochromatic, in-phase, and unidirectional. In the case of KTP laser, the beam is generated using a neodymium-doped yttrium aluminum garnet (Nd:YAG) medium. This beam is then passed through a potassium-titanyl-phosphate (KTiOPO₄) crystal that doubles the frequency and generates a laser with a wavelength of 532 nm. It has long been recognized that many features of this wavelength are optimal for otology [1]. These advantages include wavelength within the visible spectrum, delivery via a fiber-optic cable, application in a non-contact fashion, and removal of tissue without the generation of acoustic energy. Because the 532-nm beam can be transmitted via a hand-held semi-flexible fiber-optic cable, it can be precisely directed to safely work in relatively inaccessible recesses of the middle ear space. The slender handpiece is also ideally suited to work alongside endoscopes that further extend the surgeon's ability to remove cholesteatoma, beyond what can be achieved using an operating microscope [2-5]. In contrast, the CO₂ laser can be administered using a micromanipulator along straight lines of sight or a less flexible mirrored-fiber handpiece [1, 6]. Neither of the devices permits such ready access into the sequestered middle ear recesses. Higher wavelength lasers used in other surgical applications (e.g., Erbium-doped yttrium aluminum garnet and Nd:YAG lasers) generate acoustic energy with tissue vaporization, potentially leading to acoustic trauma and making these lasers ill-suited to otologic surgery [7].

The green 532-nm wavelength of KTP laser is optimally absorbed by red pigments, such as hemoglobin. Consequently, structures containing blood are preferentially heated and denatured or vaporized by the laser. Within the ear, this allows effective removal of granulation tissue and other tumors rich in blood vessels [8]. In practice, KTP laser may be used to ablate keratin, divide fibrous adhesions, shrink atelectatic segments of the tympanic membrane, and remove bone [1, 9-13]. By applying these techniques, cholesteatoma can be precisely dissected without the risk of mechanical trauma to the cochlea that may occur from manipulation of the ossicular chain with surgical instruments.

In this study, a systematic search for level 1 evidence on the use of laser in cholesteatoma surgery was conducted in April 2016 using PubMed and the Cochrane Library. The Cochrane Library of randomized controlled trials was searched using the terms [laser] and [ear] yielding one hit considered relevant for the treatment of cholesteatoma [14]. Searching PubMed with the search terms [laser], [ear], and [meta-analysis] yielded no relevant articles; search with the terms [laser], [ear], [surgery], and [systematic review] yielded 215 results of which 205 were discarded as having manuscript titles unrelated to the topic. PubMed search using [laser], [ear],
and [randomized] generated 125 hits of which 124 were discarded. Review of the references from publications identified using the aforementioned search identified 23 additional relevant publications. These abstracts were reviewed and the salient manuscripts were read in detail to yield evidence on the primary outcomes of changes in hearing threshold postoperatively and rate of residual cholesteatoma. A narrative review is provided incorporating these studies. In the absence of level 1 evidence, supporting information is provided by reference to other available literature and is summarized in the form of subsequent recommendations based on criteria established by the Oxford Centre for Evidence-based Medicine [15].

Published Evidence Evaluating KTP Laser Use in Cholesteatoma Surgery

a) Treatment of Cholesteatoma

Multiple reports provide support for use of KTP laser in cholesteatoma removal [5, 10, 11, 13, 14, 16-21]. KTP laser is widely recommended as having appropriate technical and operational characteristics for the removal of cholesteatoma from the middle ear and from the ossicles without causing any mechanical traction or trauma. One of the earliest reports by Saeed and Jackler [13] in 1996 found that the most valuable application was the atraumatic removal of cholesteatoma from a mobile stapes. Additional reported benefits include precise and hemostatic removal of diseased tissues (polyps, granulations, and adhesions) and manipulations on an intact ossicular chain without the induction of vibrational trauma. Furthermore, KTP laser is an effective tool to remove cholesteatoma, which is otherwise irretrievably stuck to the dura [17]. Although the utility of KTP laser in cholesteatoma has been widely published, there is little literature reviewing the effectiveness of other surgical lasers for cholesteatoma surgery [22, 23].

The clinical significance of these claims is that (a) cholesteatoma removal by KTP laser may be more effective than mechanical dissection, which reduces the likelihood of leaving residual cholesteatoma in situ, and (b) KTP laser may be better suited to remove cholesteatoma from the ossicles. The latter could improve hearing outcomes by reducing the risk of sensorineural hearing loss from over-zealous mechanical manipulation and reducing the risk of conductive hearing loss by making preservation of a functionally intact ossicular chain more feasible.

b) Prevention of Residual Cholesteatoma

An early narrative report including data from a retrospective case series indicated the possibility that KTP laser could reduce the risk of residual cholesteatoma by half [19]. In this series, 95 ears underwent laser surgery in this series. This impressive claim was supported by a subsequent retrospective review of 514 surgeries in which application of the KTP laser was found to reduce the presence of residual cholesteatoma at the second stage of surgery from 26.5% to 10.4% (p<0.0001) [11]. In total, 201 ears were treated using laser surgery in that series.

Following these encouraging retrospective studies, a prospective controlled parallel-group study was set up by Hamilton in two neighboring hospitals, one with a KTP laser and one without [24]. The same otologic surgeon operated at both hospitals. In total, 36 patients were operated using KTP laser and 33 were operated without KTP laser. One patient had residual disease after laser treatment, whereas 10 patients had residual disease without laser (p=0.003, Fisher exact test). Logistic regression analysis was performed to control for other factors predictive of residual cholesteatoma, and multivariate analysis continued to show a significantly beneficial effect on the prevention of residual disease (p=0.013). From this study, use of KTP laser for removal of cholesteatoma in four patients would result in one less case of residual cholesteatoma than if laser were not used (number needed to treat=4). Contemporary commentary on this study recognized the merit of the study design and the dramatic degree of benefit, concluding that the findings “certainly support the argument that such a surgery should be centered on hospitals that have a KTP laser” [24].

No evidence portrays KTP laser as being ineffective at removing cholesteatoma. However, a single narrative review on the treatment of pediatric cholesteatoma from French authors provides the unsubstantiated claim in the abstract that laser treatment of cholesteatoma has “proved unsuccessful” [25]. The remainder of the manuscript simply states that “attempts at laser treatment, mainly to reduce the rate of residual lesion in second-stage surgery, have not been greatly followed up” [25]. It is not reported whether the authors had significant experience in using KTP laser. Although residual cholesteatoma is thought to more commonly occur in children [26], there is no evidence to suggest that the effectiveness of laser treatment would differ in adults. Other reports have suggested that KTP laser is beneficial in pediatric cholesteatoma [14, 27-29].

c) Improved Hearing Outcome

It has long been recognised that KTP laser surgery facilitates atraumatic dissection of cholesteatoma from mobile ossicles, reducing the risk of trauma to the cochlea from mechanical traction [13]. Without such technology, surgeons may need to disarticulate the ossicular chain or completely remove ossicles before proceeding with mechanical dissection. KTP laser surgery thus provides the opportunity to prevent conductive hearing loss from surgery. Surgically induced sensorineural hearing is rare in cholesteatoma to preclude evaluation of this outcome with high-level evidence.

Despite the hypothetical advantage of using laser surgery to improve hearing in cholesteatoma surgery, there appears to be no comparable studies that corroborate this. The prospective study by Hamilton showing reduction of residual cholesteatoma did not include hearing as an outcome measure [14]. Limited evidence is available from retrospective studies. Another study by Hamilton compared KTP laser surgery in ears with intact versus discontinuous ossicular chains (n=80 versus n=69 ears, respectively) [19]. He found that an intact ossicular chain could be preserved in 90% of cases using the laser. The odds ratio for normal hearing was 2.73 (95% CI, 1.1-6.6; p=0.03) in favor of ears with an intact ossicular chain. Another center combined KTP laser surgery with endoscopes as well as the conventional operating microscope and preserved intact ossicular chain in 47 of 49 (96%) ears [18]. In comparison, a third center preserved an intact ossicular chain in only 17 of 32 cases (53%) without access to KTP laser [30]. Furthermore, no sensorineural hearing loss occurred in either study when KTP laser was used to dissect the disease off the ossicles. These figures merely illustrate the potential for ossicular preservation and improvement in postoperative hearing by the use of the laser. However, too many uncontrolled variables between different surgeons...
including those from CO₂, argon, and erbium lasers [7]. Although other laser wavelengths can also be used in middle ear surgery, in-site, limiting access to the recesses of the middle ear space [6]. More usually aimed using a micromanipulator, requiring a direct line of the mirrored fiber compared with the KTP carrier. Furthermore, the principle risks to the patient from using KTP laser in the ear are from collateral thermal injury. The facial nerve and cochlea have been long recognized as the two sensitive structures at risk, potentially giving rise to facial nerve palsy and sensorineural hearing loss [13]. Surgery adjacent to and on the stapes is particularly risky because it lies over the cochlea in close proximity to the facial nerve.

In cholesteatoma surgery, the reported safety profile has been good, with the largest series reporting no complications in 201 cases [11]. Nevertheless, a cadaveric study has indicated that spread of heat from the stapes may be sufficient to provoke facial nerve injury [36], and facial palsy has been reported after stapedotomy with KTP laser [27, 38]. Delayed facial nerve palsy has been reported after KTP laser use in three children with cholesteatoma [38]. It is not certain from this report whether the laser was responsible for the complication because the laser was not directly applied to the nerve and there was no response from intraoperative facial nerve monitoring during its use. All three children made a complete recovery within 2 months. Facial nerve injury is usually considered a rare complication of cholesteatoma surgery (e.g., 0.1% cases) [26], although even recent studies show much higher rates on some occasions [e.g., four of 273 cases (1.5%)] [40], which highlights the limitation of comparing outcomes in uncontrolled studies. It is reassuring to note that there appears to be no reports of permanent complications, including facial nerve or cochlear injury, attributable to KTP laser cholesteatoma surgery.

In summary, available evidence suggests that KTP laser appears to be safe for use in otologic surgery if appropriate safety guidelines are followed. Care must be taken to avoid collateral thermal injury.

Cost Effectiveness of KTP Laser
Published reports and personal communication between the reviewers and international colleagues indicate that KTP laser is used for cholesteatoma around the world, but most certainly not in every otologic center. The cost of purchase of the KTP laser device appears to be the principle deterrent to more widespread adoption. A high-volume practice is likely to be necessary in order to spread the cost of purchase over a sufficiently large number of surgeries to justify the

and patient groups make it inappropriate to make a direct comparison. The large number of variables, including extent of ossicular erosion and other surgical techniques, coupled with the relatively low volume of cholesteatoma in many centers make it seem unlikely that a comparative prospective study could be powered or completed to address hearing as an outcome measure. Furthermore, it has been suggested that the efficacy of KTP laser in eradicating cholesteatoma would make it unethical to withhold KTP laser treatment in centers where it is available [24].

Currently Available Alternatives to KTP Laser in Otologic Surgery

a) Mechanical Instrumentation
Conventional mechanical instruments are used for middle ear surgery in institutions where KTP laser is unavailable, but conventional mechanical instruments have inherent limitations. In cholesteatoma surgery, simple elevators are used to peel cholesteatoma away from the middle ear and mastoid structures. It is often impossible to completely remove the cholesteatoma using mechanical dissection, as demonstrated by the prevalence of residual disease, which may be present in more than one-third of the cases [31].

Furthermore, it may be necessary to disarticulate or remove ossicles in order to safely clear the disease as it may be impossible to peel cholesteatoma from delicate and partially mobile ossicles, thereby adversely affecting postoperative hearing levels [16, 18, 30]. Application of excessive force on the ossicular chain from mechanical dissection risks sensorineural hearing loss, although this rarely occurs. Granulation tissue removal from the ossicles using mechanical dissection may present additional challenges: it is frequently too friable and bleeds profusely, thereby compromising surgical field clarity and potentially increasing the risk of residual cholesteatoma and inadvertent injury [29].

The surgical drill is a fundamental tool in otologic surgery, which is used in cholesteatoma surgery to remove bone from the mastoid to provide visualization and access to the disease. In some respects, more extensive drilling can be used as an alternative approach to cholesteatoma removal when a laser is unavailable. By performing greater mastoid resection, including removal of the canal wall, it is possible to gain access to the cholesteatoma that would otherwise be inaccessible to mechanical dissection. However, this wider surgical approach does not completely eliminate the risk of residual cholesteatoma and may come at the expense of greater morbidity for the patient [32, 33].

b) Other Lasers
Other laser wavelengths can also be used in middle ear surgery, including those from CO₂, argon, and erbium lasers [7]. Although popular in stapedotomy, CO₂ laser has not been widely used in cholesteatoma surgery as it cannot be carried in a glass fiber. CO₂ laser is usually aimed using a micromanipulator, requiring a direct line of site, limiting access to the recesses of the middle ear space [40]. More recently, mirrored fibers have been developed that could allow wider use of CO₂ laser in otologic surgery [34]. The two relative disadvantages of this newer technology are the greater cost and lower flexibility of the mirrored fiber compared with the KTP carrier. Furthermore, the CO₂ laser beam is invisible, adding complexity to its use.

The erbium laser can be carried via fiber optics (although the special fibers are also expensive) and has been recommended as having ideal absorption characteristics for otologic surgery [7]. However, the loud bang emitted by tissue ablation is dangerously distracting to the surgeon and potentially carries a risk of sensorineural hearing loss from acoustic trauma [35]. Nearly 20 years ago, the Nd:YAG laser was described as “useful” in otology [22], but there are no other reports of its use and is not thought to have been widely adopted. Based on limited experience, it is assumed that this is also because of the distractingly loud bang emitted upon tissue vaporization. There are many reports on the successful use of the fiber-guided argon laser in stapedotomy and a single report on its use in a small number of cholesteatoma surgeries [23].

Safety Profile of KTP Laser
As with all lasers, standard operating room safety procedures should be followed to guard against the risk of fire or inadvertent injury to operating room personnel. This includes the availability of appropriate eye protection and staff training.

The principle risks to the patient from using KTP laser in the ear are from collateral thermal injury. The facial nerve and cochlea have been long recognized as the two sensitive structures at risk, potentially giving rise to facial nerve palsy and sensorineural hearing loss [13]. Surgery adjacent to and on the stapes is particularly risky because it lies over the cochlea in close proximity to the facial nerve.

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cost per case. Fortunately, for lower volume centers, rental of a device or sharing the purchase of a device with other departments provides realistic opportunities. KTP laser can also be used in laryngeal, ophthalmological, urological, and dermatological procedures. When a device is available, KTP laser use for cholesteatoma removal is easy to justify based on the impressive reduction in residual disease rates quoted above because the cost per case of the laser carrier fiber is relatively low, being equivalent to the cost of a disposable burr. Some devices can use reusable fibers to enhance cost effectiveness.

Summary & Clinical Recommendations
Clinical recommendations regarding KTP laser use in otologic surgery can be based on available published evidence. The strength of the recommendations can be weighted according to established criteria as follows: A (consistent with level 1 studies), B (consistent level 2 or 3 studies or extrapolations from level 1 studies), C (level 4 studies or extrapolations from level 2 or 3 studies), and D (level 5 evidence or troublingly inconsistent or inconclusive studies of any level) [17].

KTP laser use in cholesteatoma surgery

- Recommended to reduce the risk of residual cholesteatoma (B: pseudo-randomised comparative trial versus mechanical dissection)
- Suggested as beneficial to preserve ossicular function and improve hearing (C: case series)

KTP laser enables the surgeon to avoid mechanical trauma of more traditional instrumentation and obtain more effective and safe disease removal. A single well-designed comparative study has shown sufficient benefit to lead to an independent claim that cholesteatoma surgery should be concentrated at centers where KTP laser is available [14, 24]. KTP laser therapy use in cholesteatoma surgery has been shown to reduce the risk of residual cholesteatoma with a number needed to treat of four cases [14]. Cost effectiveness of KTP laser therapy in cholesteatoma can be calculated from this finding according to local health care costs. The cost per case of using the KTP laser is comparable with other surgical disposables and the KTP laser may also be used for granulation tissue removal, adhesiolysis, and atelectasis reduction. Available literature suggests that KTP laser may safely improve hearing outcomes in addition to its established role in prevention of residual cholesteatoma.

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REFERENCES