**Name of Journal: *World Journal of Otorhinolaryngology***

**ESPS Manuscript NO: 23562**

**Manuscript Type: Original Article**

***Retrospective Study***

**Use of Ho:Yag Laser in early stage oropharyngeal squamous cell cancer**

Virk JS *et al*. Ho:Yag Laser in oropharyngeal SCC

**Jagdeep S Virk, Mike Dilkes**

**Jagdeep S Virk, Mike Dilkes,** Department of Head and Neck ENT, Barts and Royal London Hospitals, London E1 1BB, United Kingdom

**Author contributions:** Virk JS drafted the manuscript and performed literature searches; Dilkes M performed, collated and analysed all data.

**Institutional review board statement:** This study was registered with the clinical governance and ethics team. This study was approved and ratified by the ethics board.

**Informed consent statement:** All patients agreed to undergo this surgery after a multi-step consent process in keeping with GMC guidelines (UK).

**Conflict-of-interest** **statement:** We have no financial relationships to disclose.

 **Data sharing statement:** There is no further data to share.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Correspondence to: Jagdeep Singh Virk, MA MRCS DOHNS,** E Department of Head and Neck ENT, Barts and Royal London Hospitals, Whitechapel Road, Whitechapel, London E1 1BB, United Kingdom. j\_v1rk@hotmail.com

**Received:** December 1, 2015

**Peer-review started:** December 1, 2015

**First decision:** January 15, 2016

**Revised:** January 16, 2016

**Accepted:** March 9, 2016

**Article in press:**

**Published online:**

**Abstract**

**AIM*:*** To evaluate the efficacy of Holmium:Yag laser resection for oropharyngeal squamous cell cancer.

**METHODS:** A prospectively collected case series of all patients with oropharyngeal squamous cell carcinoma undergoing laser resection using the Holmium:Yag laser technique only over a 15 year period at a tertiary referral centre. All patients underwent long term follow up with regular clinical and radiological surveillance, when indicated. All patients were operated on under general anaesthetic with a laser-safe endotracheal tube. Typically laser resection was performed first using an operating microscope, followed by neck dissection. The tumour was held with a Luc’s forceps or Allis clamp. The Ho:Yag laser was implemented via a fibre delivery system. The Holmium:Yag laser fibre, of 550 micron diameter, was inserted through a Zoellner sucker and attached *via* steri-strips to a second Zoellner suction to provide smoke evacuation. The settings were 1J/pulse, 15 Hz, 15W in a continuous delivery modality *via* a foot pedal control. The procedure is simple, bloodless, effective and quick. All surgeries were performed as day cases.

**RESULTS*:*** 27 oropharyngeal squamous cell cancer patients identified, at the following subsites: 23 lateral pharyngeal wall/tonsil, 2 anterior faucal and 2 tongue base. Of the 23 tonsil tumours, 19 required no further treatment (83% therefore had negative histopathological margins) and 4 required chemoradiotherapy (17% were incompletely excised *or* had aggressive histopathological features such as discohesive, perineural spread, vascular invasion). The 2 patients with anterior faucal pillar neoplasia needed no further treatment. Both tongue base cancer cases required further treatment in the form of chemoradiotherapy (due to positive histopathological margins). Postoperatively, patients complained of pain locally, which resolved with regular analgesia. There were no postoperative haemorrhages. Swallowing and speech were normal after healing (10-14 d). There was one case of fistula when neck dissection was carried out simultaneously; this resolved with conservative management. All patients were followed up with serial imaging and clinical examination for a minimum of five years. Median follow up was 84 mo.

**CONCLUSION:** Holmium:Yag lasers are a safe and effective treatment for Stage 1 and 2 squamous cell carcinoma of the oropharynx, excluding the tongue base.

**Key words:** Holmium:yag; Laser; Squamous cell carcinoma; Oropharyngeal; Human papillomavirus; Cancer; Squamous cell cancer

**© The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Oropharyngeal squamous cell carcinoma is increasing in incidence. Management is controversial due to the large human papillomavirus cohort. The gold standard remains single modality therapy for early stage disease, either primary surgery or radiotherapy. Laser resection is one of the viable surgical options. We present a series of patients treated with Holmium:Yag laser resection. Holmium:Yag lasers are a safe and effective treatment for Stage 1 and 2 squamous cell carcinoma of the oropharynx, excluding the tongue base. Its uses could be extended within the speciality and elsewhere, particularly with a robotic arm.

Virk JS, Dilkes M. Use of Ho:Yag Laser in early stage oropharyngeal squamous cell cancer. *World J Otorhinolaryngol* 2016; In press

**INTRODUCTION**

Oropharyngeal squamous cell carcinoma (SCC) is increasing in incidence. This has been confirmed in large epidemiological studies both in the United States and the UK recently[1]. This is principally due to the human papilloma virus (HPV) infected cohort of patients, particularly subtype HPV-16. HPV-associated oropharyngeal SCC comprises the vast majority of oropharyngeal SCC[1].

All patients undergo cross-sectional imaging and biopsy for pathological and radiological staging (Table 1)[2]. The gold standard of management remains single modality therapy for early stage disease (T1-2 NO-2a MO) [3], either primary surgery or radiotherapy, with both reported to be equally successful[4]. Decisions are based upon patient choice and co-morbidities (i.e. ability to undergo general anaesthetic), size and position of the tumour (less than 4cm and preservation of superior pharyngeal constrictor) and the functional deficit[5].

Early stage disease incorporates N1 and N2a neck disease. Hence, neck dissection should also be considered if there are positive nodes (with no radiological evidence of extra capsular spread). Ipsilateral selective level II-IV neck dissection may be warranted even with negative imaging.

Laser resection is one of the viable surgical options. Many modalities have been described but fall into two broad groups of trans-oral carbon dioxide laser surgery or trans-oral robotic surgery. Other options, apart from radiotherapy, include photodynamic therapy, diathermy excision or through open approaches with reconstruction (such as transmandibular with free flap reconstruction)[2,5].

In contrast to the commonly used carbon dioxide laser resections, we present a series of patients treated with Holmium:Yag laser resection in the oropharynx for these squamous cell carcinomas. We believe that the properties of the Holmium:Yag laser system is well suited to implementation in the oropharynx in view of its unique ability to vaporize, ablate (due to its longer wavelength of 2100 nm), coagulate soft tissues, a relatively low depth of thermal penetration (0.4mm), excellent haemostasis and a wide range of tissue effects.

**MATERIAL AND METHODS**

A prospectively collected case series of all patients with oropharyngeal squamous cell carcinoma undergoing laser resection using the Holmium:Yag laser technique only over a 15 year period at a tertiary referral centre. The hospital ethics committee approved this study as it did not affect the standard of care offered to the patients.

***Surgical technique***

All patients were operated on under general anaesthetic with a laser-safe endotracheal tube. Typically laser resection was performed first using an operating microscope, followed by neck dissection. The tumour was held with a Luc’s forceps or Allis clamp. The Ho:Yag laser was implemented via a fibre delivery system. The Holmium:Yag laser fibre, of 550 micron diameter, was inserted through a Zoellner sucker and attached via steri-strips to a second Zoellner suction to provide smoke evacuation. The settings were 1J/pulse, 15 Hz, 15W in a continuous delivery modality via a foot pedal control. The procedure is simple, bloodless, effective and quick. All surgeries were performed as day cases.

**RESULTS**

27 oropharyngeal squamous cell cancer patients identified, at the following subsites: 23 lateral pharyngeal wall/tonsil, 2 anterior faucal and 2 tongue base. Of the 23 tonsil tumours, 19 required no further treatment (83% therefore had negative histopathological margins) and 4 required chemoradiotherapy (17% were incompletely excised *or* had aggressive histopathological features such as discohesive, perineural spread, vascular invasion). The 2 patients with anterior faucal pillar neoplasia needed no further treatment. Both tongue base cancer cases required further treatment in the form of chemoradiotherapy (due to positive histopathological margins).

Postoperatively, patients complained of pain locally, which resolved with regular analgesia. There were no postoperative haemorrhages. Swallowing and speech were normal after healing (10-14 d). There was one case of fistula when neck dissection was carried out simultaneously; this resolved with conservative management.

All patients were followed up with serial imaging and clinical examination. Median follow up was 84 mo. At this longer term follow up, there were no recurrences in the 19 patients who received laser resection alone. Of the remaining 6 patients who had multimodality therapy in the form of surgery and chemoradiotherapy, there was nodal recurrence in one of the tongue base cancers.

**DISCUSSION**

Over the last 20 years, the applications of lasers in otolaryngology have increased exponentially. Holmium:Yag lasers have the unique ability to vaporize, ablate (due to its longer wavelength of 2100 nm) and coagulate soft tissues alongside extremely hard materials, such as calculi, making it the laser of choice for a range of interventions for not only otolaryngologists but also in the fields of urology, orthopaedics, gastroenterological and general surgeons[6,7]. Ho:Yag has a relatively low depth of thermal penetration (0.4mm), excellent haemostasis and a wide range of tissue effects, allowing use for urological stone surgery, urethral strictures, benign prostatic hypertrophy, biliary stones, nephrectomy, laryngeal lesions, nasal polyposis, turbinoplasty and orthopaedic procedures[6]. We present a novel role for the Ho:Yag laser.

The Ho:Yag system, in its role for oropharyngeal SCC, is particularly useful as it allows a bloodless field, a lateral thermal necrosis of 2mm (thus generating an extended clearance margin from tumour) and, when used in conjunction with an operating microscope, permits magnification and closer inspection of these margins. The latter precision inspection is particularly important with regard to the superior pharyngeal constrictor, as tumours are often adjacent or partially involving this muscle and, magnification can allow at least partial preservation, which is important to prevent exposure of parapharyngeal fat and the vital structures within. A further advantage of the Ho:Yag system is that, as a result of the pulsed effects, no laser tip cooling is necessary[7,8]. In addition, these operative procedures are quick, with each taking around 20 min, and can be performed as day cases with the associated lower costs. These features make this type of laser system preferable to the standard carbon dioxide laser.

Disadvantages reported include post-operative oedema in comparison with standard techniques and pain. To avoid the potential for fistula formation, some centres recommend staged procedures, with the neck dissection performed a few weeks after the initial laser resection[6].

Overall the Ho:Yag laser was safe and effective for lateral pharyngeal wall, tonsil and faucal pillar tumours. Only a small proportion required any further treatment at long term follow up. The main group of failures were tongue base tumours as they were too difficult to access and identify. This is confirmed in recent literature and so, radiotherapy remains an important treatment regime[9]. However, trans-oral robotic surgery or lateral pharyngotomy are better surgical options at this subsite and have shown comparable outcomes to radiotherapy in experienced centres[10-12]. In addition, minimally invasive surgical techniques are associated with superior quality of life, as compared to the historically extensive open procedures and are cost-effective due to the short stays[11-13]. Further research (ECOG-3311, NTC01898494) is currently underway to ascertain the best options for these patients, particularly in the context of HPV-16 associated outcomes[14].

We recommend the addition of the Holmium:Yag laser into the armamentarium of the otolaryngologist, particularly in cases of oropharyngeal SCC, where it has been shown to be safe, cost-effective with comparable outcomes to standard therapies.

**COMMENTS**

***Background***

Oropharyngeal squamous cell carcinoma is increasing in incidence. Management is controversial due to the large human papilloma virus (HPV) cohort. The gold standard remains single modality therapy for early stage disease, either primary surgery or radiotherapy.

***Research frontiers***

Laser resection is one of the viable surgical options. Currently carbon dioxide laser is favoured but further research is warranted in different modalities.

***Innovations and breakthroughs***

In this study, the authors demonstrated through a series of patients that, Holmium:Yag laser is safe, cost-effective with comparable outcomes to standard therapies in the treatment of oropharyngeal squamous cell carcinoma (SCC).

***Applications***

Hol:Yag Laser should be added to the head and neck surgeon’s armamentarium for consideration for use on oropharyngeal SCC, excluding the tongue base.

***Peer-review***

All relevant current literature was studied and referenced.

**REFERENCES**

1 **Stein AP**, Saha S, Kraninger JL, Swick AD, Yu M, Lambert PF, Kimple RJ. Prevalence of Human Papillomavirus in Oropharyngeal Cancer: A Systematic Review. *Cancer J* 2015; **21**: 138-146 [PMID: 26049691 DOI: 10.10.1097/PPO.0000000000000115]

2 **National Cancer Institute**. Oropharyngeal cancer treatment for health professionals. Available from: URL: http//www.cancer.gov/types/head-and-neck/hp/oropharyngeal-treatment-pdq

3 **National Cancer Institute**. Oropharyngeal cancer staging. Available from: URL: http//www.cancer.org/cancer/oralcavityandoropharyngealcancer/detailedguide/oral-cavity-and-oropharyngeal-cancer-staging

4 **Parsons JT**, Mendenhall WM, Stringer SP, Amdur RJ, Hinerman RW, Villaret DB, Moore-Higgs GJ, Greene BD, Speer TW, Cassisi NJ, Million RR. Squamous cell carcinoma of the oropharynx: surgery, radiation therapy, or both. *Cancer* 2002; **94**: 2967-2980 [PMID: 12115386 DOI: 10.1002/cncr.10567]

5 **National Cancer Institute**. Oropharyngeal Cancer Treatment–for health professionals. Available from: URL: http//www.cancer.gov/types/head-and-neck/hp/oropharyngeal-treatment-pdq#link/stoc\_h2\_4

6 **Joseph J**, Jaberoo MC, Dilkes M. Holmium: YAG laser: 12-year study of indications for use and outcomes in benign and malignant otolaryngological conditions. *J Laryngol Otol* 2010; **124**: 896-898 [PMID: 20370948 DOI: 10.1017/S002221510000654]

7 **Gleich LL**, Rebeiz EE, Pankratov MM, Shapshay SM. The holmium: YAG laser-assisted otolaryngologic procedures. *Arch Otolaryngol Head Neck Surg* 1995; **121**: 1162-1166 [PMID: 7546585 DOI: 10.1001/archotol.1995.01890100070012]

8 **Fong M**, Clarke K, Cron C. Clinical applications of the holmium: YAG laser in disorders of the paediatric airway. *J Otolaryngol* 1999; **28**: 337-343 [PMID: 10604163]

9 **Mendenhall WM**, Morris CG, Amdur RJ, Hinerman RW, Werning JW, Villaret DB. Definitive radiotherapy for squamous cell carcinoma of the base of tongue. *Am J Clin Oncol* 2006; **29**: 32-39 [PMID: 16462500 DOI: 10.1097/01.coc.0000189680.60262.eb]

10 **Patel SH**, Munson ND, Grant DG, Buskirk SJ, Hinni ML, Perry WC, Foote RL, McNeil RB, Halyard MY. Relapse patterns after transoral laser microsurgery and postoperative irradiation for squamous cell carcinomas of the tonsil and tongue base. *Ann Otol Rhinol Laryngol* 2014; **123**: 32-39 [PMID: 24574421 DOI: 10.1177/0003489414521383]

11 **Grant DG**, Salassa JR, Hinni ML, Pearson BW, Perry WC. Carcinoma of the tongue base treated by transoral laser microsurgery, part two: Persistent, recurrent and second primary tumors. *Laryngoscope* 2006; **116**: 2156-2161 [PMID: 17146389 DOI: 10.1097/01.mlg.0000244176.74302.e6]

12 **Eckel HE**, Volling P, Pototschnig C, Zorowka P, Thumfart W. Transoral laser resection with staged discontinuous neck dissection for oral cavity and oropharynx squamous cell carcinoma. *Laryngoscope* 1995; **105**: 53-60 [PMID: 7837914 DOI: 10.1288/00005537-199501000-00013]

13 **Chen AM**, Daly ME, Luu Q, Donald PJ, Farwell DG. Comparison of functional outcomes and quality of life between transoral surgery and definitive chemoradiotherapy for oropharyngeal cancer. *Head Neck* 2015; **37**: 381-385 [PMID: 24431059 DOI: 10.1002/hed.23610]

14 **National Cancer Institute: Clinical trials**. Transoral Surgery Followed by Low-Dose or Standard-Dose Radiation Therapy with or without Chemotherapy in Treating Patients with HPV Positive Stage III-IVA Oropharyngeal Cancer. Available from: URL: http//www.cancer.gov/about-cancer/treatment/clinical-trials/search/view?cdrid=758406

**P-Reviewer:** Coskun A, Noussios GI **S-Editor:** Qiu S **L-Editor: E-Editor:**

**Table 1 Oropharyngeal squamous cell carcinoma staging**

|  |  |
| --- | --- |
| Tx | Primary tumour could not be assessed; information unknown |
| T0 | No evidence of primary tumour |
| Tis | Carcinoma in situ |
| T1 | Tumour less than 2 cm |
| T2 | Tumour between 2 and 4 cm |
| T3 | Tumour larger than 4 cm (or affecting epiglottis) |
| T4 | A. Moderately advanced local disease growing into local structures (larynx, tongue, palate, medial pterygoid)B. Advanced local disease, affecting internal carotid, lateral pterygoid, nasopharynx |
| Nx | Lymph nodes cannot be assed or information unknown |
| N0 | No lymph nodes affected |
| N1 | One ipsilateral lymph node, less than 3 cm |
| N2 | A. One ipsilateral lymph node between 3 and 6 cmB. Two or more ipsilateral lymph nodes, less than 6 cmC. Contralateral lymph nodes, less than 6 cm |
| N3 | Any lymph node greater than 6cm |
| M0 | No distant spread |
| M1 | Distant site affected  |