

Femtosecond laser used in penetrating keratoplasty

The Femtec laser creates graft buttons and host trephinations to match.

by Mark Tomalla, MD

Special to Ocular Surgery News

The Femtec femtosecond laser from 20/10 Perfect Vision, which was approved for penetrating keratoplasty procedures in July 2005, makes it possible

to perform the procedure from endothelium to epithelium with no mechanical pressure or torque exerted on the tissue to be cut.

The precise cut of the femtosecond laser begins at a depth of up to 1,200

µm and is brought up to the epithelium. The mechanical pressure on the globe during the procedure is only about 40 mm Hg. The curvature of the cornea is flattened to 35 D.

Both the graft and the excised tissue are cut with such high precision that the two diameters can be of the same selected size, resulting in an optimal fit of the graft.

Femtosecond laser technology makes into reality a procedure that spares endothelial cells and offers other advantages as well. The graft and the host cornea can be prepared in any desired cut size with any desired diameters and angles of incision. Thus, every patient can be given individual treatment with a perfect fit.

Apart from experimental studies using the Femtec femtosecond laser, the technology is so new that there are as yet no publications on its clinical use. I would like to share the following case studies.

Patient 1

In 1999, a female patient, now 80 years old, was first referred to us in Duisburg at the Centre for Ophthalmology, Clinic for

acuity was 0.03.

In 2003, patient records showed corneal decomposition with dense scarring to the limbus. Vision was limited now to only hand movement.

In July 2005, we decided to perform re-transplantation, which was performed using the femtosecond laser.

Patient 2

A 79-year-old woman suffered from Fuchs's endothelial dystrophy. In 1992, the first corneal transplantation was performed in the left eye. Since then, the cornea was again totally clouded and presented an inhomogeneous tissue structure. When the patient came to us in July 2005, her vision was limited to hand movement. IOP was 16 mm Hg. The patient also had a cataract.

Patient 3

A third female patient, 62 years old, suffered from bilateral keratoconus.

The left eye had preoperative visual acuity limited to hand movement, a cataract, and a totally cloudy cornea with central and peripheral corneal scars.

Preparing donor cornea

In preparing the donor cornea, the back surface is first coated with viscoelastic, as in mechanical preparation, and then clamped into the artificial chamber. A pressure of 22 mm Hg is created.

The cornea and the patient interface of the laser, which has a curva-



IMPORTANT:
Correction of Drug Information About
VisionBlue® (trypan blue ophthalmic solution)

Dear Healthcare Provider:

The U.S. Food and Drug Administration's (FDA) Division of Drug Marketing, Advertising, and Communications (DDMAC) have asked us to contact you because we recently received a Warning Letter from the FDA concerning our promotion of VisionBlue® (trypan blue ophthalmic solution).

The FDA determined that our promotional materials were false or misleading because they presented numerous efficacy claims for VisionBlue®, but failed to communicate any risks associated with its use. These violative promotional materials raised public health and safety concerns through their complete omission of risk information for VisionBlue® by suggesting that it is safer than has been demonstrated.

This letter provides the approved indication and important safety information about VisionBlue® and corrects our violative promotional materials.

Indication Information

VisionBlue® is indicated for use as an aid in ophthalmic surgery by staining the anterior capsule of the lens.

Important Safety Information

VisionBlue® is contraindicated when a non-hydrated (dry state), hydrophilic acrylic intraocular lens (IOL) is planned to be inserted into the eye because the dye may be absorbed by the IOL and stain the IOL.

It is recommended that after injection all excess VisionBlue® be immediately removed from the eye by thorough irrigation of the anterior chamber.

A brief summary of the prescribing information is available on the adjacent page. Full prescribing information for VisionBlue® may be accessed on our website at www.dorc.nl by clicking "Click here for full Prescribing Information." If you have additional questions, please contact us at (800) 753-8824 or (603) 642-8468.

Sincerely,

Ger Vijfvinkel
President



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Mark Tomalla

Table.

Postoperative uncorrected visual acuity

	Patient 1	Patient 2	Patient 3
1 day postop	0.05	0.1	0.1
1 month postop	0.125	0.32	0.4
Postoperative findings	Cornea well adapted; transplant clear and without folds	Transplant evenly integrated; discrete Descemet folds	Transplant evenly integrated; discrete Descemet folds

Source: Tomalla M

Refractive and Ophthalmic Surgery.

The patient had undergone several operations on her right eye. As early as 1981, she received a scleral buckle after vitrectomy and after laser coagulation in the retinal foramen. In 1988, a cataract operation was performed with implantation of an anterior chamber lens, after which scleral buckle repositioning was performed. The patient had suffered since 1999 under pronounced corneal decomposition after a vitrectomy with silicone oil filling. Her vision at the time was already limited to light perception and hand movement. After the first keratoplasty, her postoperative visual

of 35 D, are placed together under vacuum. First, the donor cornea is prepared under the femtosecond laser (Figure 1). The light source for the microscope consists of fluorescent diodes arranged in a circle, and the reflex of this illumination is directed centrally (Figure 2).

The cornea is cut with a selected cutting depth of 1,100 µm and a laser spot spacing of 8/11 from the endothelium to the epithelium using the femtosecond laser (Figure 3). In clouded corneas, a narrower spot distance of 3/6 was chosen. The laser energy is set at 4 µJ. The cutting angle is programmed at 90° to the corneal curvature.

The entire preparation is performed under visual control.

In these three cases, the diameter of the transplant varied in size, depending on the findings of the patient. For patient 1 and patient 2, we selected 8.2 mm as the size of the transplant. The size of the cloudy

cornea to be replaced was 8 mm, so we left a difference of 0.2 mm. We deviated from this procedure in patient 3 and selected 8 mm as the size of the transplant; the size of the cloudy cornea to be replaced was 7.8 mm. On the one hand, we wanted to remove as little of the

patient's tissue as possible; on the other hand, the transplantation was to lie directly under the protrusion. In a possible repeated keratoplasty, a larger diameter could then be selected. (We have since changed our operating procedure in that we select identical sizes for the donor and recipient cornea. Thanks to the precise cutting quality, we can expect even better postoperative results.)

Decisive advantages of performing corneal transplantation with the femtosecond laser became apparent in the

preparation of the donor cornea.

The transplant size can be selected at will. There are no limitations due to mechanical microkeratomers in preparing the transplant.

Preparation of the donor cornea is made from bottom to top, so that this procedure is particularly sparing for the corneal endothelium. This remains largely intact, and there is only minimal damage.

Preparation is considerably quicker than in the usual methods.

(Keratoplasty, continued on page 84)




The donor cornea is prepared under the femtosecond laser. Images: Tomalla M



Light source for microscope consists of fluorescent diodes arranged in a circle.



The cornea is cut with a selected cutting depth of 1,100 μm .




Vision Blue®

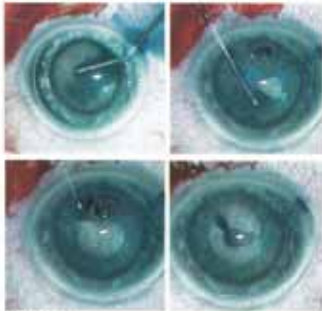
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Please see adjacent page for brief prescribing information.

1 Melles GJR, de Waard PWT, Pameyer JH, Houdijn Beekhuis W. Trypan blue capsule staining to visualize the capsulohexis in cataract surgery. J Cataract Refractive Surgery 1999; 25:7-9

Keratoplasty

(continued from page 83)

Host trephination

First, the patient interface, which is the connecting site between the laser and the globe, is mounted. Similar to a contact lens, the patented patient interface enables optimal fitting to the cornea, and the curvature remains the same during the entire procedure (Figure 4). In coupling the patient interface to the cornea, care must be taken that a vacuum space forms between the pa-

tient interface and the cornea to guarantee proper intrastromal laser application (Figure 5).

In patient 3, who had keratoconus, the ideal contact between the cornea and the patient interface could only be achieved using balanced salt solution.

Irrigating fluid smoothes the unevenness during the coupling phase.

After the eye was positioned and centered under the microscope, we performed penetrating keratoplasty. We selected a corneal diameter of 8 mm for the first two patients. For the third patient, 7.8 mm was selected as

the diameter.

In patient 1, we began at a cutting depth of 700 μm . Since this was too shallow, the eye subsequently had to be mechanically opened. In the next two procedures, we went to a maximum depth of 1,100 μm .

After the laser procedure, the cornea was well-released in all areas. On removal, there were only isolated epithelial bridges, which were released with a blade.

The laser energy was set at 4 μJ , spacing was 3/6, and an angle of 90° was selected in all patients.

We performed penetrating keratoplasty under total visual control from inside the cornea to outside. This can be considered especially safe because

the upper third of the stroma, where the scar tissue was more dense.

Total visual control

The cornea was removed, and with application of viscoelastic, the previously prepared donor cornea nestled perfectly in the opened eye. Here we see the effect of the exact cutting edges of both the patient cornea and the prepared donor cornea. They fit almost exactly.

To complete the procedure, four cardinal sutures were made for fixation before a continuous suture was made.

Postoperative results

Patient 1 improved after surgery, and her postoperative vision was 0.05. The cornea was well adapted immedi-

VisionBlue® (trypan blue ophthalmic solution)



Brief Summary of Prescribing Information

Indications and Usage

VisionBlue® is indicated for use as an aid in ophthalmic surgery by staining the anterior capsule of the lens.

Contraindications

VisionBlue® is contraindicated when a non-hydrated (dry state), hydrophilic acrylic intraocular lens (IOL) is planned to be inserted into the eye because the dye may be absorbed by the IOL and stain the IOL.

Precautions

General:

It is recommended that after injection all excess VisionBlue® be immediately removed from the eye by thorough irrigation of the anterior chamber.

Carcinogenesis, mutagenesis, impairment of fertility:

Trypan blue is carcinogenic in rats. Wistar/Kyoto rats developed lymphomas after receiving subcutaneous injections of 1% trypan blue dosed at 50 mg/kg every other week for 52 weeks (total dose approximately 1,250,000-fold the maximum recommended human dose of 0.06 mg per injection in a 60 kg person, assuming total absorption).

Trypan blue was mutagenic in the Ames test and caused DNA strand breaks *in vitro*.

Pregnancy: Teratogenic Effects: Pregnancy Category C:

Trypan blue is teratogenic in rats, mice, rabbits, hamsters, dogs, guinea pigs, pigs, and chickens. The majority of teratogenicity studies performed involve intravenous, intraperitoneal, or subcutaneous administration in the rat. The teratogenic dose is 50 mg/kg as a single dose or 25 mg/kg/day during embryogenesis in the rat. These doses are approximately 50,000- and 25,000-fold the maximum recommended human dose of 0.06 mg per injection based in a 60 kg person, assuming that the whole dose is completely absorbed. Characteristic anomalies included neural tube, cardiovascular, vertebral, tail, and eye defects. Trypan blue also caused an increase in post-implantation mortality, and decreased fetal weight. In the monkey, trypan blue caused abortions with single or two daily doses of 50 mg/kg between 20th to 25th days of pregnancy, but no apparent increase in birth defects (approximately 50,000-fold maximum recommended human dose of 0.06 mg per injection, assuming total absorption). There are no adequate and well-controlled studies in pregnant women. Trypan blue should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.

Nursing mothers:

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when trypan blue is administered to a nursing woman.

Pediatric use:

The safety and effectiveness of trypan blue have been established in pediatric patients. Use of trypan blue is supported by evidence from an adequate and well-controlled study in pediatric patients.

Geriatric use:

No overall differences in safety and effectiveness have been observed between elderly and younger patients.

Adverse Reactions

Adverse reactions reported following use of VisionBlue® include discoloration of high water content hydrogen intraocular lenses (see Contraindications) and inadvertent staining of the posterior lens capsule and vitreous face. Staining of the posterior lens capsule or staining of the vitreous face is generally self limited, lasting up to one week.

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Revised: July 2005

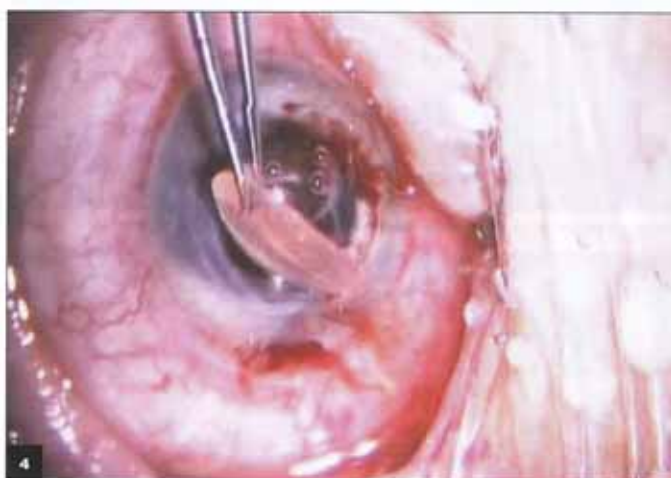
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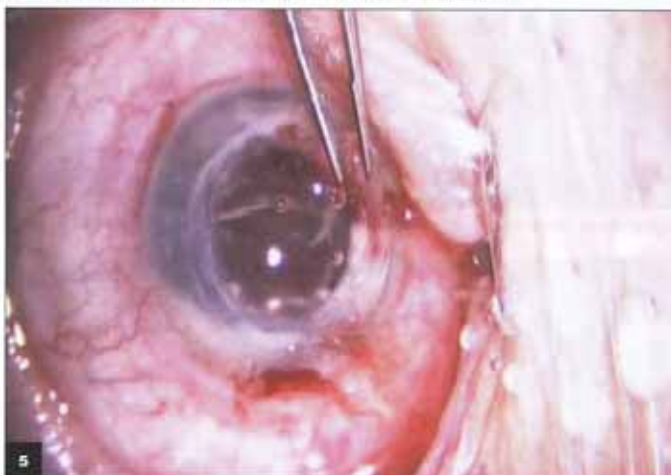
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U.S. PAT. 6,367,480; 6,720,314



The patient interface is mounted. It is similar to a contact lens.



A vacuum space must form between the patient interface and the cornea.

the eye remains a closed and thus stable system for as long as possible.

Penetrating keratoplasty was performed in patient 1 and patient 2 accurately as planned, despite cloudy corneas. In patient 3, continuous separation of the tissue was achieved, despite inhomogeneous tissue thickness and thickly scarred zones. On removing the cornea, we found a broad-based tissue bridge in

ately after the procedure. Subjectively, the patient was happy and satisfied.

One month later, the patient's visual acuity was 0.125, and IOP was 14 mm Hg. The transplant was clear and without folds.

One day postoperative, patients 2 and 3 had uncorrected vision of 0.1. The transplants were integrated without unevenness into the remaining recipient

cornea, and there were only discrete Descemet folds because of slight swelling of the transplants. Both patients had an improvement in vision.

Discussion

The following parameters characterize a penetrating keratoplasty performed with the Femtec femtosecond laser and how it differs from usual methods. The incision is performed from the endothelial side of the cornea, ie, from inside the tissue upward and outward. Thus, the endothelial cells are subjected to low mechanical stress. The eye remains closed as long as possible during the operation. This makes the operation safer. But most of all, there is no epithelial invasion into the anterior chamber thanks to the direction of the incision. Handling of the tissue is without mechanical pressure and torque motion and is of high-quality cutting. Any desired transplant size can be selected. The

standard in the performance of penetrating keratoplasty. Likewise, further developments in cut configurations are expected to bring reductions in post-operative astigmatism because rotation movements of the transplants could be considerably reduced. Finally, a reduction in the number of sutures needed can also be expected.

For Your Information:

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49-203-5081713; e-mail: mark.tomalla@ejk.de; Web: www.augenklinik-duisburg.de. Dr. Tomalla has no direct financial interest in the products mentioned in this article.

■ **20/10 Perfect Vision**, maker of the Femtec femtosecond laser, can be reached at Optische Geräte GmbH, Am Taubenfeld 21/1, D-69123 Heidelberg, Germany; 49-6221-7502-0; fax: 49-6221-7502-122; e-mail: info@2010pv.com; Web site: www.2010pv.com.

■ **References:**

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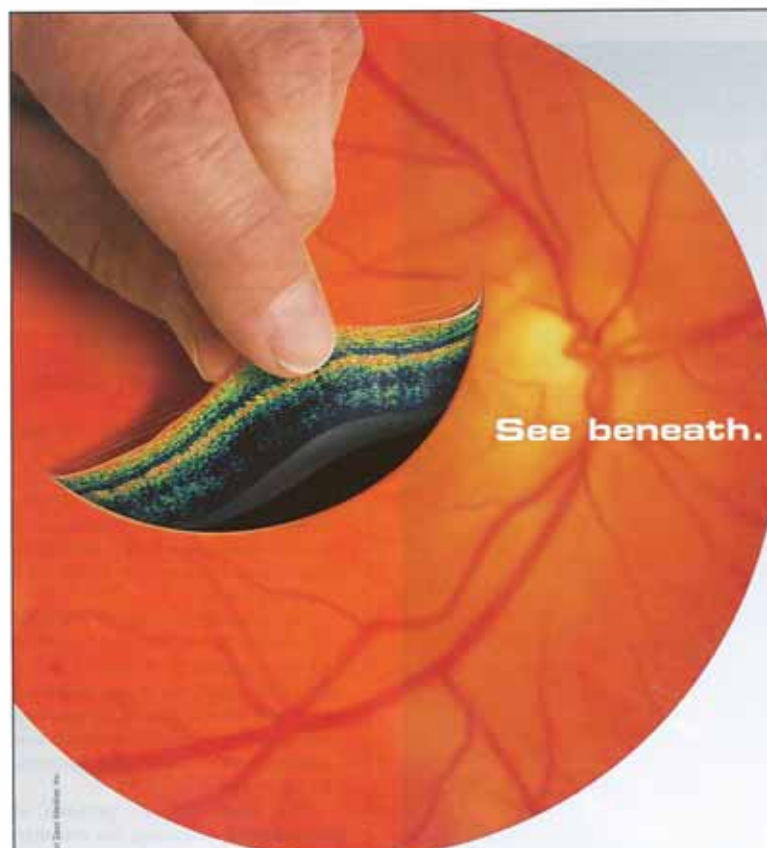
“Apart from experimental studies using the Femtec femtosecond laser, the technology is so new that there are as yet no publications on its clinical use.”

— Mark Tomalla, MD

surgeon can also select any cut configuration, which means a broad variability of form is available to him and he is no longer limited by his equipment. The cut quality is high, so the prepared donor transplant nestles perfectly in the opened eye. Fewer wound scars can be expected, and it may be possible in the future to do away with some sutures or even perform this procedure with no sutures. The operation is performed under complete visual control. The surgeon can follow the cut through his OP microscope and through the patient interface at the same time.

The femtosecond laser technology is suitable not only for treatment of transparent corneal tissue, but it can also be used with extreme precision in scarred corneal tissue. Another aspect is that varying tissue homogeneity has almost no influence on the cut quality, although the laser cuts were performed with the same energy. The only criteria here were discrete tissue bridges, but they could be released using a Sato knife or blade without problems and without tensile stress.

We must, of course, wait until long-term and more numerous postoperative patient data are available. But we can already say that the use of the femtosecond laser will set a new stan-

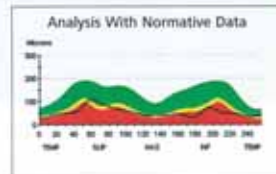
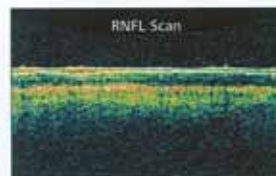
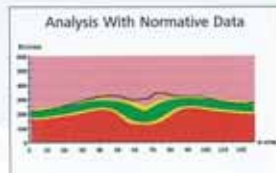
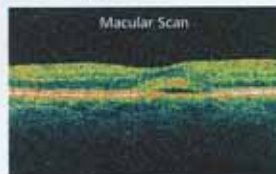


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