NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of phototherapeutic laser keratectomy for corneal surface irregularities

Eye disorders in which the outer clear layer of the eye (the cornea) becomes scarred, uneven, less flexible, or develops recurrent ulcers may result in loss of ability to focus sharply.

Phototherapeutic keratectomy uses a laser to remove layers of the cornea in order to produce a smooth, even surface with the aim of improving vision.

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 2010.

Procedure name

- Phototherapeutic laser keratectomy for corneal surface irregularities

Specialty societies

- Royal College of Ophthalmologists
- The College of Optometrists

Description

Indications and current treatment

Symptomatic corneal surface irregularities may result from a range of pathologies including band keratopathy, corneal scarring, nodular degeneration, epithelial basement membrane dystrophy or other dystrophies. Symptoms may include loss of visual acuity, pain, sensitivity to light and foreign body sensation.

Treatment aims to restore a normal regular corneal surface and adherence between the epithelium and Bowman's membrane (a basement membrane that lies between the outer layer of stratified epithelium and the substance of the cornea), with associated improvement in visual acuity and comfort.

Depending on severity and the underlying condition, treatment options may include lubrication of the ocular surface, bandage contact lens placement, or topical medication. Surgical procedures may include anterior stromal puncture, mechanical debridement, lamellar keratoplasty or resurfacing keratectomy using a diamond burr. Refractory eyes may require corneal transplantation.

What the procedure involves

Local anaesthetic eyedrops are applied and the corneal epithelium is mechanically removed. A laser is used to sequentially ablate uniformly thin layers of corneal tissue, to create a smooth surface which then becomes re-epithelialised. Postoperative management consists of an eye pad, topical antibiotics, sedatives and non-steroidal anti inflammatory drugs (NSAIDs).

The proposed advantage of this procedure is that it creates a smooth stromal surface which may improve postoperative corneal clarity, decrease existing scarring, and facilitate subsequent epithelial adhesion.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to phototherapeutic laser keratectomy for corneal surface irregularities. Searches were conducted of the following databases, covering the period from their commencement to 6 January 2010 and updated to 6 May 2010: 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 corneal surface irregularities
Intervention/test	Phototherapeutic laser keratectomy (PTK)
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 approximately 661 patients from 1 non-randomised controlled study[1], 3 case series[2,3,4], and 4 case reports[5,6,7,8].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on phototherapeutic laser keratectomy for corneal surface irregularities

Abbreviations used: BCVA, best corrected visual acuity; PTK, photo therapeutic keratectomy; D, Diopters; UCVA, uncorrected visual acuity

Study details	Key efficacy findings	Key safety findings	Comments
Sridhar M S (2002) [1] **Non-randomised controlled study** USA Recruitment period: 1992 to 2000 Study population: Symptomatic recurrent corneal erosions associated with anterior basement membrane dystrophy. **n = 39 (42 eyes) (15 PTK Vs 27 Diamond burr)** Age: 48 years (mean) Sex: 54% female Patient selection criteria: Painful episodes at night or on waking in conjunction with epithelial irregularity on slit lamp examination. Anterior basement membrane dystrophy Technique: Topical anesthesia and removal of epithelium with a blunt spatula. PTK with excimer laser with attempt not to leave the border of the epithelial defect within the visual axis Vs diamond burr to gently and uniformly polish Bowman's membrane in the area of defect. Standard cycloplegic, NSAID, and antibiotic postoperative regimen in both groups **Follow-up: 7 months mean** Conflict of interest/source of funding: One author supported by a grant	Number of patients analysed: **35 eyes (14 PTK Vs 21 Diamond burr)** Outcome — PTK — diamond burr BCVA Better — 35.7% (5/14) — 14.3% (3/21) Unchanged — 64.3% (9/14) — 81.0% (17/21) Worse — 0% (0/14) — 4.8% (1/21) (p=0.6)	**Complications** Rate per eye Outcome — PTK — diamond burr Mild Haze — 33.3% (5/15) — 25.9% (7/27) (p=0.38) Erosion recurrence — 26.7%(4/15) — 11.1% (3/27) (p=0.73) Mean time to 1st recurrence (months) — 9.7 ± 6.1 — 5.9 ± 2.1 Measurement of significance not reported.	**Follow-up issues**: Retrospective study. BCVA outcomes for the PTK group are calculated without 1 patient, and the diamond burr group without 6 patients who were lost to follow up. **Study design issues**: Patients self selected for treatment group. **Study population issues**: In the PTK group 1 patient had a history of eye trauma, 3 had undergone previous epithelial debridement, 1 an anterior stromal puncture, and 1 a bandage contact lens. In the diamond burr group 5 patients had a history of eye injury, one had undergone anterior stromal puncture, and two had bandage contact lens There was no statistically significant difference between group at baseline in terms of age or gender. **Other issues**: Rate of mild haze in the PTK group was calculated per patients and not per eye. Percentage has been recalculated here.

Abbreviations used: BCVA, best corrected visual acuity; PTK, photo therapeutic keratectomy; D, Diopters; UCVA, uncorrected visual acuity

Study details	Key efficacy findings	Key safety findings	Comments
Föster W (1997)[2] **Case series** Germany Recruitment period: not reported Study population: patients with recurrent erosions, pterygia, band-like keratopathy, or 'special indications' n = **216 (252 eyes)** Age: not reported Sex: not reported Patient selection criteria: patients without herpes infection, conjunctivitis, blepharitis, uncontrollable uveitis, or systemic disease that might influence corneal healing. Technique: topical or local anaesthesia, PTK with excimer laser ablating a zone of 3 to 8 mm. **Follow-up: 9 months (minimum)** Conflict of interest/source of funding: supported by manufacturer	**Number of patients analysed: 216 (252 eyes)** Group 1: recurrent erosion 103 eyes Further recurrent erosion occurred in 8.7% (9/103) of eyes at a minimum follow up of 12 months. 6 of these patients had idiopathic recurrent erosions. Group 2: pterygia 86 eyes 44.2% (38/86) of eyes had recurrence of pterygia at a minimum follow up of 11 months. Group 3: band-like keratopathy 29 eyes All patients were pain free after epithelial closure by 6 days follow up. Recurrence occurred in 24.1% (7/29) of eyes at 9 months follow up. In all eyes with recurrence there was rough band-like keratopathy at baseline and not all calcifications were removed. Postoperatively the maximm hypermetropioa measured was +4D, and maximum astigmatism -4.5D. Group 4: special indication (including scarring) 34 eyes Two patients with an amyloid of the cornea had an almost clear cornea after surgery and visual acuity improved from 10/200 to 20/30. In a patient with alkali burn there was no improvement in visual acuity. In a patient with acanthamoebic keratitis after epithelial closure visual acuity improved, the central cornea was almost clear and the patient was pain free at 4 moths follow up. All patients with map-dot-fingerprint dystrophy were pain free, without recurrence , with clear corneas in the ablated area and visual acuity improved in all patients. .	**Complications:** Group 1: recurrent erosion 103 eyes There was no decrease in BCVA, or induced superficial haze. Group 2: pterygia 86 eyes 1.2% (1/86) of eyes had drastic scarring in the region of the pterygium following PTK (length of follow up or treatment not reported). There was no decrease in BCVA, or induced central corneal haze worse than grade 1 Group 3: band-like keratopathy 29 eyes There was no induced central corneal haze worse than grade 1 Group 4: special indication (including scarring) 34 eyes In a patient with alkali burn there was severe inflammation of the cornea and deep vascularisation of the cornea at 1 day follow up requiring systemic corticosteroids. Visual status returned to baseline level at 5 to 6 weeks follow up.	**Follow-up issues**: Prospective follow up 5 eyes of 5 patients (all in the recurrent erosion group) were lost to follow up. Some follow up collected from patients' local ophthalmologist rather than the study centre **Study design issues**: Variation in intervention protocol within study with different indications received slightly different treatment. Operator experience not reported. Outcomes not well described and not reported systematically for all patient groups. **Study population issues**: Wide patient selection criteria and outcomes reported by indication grouping. **Other issues**: None

Abbreviations used: BCVA, best corrected visual acuity; PTK, photo therapeutic keratectomy; D, Diopters; UCVA, uncorrected visual acuity

Study details	Key efficacy findings	Key safety findings	Comments
Maloney R K (1996)[3] **Case series** USA Recruitment period: 1989 to 1993 Study population: patients with anterior corneal pathology sufficiently severe to reduce visual acuity (various diagnoses) n = **211 (232 eyes)** Age: 62 years (mean) Sex: 57% female Patient selection criteria: central corneal thickness > 400µm, central opacity in the anterior 100µm of the corneal stroma, corneal surface irregularity, or both. No pathology that would prevent improvement in BCVA. Technique: Topical anaesthesia, debulking of cornea with blunt or sharp dissection. Excimer laser ablation of 1 to 5 mm (mean 643 pulses). Postoperative antibiotic / corticosteroid ointment applied. **Follow-up: 1 month to 2 years (range)** Conflict of interest/source of funding: Supported by manufacturer	**Number of patients analysed: 211 (232 eyes)** **Eye characteristics** All eyes had epithelial defect following the procedure. At 1 day follow up 82% had defect remaining, at day 3 61%, at day 7 26%, and at 1 month 3%. **Visual Acuity** BCVA Group mean and standard deviation Follow up time / Improvement (lines) / p= 6 months (n=169) / 1.3 ± 2.7 / <0.002 1 year (n-111) / 1.6±2.8 / <0.002 2 years (n=40) / 1.4±2.9 / <0.002 UCVA improved compared to baseline at all time periods (p<0.02) except 24 months (p=not significant) There was no significant difference in improvement in BCVA between subgroups of patients with corneal dystrophy, nodular degeneration, corneal scar, or band keratopathy (p=0.15) Mean change in visual acuity and standard deviation (all more hyperopic) Follow up time / Improvement (D) 6 months (n=166) / 1.04 ± 3.32 1 year (n=87) / 0.87 ± 2.60 2 years (n=27) / 1.25 ± 2.50 .(measurement of significance not reported) Mean change in astigmatism and standard deviation Follow up time / Change (D) / p= 6 months (n=137) / -0.44 ± 2.14 / <0.004 1 year (n=87) / -0.36 ±2.35 / >0.2 2 years (n=27) / -0.45±2.28 / >0.2	**Complications:** There was a loss of BCVA of 2 or more lines in 12.5% (3/24) of patients at 24 months follow up. Outcome / rate Recurrence (nodular degeneration) / 0.8% (2/232) Recurrent lattice dystrophy / 1.3% (3/232) Poor visual result –penetrating keratoplasty / 1.3% (3/232) Corneal scraping (not otherwise described) / 0.4% (1/232) Recurrent herpetic keratitis – penetrating keratoplasty / 1.3% (3/232) Idiopathic iritis / 0.4% (1/232) Bacterial keratitis / 0.4% (1/232) Marginal corneal ulcer / 0.4% (1/232) Progression of macular degeneration (probably unrelated to laser treatment) / 0.8% (2/232) Progressive cataract (probably unrelated to laser treatment) / 1.3% (3/232) **Haze** Haze was rated using the following scale Grade 0: clear cornea Grade 1: trace haze Grade 2: mild haze Grade 3: moderate haze obscuring iris detail Grade 4: severe opacity	**Follow-up issues**: Prospective study. 7 eyes underwent retreatment during the course of the study but were censored at time of retreatment and no longer followed up. 7 further eyes underwent an additional surgical procedure and were similarly excluded from subsequent follow up **Study design issues**: Multicentre study 13 sites. Outcome assessment was not blinded. **Study population issues**: For phase II of the study inclusion criteria of BCVA ≤20/40 was introduced. **Other issues**: Authors state that PTK is best for eyes with recurrent corneal irregularity after scraping. Authors state that surgeon's level of experience is an important factor in successful outcome.

Abbreviations used: BCVA, best corrected visual acuity; PTK, photo therapeutic keratectomy; D, Diopters; UCVA, uncorrected visual acuity			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
		Mean haze grade and standard deviation Follow up time Grade p= 6 months (n=69) 1.0 ± 0.8 <0.04	

Abbreviations used: BCVA, best corrected visual acuity; PTK, photo therapeutic keratectomy; D, Diopters; UCVA, uncorrected visual acuity

Study details	Key efficacy findings	Key safety findings	Comments
Sharma N (2008)[4] **Case series** India Recruitment period: 2000 to 2006 Study population: various indications of patients with bullous keratopathy secondary to cataract surgery (n=107), Salzmann nodular or spheroidal degeneration(n=47), Band keratopathy (n=22) n = **191 (203 eyes)** Age: 54 years (mean) Sex: 41% female Patient selection criteria: not reported Technique: Topical anaesthesia, scraping of epithelium with blunt spatula. Excimer laser ablation to 6 mm zone. Postoperative antibiotic and corticosteroids **Follow-up: 6 months (median)** Conflict of interest/source of funding: none	**Number of patients analysed: 191 (203 eyes)** **Eye symptoms** Pain, photophobia, and watering symptoms (number of patients) Bullous Keratopathy: Baseline 0, 6 months 0 Asymptomatic: 0, 0 Minimal: 0, 18 Mild: 7, 34 Moderate: 44, 40 Severe: 56, 15 (p<0.017 severe Vs all other category) Corneal scarring: Baseline 0, 6 months 0 Asymptomatic: 0, 0 Minimal: 0, 16 Mild: 13, 24 Moderate: 26, 8 Severe: 13, 4 (p<0.0001 severe Vs all other category) Mean (standard deviation) time to epithelialisation Days Bullous keratopathy: 6.44±3.51 Corneal scarring: 3.54±1.17 **Visual Acuity** Mean BCVA Bullous keratopathy: Baseline 20/384, 6 months 20/202, p= <0.0001 Corneal scarring: Baseline 20/222, 6 months 20/86, p= <0.0001 Change in BCVA was significantly correlated with baseline BCVA (p <0.0001 and = 0.03 respectively) but not to baseline pachymetry or depth of ablation.	**Complications:** Outcome: Rate per eye Mild postoperative haze (resolved by last follow up in 12 eyes): 10.8% (22/203)	**Follow-up issues**: Retrospective study. Loss to follow up not reported. **Study design issues**: Comparison made between groups of patients with bullous keratopathy and those with corneal scarring. All procedures undertaken at one study centre **Study population issues**: Patients included had a range of indications. Possibly more patients with a complication from Cataract surgery than would be expected in a UK setting. **Other issues**: None

Abbreviations used: BCVA, best corrected visual acuity; PTK, photo therapeutic keratectomy; D, Diopters; UCVA, uncorrected visual acuity			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Teichman K D (1996)[5] **Case report** Saudi Arabia Recruitment period: not reported Study population: bilateral central coreal opacity of unknown origin. **n = 1** Age:25 years Sex: 0% female Patient selection criteria: not reported Technique: PTK with Excimer laser, 5mm ablation zone, 294 pulses. Postoperative nonsteroidal anti inflammatory eyedrops. **Follow-up: 9 months** Conflict of interest/source of funding: not reported	Patient with bilateral central corneal opacity from childhood of unknown origin. Mainly in the anterior third of the corneal stroma. Visual acuity 20/125 in both eyes at baseline. PTK performed to the left eye. Bandage contact lens applied at 2 days follow up for large epithelial defect. By 4 days follow up an incomplete dense, white ring partially covered by epithelium formed in the corneal periphery. The bandage lens was removed, corneal scrapings taken and hourly antibiotic given. Cultures were found to be negative and sterile corneal (Wessely-type) immune ring was diagnosed. The epithelium healed at 4 weeks follow up. At 9 months follow up after PTK the ring was still visible and visual acuity remained the same as baseline.		**Follow-up issues**: None **Study design issues**: Number of patients treated at the study site is not reported. Biopsy sample was too small for immunological studies. **Study population issues**: Aetiology of corneal opacity not clearly defined. **Other issues**: None

Abbreviations used: BCVA, best corrected visual acuity; PTK, photo therapeutic keratectomy; D, Diopters; UCVA, uncorrected visual acuity			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Alaa M (1997)[6] **Case report** Saudi Arabia Recruitment period: 1994 Study population: patient with Fuchs' endothelial corneal dystrophy with stromal oedema, and subepithelial scaring. **n = 1** Age: 63 years Sex: 100% female Patient selection criteria: not reported Technique: PTK with excimer laser, 200 pulses, 5mm ablation zone. **Follow-up: 5 months** Conflict of interest/source of funding: supported by manufacturer	Before PTK procedure BCVA was 20/60. Repitheliasation was complete at 4 days, but at 1 month subepitheleal haze developed that had increased by 3 months with decreased visual acuity. Topical steroids were prescribed. At 5 months follow up the patient complained of reduced vision, uncorrected visual acuity was hand motion, and BCVA was finger count. Slit lamp microscopy revealed a central 4.5 mm circular subepithelial corneal scar, moderate corneal oedema, and diffuse cornea guttata. Penetrating keratoplasty was performed and uncorrected visual acuity improved to 20/60, 6 months later.		**Follow-up issues**: None **Study design issues**: Number of patients treated at the study site is not reported **Study population issues**: Authors state that the patient was inappropriately treated with PTK **Other issues**: None

Abbreviations used: BCVA, best corrected visual acuity; PTK, photo therapeutic keratectomy; D, Diopters; UCVA, uncorrected visual acuity

Study details	Key efficacy findings	Key safety findings	Comments
Lahners W (2001)[7] **Case report** USA Recruitment period: not reported. Study population: patient with keratoconus, Fleischer ring, Vogt's striar, minimal central thinning, and a central elevated subepithelial nodule. **n = 1** Age: 29 years Sex: 0% female Patient selection criteria: not reported Technique: exposure of the subepithelial nodule with Methyl-cellulose. PTK with excimer laser, 200 pulses until the surface was smooth at site of the nodule. **Follow-up: 13 months** Conflict of interest/source of funding: supported by grant	Patient presented with difficulty to fit a contact lens due to recurrent epithelial erosion over the subepithelial nodule. At 1 day follow up following PTK, uncorrected visual acuity was finger counting and a 2mm epithelial defect remained. At 3 days follow up uncorrected acuity improved to 20/200 and slit lamp microscopy revealed persistent epithelial defect and stromal oedema, corneal thickness was 50% less than at 1st postoperative examination. The patient was fitted with a therapeutic soft contact lens. At 8 days follow up, uncorrected acuity was finger counting, and a 2mm central descemetocele (hernia of Descemet's membrane) was observed. Because of the deep rapidly progressing keratolysis and impending perforation a penetrating keratoplasty was performed. Recovery was uncomplicated and at 13 months follow up the patient had a clear graft and BCVA of 20/25.		**Follow-up issues**: None **Study design issues**: Number of patients treated at the study site is not reported **Study population issues**: Patient with keratoconus but treated for subepithelial nodule. **Other issues**: None

Abbreviations used: BCVA, best corrected visual acuity; PTK, photo therapeutic keratectomy; D, Diopters; UCVA, uncorrected visual acuity			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Miyata K (2001)[8] **Case report** Japan Recruitment period: not reported Study population: patient with bilateral band keratopathy **n = 1** Age: 76 years Sex: 100 % female Patient selection criteria: not reported Technique: PTK with excimer laser with a transepithelial technique. 200 pulses, to ablate 48µm of the cornea in a 6mm zone. Soft contact lens placed for 3 days postoperatively **Follow-up: 12 months** Conflict of interest/source of funding: not reported	BCVA was 6/20 and the central corneal thickness was 541 µm at baseline. Following PTK re-epithelialisation was complete within 1 week follow up. At one month follow up BCVA was 20/20 and corneal thickness 517µm. BCVA deteriorated to 10/20 with corneal thickness of 513 µm at 6 months follow up. Videokeratography obtained serially since surgery showed progressive kerectasia in the central area. Scanning split lamp corneal topography at 6 months revealed a marked elevation of the posterior surface in the central area indicating anterior protrusion of the central cornea. This did not progress at 12 months follow up.		**Follow-up issues**: Final treatment and clinical outcomes not described. **Study design issues**: Number of patients treated at the study site is not reported **Study population issues**: Patient had bilateral band keratoplasty but treatment to the right eye only is described. **Other issues**: None

Efficacy

A non randomised controlled study of 39 patients reported that there was no significant difference in change in best corrected visual acuity (BCVA) between patients treated by laser phototherapeutic keratectomy and those treated by diamond burr polishing at 7 months follow up[1].

Mean BCVA improved by 1.4 lines compared to baseline in a case series of 211 patients (232 eyes) at 2 years follow up ($p<0.002$)[3]. There was no significant difference in BCVA improvement between subgroups of patients with corneal dystrophy, nodular degeneration, corneal scar, or band keratopathy ($p=0.15$).

A case series of 216 patients (252 eyes) reported that further recurrent erosion occurred in 9% (9/103) eyes at 12 months follow up, and 100% (29/29) of eyes with band-like keratopathy were pain free by 6 days follow up[2].

A case series of 191 patients (203 eyes) reported that significantly fewer patients with bullous keratopathy had severe pain / photosensitivity / watering symptoms at 6 months follow up (n=15) than at baseline (n=56) ($p<0.017$). Similarly, significantly fewer patients with corneal scaring had severe symptoms at 6 months follow up (n=4) compared to baseline (n=13) ($p<0.0001$)[4].

Safety

A case series of 211 patients (232 eyes) reported recurrent keratitis requiring penetrating keratoplasty in 1% (3/232) of eyes at follow up of up to 2 years[3]. In the same study idiopathic iritis occurred in 1 of 232 eyes, and a marginal corneal ulcer developed in 1 of 232 eyes. There was a loss of BCVA of 2 lines or more in13% (3/24) of patients at 2 years follow up.

There was one case report each of progressing keratolysis at 8 days follow up[7], and circular subepithelial corneal scaring at 5 months follow up[6] (both requiring penetrating keratoplasty), progressive kerectasia at 6 months (sequelae not reported)[8], and sterile corneal immune rings at 4 days follow up[5].

A case series of 191 patients (203 eyes) reported mild postoperative haze in 11% (22/203) eyes, which resolved in 12 eyes by 6 months follow up[4]. There was no significant difference in the occurrence of mild haze between patients treated by laser phototherapeutic keratectomy [33% (5/15)] or by diamond burr polishing [26% (7/27)] in a non randomised controlled study of 39 patients (42 eyes) at 7 months follow up ($p=0.38$)[1]. In the same study there were no cases of anterior basement dystrophy in either study group.

Validity and generalisability of the studies

- A wide variety of indications are included in the studies and the treatment aim may be slightly different in each.
- Little long-term data are available and recurrence may be an issue.
- Very little comparative data have been published at present.
- Efficacy outcomes are not well defined and vary between studies.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

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.

Mr N Hawksworth (Royal College of Ophthalmologists), Mr A Morrell (Royal College of Ophthalmologists), Prof. M Rubenstein (College of Optometrists)

- The Specialist Advisers were divided in their opinion as to the status of the procedure. One classified it as established and no longer new, one that it was novel and of uncertain safety and efficacy and one that it was a minor variation on Photo-refractive laser keratectomy.
- The main comparator to this procedure would be lamellar corneal graft surgery, or epithelial debridement and stromal puncture.
- The key efficacy outcomes for this procedure include visual acuity, ocular surface health, ocular comfort, and pain relief.

- Adverse events reported or encountered with this procedure include corneal infection.
- Additional theoretical adverse events might include epithelial defect, corneal ectasia, scarring, induction of astigmatism / refractive error, or recurrence of the disorder.
- One Specialist Advisor commented that published evidence suggests that this is a safe and effective treatment modality, providing an effective alternative treatment to more invasive procedures such as lamellar keratoplasty in certain anterior corneal disorders
- Surgeons require experience with equipment used for laser refractive procedures. A Royal College of Ophthalmologists Certificate in Laser Refractive Surgery would be desirable
- All three specialist advisors regarded the potential impact of this procedure on the NHS in terms of numbers of patients and use of resources to be minor.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme sent 60 questionnaires to 1 trust for distribution to patients who had the procedure (or their carers). NICE received 3 completed questionnaires.

The Patient Commentators raised the following issues about the safety/efficacy of the procedure which did not feature in the published evidence or the opinions of Specialist Advisers, and which the Committee considered to be particularly relevant:

- The procedure enabled walking with more confidence.
- Quality of life is improved with less photosensitivity (which had required sunglasses).

Issues for consideration by IPAC

- Non English language studies have not been included in this overview

- The procedure is similar to that for photorefractive keratectomy, however in this procedure the laser is used to smooth the corneal surface as opposed to altering the refractive characteristics.

References

1 Sridhar MS, Rapuano CJ, Cosar CB et al. (2002) Phototherapeutic keratectomy versus diamond burr polishing of Bowman's membrane in the treatment of recurrent corneal erosions associated with anterior basement membrane dystrophy. Ophthalmology 109:674-679.

2 Forster W, Atzler U, Ratkay I et al. (1997) Therapeutic use of the 193-nm excimer laser in corneal pathologies. Graefe's Archive for Clinical and Experimental Ophthalmology 235:296-305.

3 Maloney RK, Thompson V, Ghiselli G et al. (1996) A prospective multicenter trial of excimer laser phototherapeutic keratectomy for corneal vision loss. The Summit Phototherapeutic Keratectomy Study Group. American Journal of Ophthalmology 122:149-160.

4 Sharma N, Prakash G, Sinha R et al. (2008) Indications and outcomes of phototherapeutic keratectomy in the developing world. Cornea 27:44-49.

5 Teichmann KD, Cameron J, Huaman A et al. (1996) Wessely-type immune ring following phototherapeutic keratectomy. Journal of Cataract & Refractive Surgery 22:142-146.

6 Alaa M, Waring III GO, Malaty A et al (1997) Increased corneal scarring after phototherapeutic keratectomy in Fuch’s corneal dystrophy. Journal of Refractive Surgery 13: 308-309

7 Lahners WJ, Russell B, Grossniklaus HE et al. (2001) Keratolysis following excimer laser phototherapeutic keratectomy in a patient with keratoconus. Journal of Refractive Surgery 17:555-558.

8 Miyata K, Takahashi T, Tomidokoro A et al. (2001) Iatrogenic keratectasia after phototherapeutic keratectomy. British Journal of Ophthalmology 85:247-248.

Appendix A: Additional papers on phototherapeutic laser keratectomy for corneal surface irregularities

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies. Case series or case reports including less than 20 patients where no new / additional safety outcomes are reported have been excluded from this table for brevity.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Amm, M. and Duncker, G. I. (1997) Refractive changes after phototherapeutic keratectomy. Journal of Cataract & Refractive Surgery 23 (6) 839-844	n=45 FU=24 months	After PTK, all types of refractive change can occur. The greatest risk is that of a hyperopic shift.	Larger studies are included in table 2
Ashrafzadeh, A. and Steinert, R. F. (2007) Results of phototherapeutic keratectomy in the management of flap striae after LASIK before and after developing a standardized protocol: long-term follow-up of an expanded patient population. Ophthalmology 114 (6) 1118-1123	n=44 FU=3 months minimum	Phototherapeutic keratectomy treatment of LASIK flaps is well tolerated, with stable outcomes and minimal complications. A standardised treatment protocol reduced postoperative refractive variability	Larger studies are included in table 2
Baryla, J., Pan, Y. I., and Hodge, W. G (2006) Long-term efficacy of phototherapeutic keratectomy on recurrent corneal erosion syndrome. Cornea 25 (10) 1150-1152	n=33 FU=17 months	PTK is an important treatment of recurrent corneal erosion syncrome refractory to other therapies. Long-term data suggest that most patients treated with PTK do not develop recurrences, and side effects from PTK are minimal	Larger studies are included in table 2
Cavanaugh, T. B., Lind, D. M., Cutarelli, P. E. (1999) Phototherapeutic keratectomy for recurrent erosion syndrome in anterior basement membrane dystrophy. Ophthalmology 106 (5) 971-976	n=43 FU=1 year minimum	Phototherapeutic keratectomy is an effective treatment for recurrent erosions occurring in the setting of anterior basement membrane dystrophy, is well tolerated, and may improve visual acuity	Larger studies are included in table 2
Das, S., Langenbucher, A., and Seitz, B.(2005) Excimer laser phototherapeutic keratectomy for granular and lattice corneal dystrophy: a comparative study. Journal of Refractive Surgery 21 (6) 727-731	n=40 FU=3 years	Our results suggest that PTK may be tried in all patients with superficially accentuated opacities in granular and lattice dystrophy before undergoing a more invasive procedure, such as lamellar or penetrating keratoplas	Larger studies are included in table 2 Comparison between two indication subgroups
Das, S., Langenbucher, A., and Seitz, B.(2005) Delayed healing of corneal epithelium after phototherapeutic keratectomy for lattice dystrophy. Cornea 24 (3) 283-287	n=133 FU=Not reported	Eyes with lattice corneal dystrophy suffered from delayed epithelial healing after o-PTK. In addition to adequate counseling, these patients should be followed up closely until complete closure of the epithelium to avoid ulceration, scarring, or	Larger studies are included in table 2

		even infection	
Dausch, D., Landesz, M., Klein, R. (1993) Phototherapeutic keratectomy in recurrent corneal epithelial erosion. Refractive & Corneal Surgery 9 (6) 419-424	n=73 FU=not reported	Phototherapeutic keratectomy in recurrent epithelial erosions is a promising treatment, especially in recalcitrant cases with the erosion over the entrance pupil. Photoablation allows a fast reepithelialization of the affected area and quick relief for painful symptoms	Larger studies are included in table 2
Dinh, R., Rapuano, C. J., Cohen, E. J. (1999) Recurrence of corneal dystrophy after excimer laser phototherapeutic keratectomy. Ophthalmology 106 (8) 1490-1497	n=33 FU=20 months	Phototherapeutic keratectomy can restore and preserve useful visual function for a significant period of time in patients with anterior corneal dystrophies. Even though corneal dystrophies are likely to recur eventually after PTK, successful retreatment with PTK is possible	Larger studies are included in table 2
Forster, W., Ratkay, I., Krueger, R., (1997) Topical diclofenac sodium after excimer laser phototherapeutic keratectomy. Journal of Refractive Surgery 13 (3) 311-313	n=134 FU=72 hours	Topical diclofenac sodium reduces postoperative pain in patients after phototherapeutic keratectomy	Studies with longer follow up are included in table 2
Hersh, P. S., Burnstein, Y., Carr, J., (1996) Excimer laser phototherapeutic keratectomy. Surgical strategies and clinical outcomes. 103 (8) 1210-1222	n=26 FU=6 to 30 months	A number of PTK techniques are available to treat particular corneal disorders. Planning of surgical strategy is guided by careful patient selection which will minimize optical side effects and optimize visual outcome and subjective symptomatology after the PTK procedure	Larger studies are included in table 2
Ho, C. L., Tan, D. T., and Chan, W. K. (1999) Excimer laser phototherapeutic keratectomy for recurrent corneal erosions. Annals of the Academy of Medicine, Singapore 28 (6) 787-790	n=32 FU=12 months	PTK is a safe and effective procedure for RCE refractory to conventional treatment	Larger studies are included in table 2
Holzer, M. P., Auffarth, G. U., Specht, H. (2005) Combination of transepithelial phototherapeutic keratectomy and autologous serum eyedrops for	n=25 FU=16 months	Transepithelial phototherapeutic keratectomy is a safe and effective therapy for recurrent corneal erosions. Additional treatment with autologous serum eyedrops	Larger studies are included in table 2

treatment of recurrent corneal erosions. Journal of Cataract & Refractive Surgery 31 (8) 1603-1606		can support the healing process following corneal erosions and t-PTK and can be given as a long-term artificial tear treatment	
Jain, S. and Austin, D. J. (1999) Phototherapeutic keratectomy for treatment of recurrent corneal erosion. Journal of Cataract & Refractive Surgery 25 (12) 1610-1614	n=68 FU=2 years	Phototherapeutic keratectomy is a safe and effective treatment for refractory recurrent corneal erosion and, where appropriate, can be combined with photorefractive therapy	Larger studies are included in table 2
Lohmann, C. P., Sachs, H., Marshall, J., (1996) Excimer laser phototherapeutic keratectomy for recurrent erosions: a clinical study. Ophthalmic Surgery & Lasers 27 (9) 768-772	n=24 FU=3 to 12 months	Excimer laser PTK appears to be a safe and promising procedure for cases of recurrent corneal erosion refractory to medical treatment	Larger studies are included in table 2
Maini, R., Sullivan, L., Snibson, G. R., (2001) A comparison of different depth ablations in the treatment of painful bullous keratopathy with phototherapeutic keratectomy. British Journal of Ophthalmology 85 (8) 912-915	n=37 (eyes) FU=7 months	PTK can be a useful therapeutic measure in painful bullous keratopathy with poor visual potential. Deep PTK appears to be more successful in pain management than superficial treatment	Larger studies are included in table 2. Study compares 2 different depths of ablation.
McDonnell, J. M., Garbus, J. J., and McDonnell, P. J. (1992) Unsuccessful excimer laser phototherapeutic keratectomy. Clinicopathologic correlation. Archives of Ophthalmology 110 (7) 977-979	n=1 FU=3 months	The resistance of this lesion to excimer laser ablation appears to have been the consequence of marked differences in rates of ablation between normal stroma and the very long-standing scar	Larger studies are included in table 2
Migden, M., Elkins, B. S., and Clinch, T. E.(1996) Phototherapeutic keratectomy for corneal scars. Ophthalmic Surgery & Lasers 27 (5:Suppl) Suppl-7	n=22 eyes FU=3 months	PTK is a relatively safe and effective means of treating corneal scars and thereby may offer an alternative to corneal transplantation	Larger studies are included in table 2
Moniz, N. and Fernandez, S. T. (2003) Efficacy of phototherapeutic keratectomy in various superficial corneal pathologies. Journal of Refractive Surgery 19 (2:Suppl) Suppl-6	n=31 FU=12 months	Phototherapeutic keratectomy may facilitate better visual acuity and reduced photophobia in eyes with various corneal pathology. Proper case selection is crucial	Larger studies are included in table 2

Morad, Y., Haviv, D., Zadok, D., (1998) Excimer laser phototherapeutic keratectomy for recurrent corneal erosion. Journal of Cataract & Refractive Surgery 24 (4) 451-455	n=33 FU=38 months	Excimer laser PRK appears to be a safe and effective treatment for recurrent erosions of the cornea	Larger studies are included in table 2
Nghiem-Buffet, M. H., Gatinel, D., Jacquot, F., (2003) Limbal stem cell deficiency following phototherapeutic keratectomy. Cornea 22 (5) 482-484	n=1 FU=12 months	The extensive corneal mechanical debridement and laser photoablation incurred during phototherapeutic keratectomy can cause clinical limbal stem cell deficiency in patients with predisposing external diseases	Larger studies are included in table 2
O'Brart, D. P., Gartry, D. S., Lohmann, C (1993) Treatment of band keratopathy by excimer laser phototherapeutic keratectomy: surgical techniques and long term follow up. British Journal of Ophthalmology 77 (11) 702-708	n=122 FU=12 months	Excimer laser PTK is a safe and effective outpatient treatment for band keratopathy	Larger studies are included in table 2
Orndahl, M., Fagerholm, P., Fitzsimmons, T (1994) Treatment of corneal dystrophies with excimer laser. Acta Ophthalmologica 72 (2) 235-240	n=31 FU=9 months	Excimer laser ablation of corneal dystrophies seems to be a good treatment, which can improve visual functions considerably, heal corneal wounds and in this way postpone corneal grafting in many cases	Larger studies are included in table 2
Orndahl, M. J. and Fagerholm, P. P. (1998) Phototherapeutic keratectomy for map-dot-fingerprint corneal dystrophy. Cornea 17 (6) 595-599	n=24 FU=30 months	In this study, excimer laser photoablation was shown to be an effective, safe, and stable choice of treatment for map-dot-fingerprint dystrophy. A refractive change, as hyperopic shift, can be an adverse side effect in some individual cases	Larger studies are included in table 2 Possibly the same patients as Oendahl (1994)
Rapuano, C. J.(1997) Excimer laser phototherapeutic keratectomy: long-term results and practical considerations. Cornea 16 (2) 151-157	n=24 FU= 23 months	Excimer laser PTK is safe and effective for the treatment of anterior corneal pathology. Recurrence of pathology, especially corneal dystrophies, do occur with time	Larger studies are included in table 2
Rashad, K. M., Hussein, H. A., El-Samadouny, M. A (2001) Phototherapeutic keratectomy in patients with recurrent corneal epithelial	n=41 FU=23 months	Excimer laser PTK was a safe and effective procedure for the treatment of recurrent corneal erosions. Excimer laser	Larger studies are included in table 2

erosions. Journal of Refractive Surgery 17 (5) 511-518		PTK can also be useful in improving the visual acuity in these patients. A small percentage of patients may require a second PTK to prevent further episodes of corneal erosions	
Robinson, J. W., Brownstein, S., and Mintsioulis, G.(2006) Corneal myxoma arising in a patient with repeated phototherapeutic keratectomies. Cornea 25 (9) 1111-1114	n=1 FU=8 months	The pathogenesis of corneal myxomas involves a reactive process that requires an antecedent affliction, in contrast to the neoplastic mesenchymal histogenesis of myxomas characterized in other parts of the body	Larger studies are included in table 2
Sher, N. A., Bowers, R. A., Zabel, R. W (1991) Clinical use of the 193-nm excimer laser in the treatment of corneal scars. Archives of Ophthalmology 109 (4) 491-498	n=33 FU=3 to 12 months	The 193-nm excimer laser is an effective new tool in the treatment of selected patients with superficial corneal opacity from a variety of conditions	Larger studies are included in table 2
Starr, M. B.(1999) Recurrent subepithelial corneal opacities after excimer laser phototherapeutic keratectomy. Cornea 18 (1) 117-120.	n=1 FU=5 years	Post-viral keratitis subepithelial corneal opacities may recur after removal by excimer laser PTK. Recurrence of these opacities in anterior corneal stroma previously unaffected by opacities before laser treatment suggests the presence of viral antigen in deeper corneal tissue than that occupied by the original subepithelial opacities	Larger studies are included in table 2 Safety outcome reported elsewhere
Starr, M., Donnenfeld, E., Newton, M.(1996) Excimer laser phototherapeutic keratectomy. Cornea 15 (6) 557-565	n=45 FU=11 months	Excimer laser phototherapeutic keratectomy can consistently achieve a modest to a more substantial improvement in irritative ocular symptoms and/or visual acuity with significant potential for adverse results that appear to be less severe than the complications associated with alternative treatment by keratoplasty	Larger studies are included in table 2
Stewart, O. G. and Morrell, A. J. (2003) Management of band keratopathy with excimer phototherapeutic keratectomy: visual, refractive, and symptomatic outcome.	n=33 FU=12 months	Excimer PTK is an effective procedure in the management of band keratopathy whether it is performed for visual rehabilitation or for ocular surface improvement to prevent erosions.	Larger studies are included in table 2

Eye 17 (2) 233-237			
Tuunanen, T. H. and Tervo, T. M.(1995) Excimer laser phototherapeutic keratectomy for corneal diseases: a follow-up study. CLAO Journal 21 (1) 67-72	n=38 FU=9 months	Results can be improved with better patient selection criteria and by evaluating PTK on the basis of visual expectations and type and location of corneal pathology	Larger studies are included in table 2
Wei, Z., Bingji, S., Yinqi, W (2006) Excimer laser phototherapeutic keratectomy for superficial corneal dystrophy. Chinese Ophthalmic Research 18 (6) 567-570	n=26 FU= 6 to 18 months	PTK appears to be safe and benificial in the treatment of superficial corneal dystrophy. The success rate is very high and complications are rare	Larger studies are included in table 2
Zuckerman, S. J., Aquavella, J. V., and Park, S. B.(1996) Analysis of the efficacy and safety of excimer laser PTK in the treatment of corneal disease. Cornea 15 (1) 9-14	n=45 FU=3 months	Excimer PTK appears to be a valuable addition to our therapeutic armamentarium for the treatment of superficial stromal opacification and surface irregularity	Larger studies are included in table 2

Appendix B: Related NICE guidance for phototherapeutic laser keratectomy for corneal surface irregularities

There is currently no NICE guidance related to this procedure.

Appendix C: Literature search for phototherapeutic laser keratectomy for corneal surface irregularities

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	06/01/2010	Issue 4, 2009
Database of Abstracts of Reviews of Effects – DARE (CRD website)	06/01/2010	N/A
HTA database (CRD website)	06/01/2010	N/A
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	06/01/2010	Issue 4, 2009
MEDLINE (Ovid)	06/01/2010	1950 to December Week 4 2009
MEDLINE In-Process (Ovid)	06/01/2010	January 5, 2010
EMBASE (Ovid)	06/01/2010	1980 to 2009 Week 53
CINAHL (NHS Evidence)	06/01/2010	1981 to Present
BLIC (Dialog DataStar)	05/01/2010	1995 to date

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

1	(Phototherapeutic* adj3 keratectom*).tw.
2	PTK.tw.
3	or/1-2
4	Lasers, Excimer/
5	Laser*.tw.
6	Excimer*.tw.
7	Lasers, Solid-State/
8	YAG.tw.
9	Solid*State.tw.
10	or/4-9
11	3 and 10
12	Cornea/
13	Corneal Diseases/

14	Corneal Dystrophies, Hereditary/
15	Corneal Opacity/
16	(Cornea* adj3 (Opacit* or Irregularit* or Dystroph* or Degenerat* or Scar* or Trauma* or Diseas* or Erosion* or Pain*)).tw.
17	Fuchs' Endothelial Dystrophy/
18	((Fuch* or Granular* or Reis* Buckler*) adj3 Dystroph*).tw.
19	Keratopath*.tw.
20	(Salzmann* adj3 nodular* adj3 degenerat*).tw.
21	or/12-20
22	11 and 21
23	Animals/ not Humans/
24	22 not 23