

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of radiofrequency cold ablation for respiratory papillomatosis

Treating papillomas in the throat and airways using electrical energy

Respiratory papillomatosis is a condition in which non-cancerous wart-like growths called papillomas grow in the throat or airways. It affects both children and adults and can cause voice changes and shortness of breath. The condition is caused by the human papilloma virus and can keep coming back after treatment. This procedure aims to dissolve or shrink the papillomas using an electric current. The procedure uses a lower temperature than other treatments, with minimal heat damage to surrounding healthy tissue.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in March 2012.

Procedure name

- Radiofrequency cold ablation for respiratory papillomatosis

Specialty societies

- British Association of Otorhinolaryngologists, Head and Neck Surgeons (ENT UK)
- British Association of Paediatric Otolaryngologists

Description

Indications and current treatment

Respiratory papillomatosis is a condition characterised by benign papillomatous (wart-like) growths in the respiratory tract (larynx, trachea and rarely lungs). It can affect both children and adults, causing voice changes and airway obstruction. The condition tends to recur after treatment, requiring multiple procedures to control growth of the lesions. In such cases, the condition is known as recurrent respiratory papillomatosis.

Surgical therapy is aimed at complete removal of papillomas, while preserving normal structures, maintaining airway patency and improving voice quality. Treatment options include repeated surgical debulking of the papillomas, by cold steel dissection, suction diathermy, cryotherapy, carbon dioxide (CO₂) or other lasers, or microdebridement. Any of these may be followed by systemic administration or direct injection of antiviral agents (for example, cidofovir) into the resection sites, with the aim of reducing the frequency of reoperative surgery. Tracheostomy may be needed if significant airway obstruction occurs. No single treatment method has been shown to be effective in eradicating recurrent respiratory papillomatosis.

Radiofrequency cold ablation (commonly known as coblation) uses controlled energy delivery to operate at the relatively low temperature of 60-65°C. This aims to reduce surrounding tissue damage and postoperative pain and to avoid seeding of viral particles during the thermal vaporisation process.

What the procedure involves

Radiofrequency cold ablation involves passing a radiofrequency bipolar electrical current through a medium of normal saline. This produces a plasma field of sodium ions that dissects the tissue by disrupting intercellular bonds, leading to tissue vaporisation and coagulation. Radiofrequency cold ablation heats tissue to only 60–65°C, which may produce less postoperative pain and damage to surrounding structures than conventional diathermy.

The procedure is usually done with the patient under general anaesthesia. Conventional microlaryngoscopy techniques allow introduction of a single-use radiofrequency probe into the lumen of the larynx and trachea.

Once the probe tip is in contact with the papilloma, it is activated to produce controlled tissue ablation of individual lesions, together with haemostasis and suction.

Steroids and antibiotics may be given after the procedure to reduce inflammation and the risk of infection.

Clinical assessment tools

Respiratory papillomatosis is difficult to stage. One of the more accepted scoring methods is the Derkey system, in which the surgeon assigns a score of 0–3 to each site in the aero-digestive tract (0 = absent, 1 = surface lesion, 2 = raised lesion and 3 = bulky lesion). A composite score is generated by summing the score at each involved site.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to radiofrequency cold ablation for respiratory papillomatosis. Searches were conducted of the following databases, covering the period from their commencement to 28 March 2012: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with respiratory papillomatosis.
Intervention/test	Radiofrequency cold ablation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on 32 patients from 5 case series and 1 case report.

Table 2 Summary of key efficacy and safety findings on radiofrequency cold ablation for respiratory papillomatosis

Abbreviations used: CO ₂ , carbon dioxide; RRP, recurrent respiratory papillomatosis			
Study details	Key efficacy findings	Key safety findings	Comments
<p>She (2011)¹</p> <p>Case series</p> <p>China</p> <p>Recruitment period: 2008-10</p> <p>Study population: Adult patients with laryngeal papilloma</p> <p>n = 18 (14 patients with single laryngeal papilloma and 4 patients with multiple laryngeal papilloma)</p> <p>Age: not reported</p> <p>Sex: not reported</p> <p>Patient selection criteria: Not reported</p> <p>Technique: All patients were treated with Coblator™ Reflex #7070 under general anaesthesia without tracheotomy.</p> <p>Follow-up: 18 months (median)</p> <p>Conflict of interest/source of funding: Not reported</p>	<p>Number of patients analysed: 18</p> <p>Recurrence of respiratory papillomas</p> <p>88.9% (16/18) patients had no recurrence during follow-up.</p> <p>Recurrence occurred in 11.1% (2/18) of patients, 1 occurred 4 months and the other 8 months after the procedure. Both were retreated by the same procedure and followed up for 4 months and 12 months, respectively. Recurrence occurred again in 1 patient.</p>	<p>There was no postoperative bleeding or other complications.</p> <p>The volumes of blood loss during surgery varied from 1–10 ml; 2 ml was the average.</p> <p>Safety findings identified in Chinese language full-text</p> <p>Tissue scarring</p> <p>Minor scarring around the ablated tissues was reported in all patients.</p> <p>Appearance of respiratory papillomas at another location</p> <p>Four months after the procedure, there was no recurrence of respiratory papillomas at the original ablated site in 1 patient, but respiratory papillomas appeared at another location. Radiofrequency cold ablation was repeated with no recurrence at 2 month follow-up.</p>	<p>Abstract only. Full-text in Chinese language.</p> <p>Follow-up issues:</p> <ul style="list-style-type: none"> Unclear what assessment was carried out during follow-up. <p>Study population issues:</p> <ul style="list-style-type: none"> Unknown from abstract whether study population had respiratory papillomatosis before.

Abbreviations used: CO ₂ , carbon dioxide; RRP, recurrent respiratory papillomatosis												
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<p>Carney (2010)²</p> <p>Case series</p> <p>Australia</p> <p>Recruitment period: not reported</p> <p>Study population: Adult patients with advanced laryngotracheal RRP</p> <p>n = 6</p> <p>Age: 34 (median)</p> <p>Sex: 50% male</p> <p>Patient selection criteria: Patients who were treated for at least 2 years by CO₂ laser vaporisation with or without intralesional cidofovir and subsequently treated with radiofrequency cold ablation with or without intralesional cidofovir for a further 2 years.</p> <p>Technique: All patients were treated under general anaesthesia using jet ventilation. A 0° Hopkins rod endoscope and camera were used with a Storz C laryngoscope (Storz, Tuttlingen, Germany) to visualise the tracheobronchial lesions. A modified, three-electrode,</p>	<p>Number of patients analysed: 6</p> <p>Increase in time interval between radiofrequency cold ablation procedures compared with time interval between CO₂ laser procedures required to maintain disease control</p> <table border="1"> <thead> <tr> <th>Definition</th> <th>No. of patients</th> <th>Reported p-value</th> </tr> </thead> <tbody> <tr> <td>Modest increase (< 25% increased time interval)</td> <td>3</td> <td>Not reported</td> </tr> <tr> <td>Significant increase (> 50% increased time interval)</td> <td>3</td> <td>0.0342</td> </tr> </tbody> </table> <p>Other findings</p> <p>After a number of radiofrequency cold ablation resections 1 patient's papillomas became less exophytic, tending to a more sessile appearance, a finding not previously reported for laser procedures.</p>	Definition	No. of patients	Reported p-value	Modest increase (< 25% increased time interval)	3	Not reported	Significant increase (> 50% increased time interval)	3	0.0342	<p>None reported.</p>	<p>Follow-up issues:</p> <ul style="list-style-type: none"> Actual number of years patient received CO₂ laser or radiofrequency cold ablation treatment was not reported. <p>Study design issues:</p> <ul style="list-style-type: none"> This is a retrospective comparative study. There could be potential bias in patient selection. <p>Study population issues:</p> <ul style="list-style-type: none"> All patients exhibited marked differences in the severity of their RRP, from advanced laryngeal disease with only solitary tracheal lesions, to almost complete circumferential papillomas involving most of the trachea with minimal laryngeal disease. Three patients had juvenile onset RRP. It was unclear if the natural history of the disease between
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<p>bipolar radiofrequency device (Coblator I; Arthrocare, Sunnyvale, California, USA) was used to ablate papillomas. Before each insertion into the airway, the wand tip was placed in saline gel to create an adequate environment for the radiofrequency cold ablation plasma field. The power level was set to provide 800–1200 J of energy. Papillomas were ablated by placing the tip of the wand over the lesions at a 90° angle where possible to minimise surrounding thermal damage.</p> <p>Follow-up: not reported</p> <p>Conflict of interest/source of funding: One author is currently a member of the International Medical Advisory Board of the device manufacturer. He has received funding/sponsorship from the device manufacturer to lecture on radiofrequency cold ablation technology at sponsored postgraduate meetings.</p>			<p>juvenile and adult onset RRP was different.</p> <ul style="list-style-type: none"> Four patients had been treated previously with intralesional cidofovir after laser resection but were regarded as having no response, although intralesional treatment was also continued in these 4 patients after radiofrequency cold ablation. There was uncertainty about the potential impact of intralesional cidofovir on time interval in the longer term in patients who have no previous responded to it. <p>Other issues:</p> <ul style="list-style-type: none"> The radiofrequency cold ablation device used was originally designed for orthopaedic use.

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<p>Peters (2011)³</p> <p>Case series (3 case reports)</p> <p>USA</p> <p>Recruitment period: not reported</p> <p>Study population: patient with recurrent papilloma of the nasopharynx</p> <p>n = 3 (4 procedures)</p> <p>Age: 52, 55 and 66</p> <p>Sex: 67% male</p> <p>Patient selection criteria: Endoscopic examination of patient 1 revealed nasopharyngeal multifocal papillomas. Endoscopic examination of patient 2 revealed a 3 cm sessile papilloma on the nasopharyngeal surface of the soft palate. Endoscopic examination of patient 3 revealed a 2 cm papilloma on the nasopharyngeal surface of the soft palate near the midline.</p> <p>Technique: patients were treated with endoscopic transnasal radiofrequency cold ablation. An Arthrocare EVac 70 Coblator (setting:</p>	<p>Number of patients analysed: 3</p> <p>Operative success</p> <table border="1"> <thead> <tr> <th></th> <th>Patient 1</th> <th>Patient 2</th> <th>Patient 3</th> </tr> </thead> <tbody> <tr> <td>Immediately after radio frequency cold ablation</td> <td>Denied any dysphagia or symptoms of velopharyngeal insufficiency (difficulties swallowing or speaking)</td> <td>Denied dysphagia, nasopharyngeal reflux or globus</td> <td>Patient was asymptomatic</td> </tr> <tr> <td>Recurrence of respiratory papillomatosis</td> <td>A small recurrent lesion of the right fossa of Rosenmuller (3 mm) was found at about 4 months after initial treatment with radio frequency cold ablation</td> <td>No evidence of recurrence at 15-month follow-up</td> <td>No evidence of recurrence at 17-month follow-up</td> </tr> <tr> <td>Management and outcome of recurrent respiratory papillomatosis after first radio frequency cold ablation treatment</td> <td>Radio frequency cold ablation was repeated with no evidence of recurrent disease at 2-month follow-up</td> <td></td> <td></td> </tr> <tr> <td>Other notes</td> <td>Patient later</td> <td></td> <td></td> </tr> </tbody> </table>				Patient 1	Patient 2	Patient 3	Immediately after radio frequency cold ablation	Denied any dysphagia or symptoms of velopharyngeal insufficiency (difficulties swallowing or speaking)	Denied dysphagia, nasopharyngeal reflux or globus	Patient was asymptomatic	Recurrence of respiratory papillomatosis	A small recurrent lesion of the right fossa of Rosenmuller (3 mm) was found at about 4 months after initial treatment with radio frequency cold ablation	No evidence of recurrence at 15-month follow-up	No evidence of recurrence at 17-month follow-up	Management and outcome of recurrent respiratory papillomatosis after first radio frequency cold ablation treatment	Radio frequency cold ablation was repeated with no evidence of recurrent disease at 2-month follow-up			Other notes	Patient later			<p>There were no complications.</p>	<p>Follow-up issues:</p> <ul style="list-style-type: none"> There was no fixed duration of follow-up. <p>Study design issues:</p> <ul style="list-style-type: none"> Only 1 patient was reported to have received intralesional cidofovir injection after radiofrequency cold ablation. <p>Study population issues:</p> <ul style="list-style-type: none"> One patient had active acquired immune deficiency syndrome.
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coblation™-9, coagulation-5) was used. Dissections were carried out down to the underlying fascia (in 1 patient) / muscle (in all patients) to ensure complete excision. Patient 2 received cidofovir injection into the wound bed upon complete excision of the lesion. Follow-up: 6 months (patient 1); 15 months (patient 2); 17 months (patient 3) Conflict of interest/source of funding: None declared		died because of an unrelated cause			

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<p>Timms (2007)⁴</p> <p>Case series (2 case reports)</p> <p>India and United Kingdom</p> <p>Recruitment period: not reported</p> <p>Study population: adult patients with extensive and recurrent laryngeal papillomas</p> <p>n = 2</p> <p>Age: 38 and 41</p> <p>Sex: 50% male</p> <p>Patient selection criteria: One patient presented with severe hoarseness and exertional dyspnoea. She had extensive papillomas on both vocal folds. The other patient had extensive papillomas affecting the glottis and supraglottis. Both patients had previously received surgical treatment, including cold steel surgery and laser techniques for their respiratory papillomatosis.</p> <p>Technique: A microlaryngeal tube was used in 1 patient. An expandable laser</p>	<p>Number of patients analysed: 2</p> <p>Operative success</p> <p>Patient 1 (patient presented with severe hoarseness and exertional dyspnoea)</p> <table border="1"> <thead> <tr> <th>Follow-up</th> <th>Outcome</th> </tr> </thead> <tbody> <tr> <td>Immediately after the procedure</td> <td>The appearance of the larynx was normal.</td> </tr> <tr> <td>2-month</td> <td>Patient was found to have good voice and no exertional dyspnoea.</td> </tr> <tr> <td>6-month</td> <td>Remained well.</td> </tr> </tbody> </table>	Follow-up	Outcome	Immediately after the procedure	The appearance of the larynx was normal.	2-month	Patient was found to have good voice and no exertional dyspnoea.	6-month	Remained well.	<p>Patient 1 (patient presented with severe hoarseness and exertional dyspnoea)</p> <table border="1"> <thead> <tr> <th>Follow-up</th> <th>Outcome</th> </tr> </thead> <tbody> <tr> <td>Immediately after the procedure</td> <td>The appearance of the larynx was normal, with no signs of charring or bleeding. Patient's recovery was uneventful, and no signs of oedema were seen on endoscopic examination the following morning.</td> </tr> </tbody> </table> <p>Patient 2 (patient had extensive papillomas affecting the glottis and supraglottis)</p> <table border="1"> <thead> <tr> <th>Follow-up</th> <th>Outcome</th> </tr> </thead> <tbody> <tr> <td>Immediately after the procedure</td> <td>Patient discharged on same day of procedure with no complications.</td> </tr> <tr> <td>4-month</td> <td>A mucosal wave was seen bilaterally at laryngeal stroboscopy.</td> </tr> </tbody> </table>	Follow-up	Outcome	Immediately after the procedure	The appearance of the larynx was normal, with no signs of charring or bleeding. Patient's recovery was uneventful, and no signs of oedema were seen on endoscopic examination the following morning.	Follow-up	Outcome	Immediately after the procedure	Patient discharged on same day of procedure with no complications.	4-month	A mucosal wave was seen bilaterally at laryngeal stroboscopy.	<p>Follow-up issues:</p> <ul style="list-style-type: none"> Unclear what assessment was carried out during follow-up. <p>Other issues:</p> <ul style="list-style-type: none"> There was no formal tool to assess treatment efficacy for example voice recording analysis. There was no formal statistical comparison of event recurrence before and after the procedure. A mucosal wave is the ripple that passes along a normal vocal cord during phonation. It is changed when vocal fold scar is present. Vocal fold scar causes the mucosal wave to be irregular and/or reduced in both speed and extent of movement (amplitude).
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<p>laryngoscope was used to gain adequate exposure of the larynx in the other patient. The procedures were performed in the two patients using different wands, an Evac 70 wand (Arthrocare, Sunnyvale, California, USA) and an EIC070 wand (Arthrocare). No antibiotics or steroids were used in either patient.</p> <p>Follow-up: up to 6 months</p> <p>Conflict of interest/source of funding: None</p>			

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<p>Psaltis (2003)⁵</p> <p>Case series (2 case reports)</p> <p>Australia</p> <p>Recruitment period: not reported</p> <p>Study population: Adult patients with advanced laryngotracheal papillomatosis. Both patients had juvenile onset RRP diagnosed in their infant years</p> <p>n = 2</p> <p>Age: 25 and 26</p> <p>Sex: 100% male</p> <p>Patient selection criteria: Both patients had undergone multiple previous treatments to their airway with CO₂ laser.</p> <p>Technique: Both patients were treated under general anaesthesia and oxygenated using jet ventilation. A long 0-degree Hopkin's Rod endoscope through a Storz C laryngoscope was used to provide visualisation of the lesions and a modified Arthrocare orthopaedic 3-electrode probe</p>	<p>Number of patients analysed: 2</p> <p>Disease recurrence</p> <p>Patient 1</p> <table border="1"> <tr> <td>Treatment received</td> <td>CO₂ laser (treatment received before radio frequency cold ablation)</td> <td>Radiofrequency cold ablation</td> </tr> <tr> <td>No. of treatments received</td> <td>77</td> <td>Not reported</td> </tr> <tr> <td>Location of papillomas treated</td> <td>Larynx, nasal septum and upper trachea (up to 4 cm below the vocal cord)</td> <td>Superior trachea and supraglottic trachea</td> </tr> <tr> <td>Operative success immediately after the procedure</td> <td>Not reported</td> <td>The lower trachea and main bronchi appeared clear of papillomas</td> </tr> <tr> <td>Treatment interval</td> <td>Approximately 3 months</td> <td>Subsequent procedures demonstrated reduction in disease recurrence and an extended time period between ablation sessions</td> </tr> </table>		Treatment received	CO ₂ laser (treatment received before radio frequency cold ablation)	Radiofrequency cold ablation	No. of treatments received	77	Not reported	Location of papillomas treated	Larynx, nasal septum and upper trachea (up to 4 cm below the vocal cord)	Superior trachea and supraglottic trachea	Operative success immediately after the procedure	Not reported	The lower trachea and main bronchi appeared clear of papillomas	Treatment interval	Approximately 3 months	Subsequent procedures demonstrated reduction in disease recurrence and an extended time period between ablation sessions	<p>Patient 1</p> <table border="1"> <tr> <td>Treatment received</td> <td>CO₂ laser (treatment received before radio frequency cold ablation)</td> <td>Radio frequency cold ablation</td> </tr> <tr> <td>Complications</td> <td>Scarring of both cords and posterior inter-arytenoid space and anterior and posterior glottis webs; patient developed bronchospasm resulting in 1 treatment episode being abandoned</td> <td>None reported</td> </tr> </table> <p>Patient 2</p> <table border="1"> <tr> <td>Treatment received</td> <td>CO₂ laser (treatment received before radio frequency cold ablation)</td> <td>Radio frequency cold ablation for proximal lesions and CO₂ laser for distal lesions</td> </tr> <tr> <td>Complications</td> <td>Bilateral pneumo-</td> <td>None reported</td> </tr> </table>	Treatment received	CO ₂ laser (treatment received before radio frequency cold ablation)	Radio frequency cold ablation	Complications	Scarring of both cords and posterior inter-arytenoid space and anterior and posterior glottis webs; patient developed bronchospasm resulting in 1 treatment episode being abandoned	None reported	Treatment received	CO ₂ laser (treatment received before radio frequency cold ablation)	Radio frequency cold ablation for proximal lesions and CO ₂ laser for distal lesions	Complications	Bilateral pneumo-	None reported	<p>Follow-up issues:</p> <ul style="list-style-type: none"> Duration of follow-up not reported. Unclear how many times radiofrequency cold ablation was repeated. <p>Study design issues:</p> <ul style="list-style-type: none"> Patient 2 was subsequently treated with a combination of radiofrequency cold ablation and CO₂ laser. Thus, treatment effectiveness must not be attributed only to radiofrequency cold ablation. <p>Other issues:</p> <ul style="list-style-type: none"> Actual treatment interval between subsequent radiofrequency cold ablation procedures was not reported. The radiofrequency cold ablation device used for both patients was originally designed for orthopaedic use in the ablation of
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<p>radiofrequency ablation device (coblator) was used to ablate the papillomas. Before each insertion into the airway, the wand tip was placed in saline to ensure the formation of a plasma conduction field. With the controller panel set to a power level between two and four (providing 800–1200 J of energy), the tip of the wand was placed at a 90-degree angle to the papillomas to avoid collateral mucosal damage. Lesions were ablated until the underlying submucosa came into view. The distal lesions that could not be reached by the coblator™ were ablated using the CO₂ laser bronchoscope.</p> <p>Follow-up: not reported</p> <p>Conflict of interest/source of funding: not reported</p>	Patient 2		<table border="1"> <tr> <td></td> <td>thoraces, proximal tracheal strictures, delayed bronchospasm and an asystolic cardiac arrest</td> <td></td> </tr> </table>		thoraces, proximal tracheal strictures, delayed bronchospasm and an asystolic cardiac arrest		<p>knee menisci and only reached to 5 cm below the vocal cord. Thus, it cannot be used to ablate papillomas in the distal half of the trachea.</p> <ul style="list-style-type: none"> • Images of the appearance of the trachea were before and after the procedures were presented in the paper. The papillomas appeared to have been removed but this is subjective analysis based on study of the images. There was no formal assessment and statement given by the authors. • There is potential overlap of the patient population with Carney (2010)².
		thoraces, proximal tracheal strictures, delayed bronchospasm and an asystolic cardiac arrest					
	Treatment received	CO ₂ laser (treatment received before radio frequency cold ablation)		Radio frequency cold ablation for proximal lesions and CO ₂ laser for distal lesions			
	No. of treatments received	56		Not reported			
	Location of papillomas	Widespread, from base of the epiglottis to the entrance of the right main bronchus.		Massive circumferential papillomas in trachea (< 10% of the lumen visible)			
	Treatment interval	Not reported		Not reported			
Treatment effectiveness		Subsequent procedures demonstrated a reduction in papilloma regrowth					

Abbreviations used: CO ₂ , carbon dioxide; RRP, recurrent respiratory papillomatosis			
Study details	Key efficacy findings	Key safety findings	Comments
<p>Rachmanidou (2011)⁶</p> <p>Case report</p> <p>United Kingdom</p> <p>Recruitment period: not reported</p> <p>Study population: paediatric patient with laryngeal papillomatosis n = 1</p> <p>Age: 32 months</p> <p>Sex: female</p> <p>Patient selection criteria: paediatric patient with hoarse cry and very croaky voice since birth, presenting with a large laryngeal papilloma occupying the anterior commissure and the anterior thirds of both vocal folds. Derkay staging of lesion score: 12.</p> <p>Technique: The papillomatous lesion was excised using an Evac 70Xtra wand (Arthrocare, USA). Saline-soaked neuropatties were used in the subglottis to prevent distal airway seeding of papilloma lesions. The lesion was ablated at a setting of 7 and a</p>	<p>Number of patients analysed: 1</p> <p>Recurrence of respiratory papillomatosis</p> <p>No sign of recurrence during follow-up at 3 and 18 months.</p> <p>Voice quality</p> <p>Dramatic improvement (with additional assistance from speech therapy sessions).</p>	<p>There was minimal bleeding during the procedure.</p>	<p>Study design issues:</p> <ul style="list-style-type: none"> The authors commented that the EIC 7070 laryngeal wand would have been more suitable but was not available for the procedure. This wand is slimmer (4 mm in diameter), longer (25 cm in length) and has a 30° bend at its distal tip. The malleable tip design provides easier access to the anterior commissure, together with optimal visibility for the surgeon. <p>Other issues:</p> <ul style="list-style-type: none"> This case report involves the use of radiofrequency cold ablation for de novo respiratory papillomatosis. A formal tool to assess voice quality was not defined, potentially subjective measures were used. There is thus the potential for biased assessment.

Abbreviations used: CO ₂ , carbon dioxide; RRP, recurrent respiratory papillomatosis			
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<p>coagulation setting of 3. Saline irrigation and suction were used throughout the operation. Follow-up: 18 months</p> <p>Conflict of interest/source of funding: none declared</p>			

Efficacy

Recurrence of respiratory papillomatosis

In a case series of 3 adult patients with recurrent papillomas of the nasopharynx, only 1 patient had a recurrent lesion at 4-month follow-up, which was successfully re-excised with endoscopic transnasal radiofrequency cold ablation³.

A case series reported 'reduced disease recurrence' (no further details provided) in 2 adult patients with juvenile-onset recurrent respiratory papillomatosis who had previously been treated repeatedly by CO₂ laser ablation; 1 was treated by radiofrequency cold ablation treatment alone and 1 by radiofrequency cold ablation together with CO₂ laser ablation⁵.

In a case report of 1 paediatric patient with a large de novo laryngeal papilloma treated by radiofrequency cold ablation alone, there was no sign of recurrence at 18-month follow-up⁶.

Interval between treatment sessions

In a case series of 6 adult patients with advanced laryngotracheal recurrent respiratory papillomatosis who had previously received at least 2 years of treatment by CO₂ laser ablation followed by at least 2 years of treatment by radiofrequency cold ablation, there was a significant increase (>50%) in the interval between treatments in 3 patients when radiofrequency cold ablation was introduced ($p=0.03$) and a modest increase (<25%) in the interval between treatments in the other 3 patients (p value not reported)².

In the case series of 2 adult patients, the interval between ablation sessions was increased in 1 patient who was initially treated by CO₂ laser ablation before being subsequently treated with radiofrequency cold ablation (actual interval between procedures not reported)⁵.

Voice quality

In another case series of 2 adult patients with extensive and recurrent laryngeal papillomas, 1 patient who presented with severe hoarseness and exertional dyspnoea was found to have a good voice with no exertional dyspnoea at 2-month follow-up (no formal assessment of voice quality reported)⁴. This patient remained well at 6-month follow-up. No results were reported for the other patient who presented with extensive papillomas affecting the glottis and supraglottis.

In the case report of 1 paediatric patient, a dramatic improvement in voice quality was observed, although the patient also had speech therapy (no formal assessment of voice quality reported)⁶.

Safety

Tissue scarring

Minor scarring around the ablated tissues was reported in all patients in the case series of 18 patients (method of assessment of scarring not described)¹.

Appearance of respiratory papillomas at another location

Respiratory papillomas appeared at a new location 4 months after radiofrequency cold ablation in 1 patient in the case series of 18 patients¹. The procedure was repeated with no further recurrence at 2-month follow-up.

Other findings

There was minimal bleeding during the procedure in the case report of 1 paediatric patient⁶.

Validity and generalisability of the studies

- The studies used different devices, some of which were modified devices originally indicated for orthopaedic procedures.
- Avoiding damage to surrounding tissue is highly dependent on the technique and skills of the surgeon performing the procedure to ensure controlled manoeuvre of the radiofrequency cold ablation device.
- The natural history of juvenile-onset and adult-onset recurrent respiratory papillomatosis might differ. The studies presented in this overview are mostly case series or case reports with no control arm.

Existing assessments of this procedure

- Aetna, a health insurer in the USA, in its Clinical Policy Bulletin: Coblation™ Non-thermal Volumetric Tissue Reduction (Number: 0475) states:

‘Aetna considers Coblation™ non-thermal volumetric tissue reduction experimental and investigational for all other indications (for example, laryngo-tracheal papillomatosis) due to insufficient evidence in the peer-reviewed literature.’

Related NICE guidance

There is currently no NICE guidance related to this procedure.

Specialist Advisers’ opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Neil Bateman, Michael Kuo and Gavin A J Morrison (British Association of Paediatric Otolaryngologists), Benjamin Hartley (British Association of Otorhinolaryngologists, Head and Neck Surgeons [ENT UK]).

- All Specialist Advisers have never performed the procedure.
- Two Specialist Advisers considered the procedure to be definitely novel and of uncertain safety and efficacy. One of the two Specialist Advisers considered it to fall between a minor change in technique with equipment that is well established for other areas and a new procedure. Two other Specialist Advisers considered it to be a minor variation of an existing procedure, which is unlikely to alter the procedure's safety and efficacy.
- CO₂ laser, microdebridement, potassium titanyl phosphate laser (KTP laser) and cold steel excision would be comparators to the procedure.
- Theoretical adverse events include laryngeal or airway scarring, with airway stenosis and dysphonia as possible consequences of scarring to the larynx, bleeding and inadequate reduction in the number and size of papillomas, leading to inability to maintain a safe airway.
- One Specialist Adviser was concerned about safety of the procedure to voice (quality) and airway (patency). One Specialist Adviser noted that it is very difficult, if not impossible, to measure scarring objectively.
- Key efficacy outcomes include reduction of the number or frequency of microlaryngoscopy procedures required to maintain a safe airway and achievement of good voice quality. Other efficacy outcomes are endoscopic and photographic evidence of ablation of papillomatosis and establishment of an airway macroscopically free of papillomatosis.
- Uncertainty remains about whether the treatment holds advantages over the current gold standard treatments. It might theoretically do so, because the low temperature could avoid collateral tissue damage and the haemostatic properties may mean no bleeding and so less risk of inadvertent spread of the virus to more distal airway sites.
- Training to use the device, including surgeon education with mentoring and support, is needed.
- All Specialist Advisers thought that this procedure would have a minor impact on the NHS.
- One Specialist Adviser thought that this procedure should be confined to larger units such as a university type tertiary centre. He added that it will not be easy to establish any level 1 or even good level 2 evidence because recurrent respiratory papillomatosis is too infrequent and surgical trials in this area are fraught with difficulty. He emphasised the usefulness of more clinical case series, comparing results with other treatments. Another Specialist Adviser also noted that respiratory papillomatosis is a relatively uncommon condition and therefore appropriately powered trials may be difficult to establish.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

- One of the studies included in table 2 of this overview is a Chinese language paper. The reason for inclusion is the report of minor scarring around the ablated tissues and appearance of respiratory papillomas at another location, which have not been reported by other studies.

References

1. She CP, Zhang QF and Cheng CJ (2011) Coblation treatment for laryngeal papilloma in adult [Chinese]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi = Chinese Journal of Otorhinolaryngology Head and Neck Surgery* 46(4) 336–338
2. Carney AS, Evans AS, Mirza S and Psaltis A (2010) Radiofrequency coblation for treatment of advanced laryngotracheal recurrent respiratory papillomatosis. *Journal of Laryngology and Otology* 124(5) 510–514
3. Peters G, McLaughlin K and Nuss DW (2011) Treatment of nasopharyngeal papillomatosis with coblation: a case series. *International Forum of Allergy and Rhinology* 1(5) 405–408
4. Timms MS, Bruce IA and Patel NK (2007) Radiofrequency ablation (coblation): A promising new technique for laryngeal papillomata. *Journal of Laryngology and Otology* 121(1) 28–30
5. Psaltis A. and Carney AS (2003) The use of radiofrequency ablation in the treatment of tracheal papillomatosis: A case report. *Australian Journal of Otolaryngology* 6(2) 86–88
6. Rachmanidou A. and Modayil PC (2011) Coblation resection of paediatric laryngeal papilloma. *Journal of Laryngology and Otology* 125(8) 873–876

Appendix A: Additional papers on radiofrequency cold ablation for respiratory papillomatosis

There were no additional papers identified.

Appendix B: Related NICE guidance for radiofrequency cold ablation for respiratory papillomatosis

There is currently no NICE guidance related to this procedure.

Appendix C: Literature search for radiofrequency cold ablation for respiratory papillomatosis

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	28/03/12	Issue 3 of 12, Mar 2012
Database of Abstracts of Reviews of Effects – DARE (CRD website)	28/03/12	-
HTA database (CRD website)	28/03/12	-
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	28/03/2012	Issue 3 of 12, Mar 2012
MEDLINE (Ovid)	28/03/12	1946 to March Week 2 2012
MEDLINE In-Process (Ovid)	28/03/12	<March 27, 2012
EMBASE (Ovid)	28/03/12	1980 to 2012 Week 12
CINAHL (NLH Search 2.0/)	28/03/12	1981-present

Trial sources searched on 28/03/2012

- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov
- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database

Websites searched

- National Institute for Health and Clinical Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference search
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Papilloma/
2	Papillom*.tw.
3	RRP.tw.
4	JORRP.tw.
5	AORRP.tw.
6	Papillomavirus Infections/
7	Laryngeal Neoplasms/
8	(Laryng* adj3 (neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or

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tumor* or malignan*).tw.

9 or/1-8

10 Cryosurgery/

11 (cryosury* or cryoablat* or cryotherap* or coblat*).tw.

12 ((Cold* or control* or radiofreq*) adj3 ablat*).tw.

13 radiofreq*.tw.

14 RF.tw.

15 RFA.tw.

16 (coblat* adj3 radiofreq*).tw.

17 Debulk*.tw.

18 Ablation Techniques/

19 (ablat* adj3 techniq*).tw.

20 Debridement/is [Instrumentation]

21 debride*.tw.

22 (plasma* adj3 wand*).tw.

23 or/10-22

24 9 and 23

25 Animals/ not Humans/

26 24 not 25