For a number of years there has been a growing interest in the possibility of changing the focusing properties of the human eye by surgical means rather than the use of spectacles or contact lenses. Surgical procedures to change corneal curvature are basically of two types, those involving the optical zone and those involving the peripheral cornea.

In the central zone procedures, the surgeon decides upon the desired correction and a disc of Bowman's membrane and anterior stroma is then carefully cleaved off the surface of a patient's (keratomileusis) or of a donor's (epikeratophakia) eye and then stained with a vital dye before being frozen. The stain is merely for the surgeon to visualise the specimen. The frozen corneal segment is then placed in a microcryolathe and the stromal surface is turned to the correct curvature to achieve the desired optical correction. The corneal specimen is then thawed and sutured, Bowman's surface outwards, on to either the patient's Bowman's (epikeratophakia) or stroma (keratophakia). In a slight variation of this procedure artificial polysulphone inlays of varying optical powers are inserted into pockets in the patient's stroma. This is high stress surgery for the surgeon and relatively few procedures are undertaken worldwide.

Peripheral zone procedures are currently the most popular refractive surgical modality for both patients and surgeons. Radial keratotomy (RK) involves the surgeon making a series of four, eight, 16, 32 or more radial incisions from the edge of the optical zone outwards to almost the edge of the cornea. These incisions go deep into the stroma penetrating up to 90% of its thickness to cause a collapse or flattening of the central cornea. RK can therefore only be used to correct myopia and certain types of astigmatism.

Three theories relate this central collapse to peripheral incision (a) that there is a circumferential band of collagen around the peripheral cornea and that cutting through this causes the centre to flatten. (b) The balloon theory which says any weakening in a device under pressure will cause bulging at the weakened part and flattening elsewhere. (c) The gape theory which says the radial wounds gape and by increasing the effective diameter of the peripheral cornea the centre flattens. There is no anatomical evidence for (a), and (b) and (c) would demand a control of predictability over wound healing subsequent to surgery that we do not have.

Even in the absence of a comprehensive theory as to why this type of surgery works, all theories demand a precise control of the depths of incisions. The depth of a given incision depends upon a number of variables including the sharpness of the cutting edge, the surgeon's hand pressure and speed, the tissue resistance and elasticity. Once the blade touches the surface of the tissue the surface deforms and cutting to within an accuracy of a few microns becomes impossible. Ophthalmologists have minimised this by using diamond and sapphire knives and by equipping them with 'blade skis', however, they still cannot cut to the accuracy demanded by refractive surgery and at best manage ±12% of the target depth.

Clinical trials reflect these problems in terms of the numbers of patients under or over corrected but even so a large number of patients are happy with the results and to be free of wearing glasses or contact lenses.

No-touch technique

Four years ago ophthalmologists began to wonder if a no-touch surgical technique could be employed for refractive surgery using lasers. Lasers have long been associated with ophthalmology, being the first sub-speciality in medicine to employ them and still being the field in which the most units and the greatest variety of types of lasers are found. This pre-eminent position has come about because the eye is the only organ of the body that is specialised to allow a portion of the optical radiation spectrum to penetrate deep within it.

In laser surgery it is the wavelength of the laser that determines where the laser energy will be absorbed and therefore which tissues are potential targets. To operate on the surface of the cornea lasers with emission wavelengths in the UVC (280-100nm) or IRB (1.4-3μm) and IRC (3μm-1mm) holds most promise as they could potentially initiate a superficial effect with no complications of excess energy penetrating into the eye and damaging the retina. A number of infra-red lasers including Hydrogen Fluoride, Colour Centre Lasers, Raman Lasers and Erbium YAG have been considered as suitable candidates but, as yet, most of the experimental work has been concentrated on UVC lasers and, in particular, Excimer lasers.

Excimer is an acronym derived from the first two and last syllables of the words that describe the physical state of the lasing media used in such lasers. Excimer dimers. Excited dimers are two atoms of an inert gas bound in a highly excited state with atoms of a halogen to form a temporary, highly unstable association as a diatomic rare gas halide. The decay of these unstable molecules is accompanied by the emission of a highly energetic photon of ultraviolet light. The energy of the photons and therefore the wavelength of the light emitted from an excimer laser is dependent upon the particular gas mixture used to fill the laser. For example, the emission from a mixture of argon and fluorine occurs at 193nm and that for krypton fluoride at 248nm. These lasers emit their radiation as a train of individual pulses whose duration is typically about 10 nano-
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seconds (10^-9 seconds), with a
selectable pulse repetition frequency of
between one and 100 pulses per second,
and typical pulse energies of 20 to
200mJ.

In the materials and electronic indus-
tries excimers are used to etch
submicron patterns into the surfaces of
plastics and other polymers with no
degradation processes being conducted
to unirradiated areas. In this situation
resolution can be considered both in
width and depth of material removed
with each pulse of laser energy. In
theory, the very best lateral resolution
would occur if only those molecules
directly irradiated were removed and
the best depth resolution would be one
layer of molecules removed per laser
pulse. In practice more than one layer
of molecules is removed with each pulse
because photons penetrate through the
surface of the target. As previously
stated, the penetration depth is a
function of the nature of the target
material and the wavelength of the
incident radiation. In biological tissue,
minimum penetration occurs at two
wavelengths, 190nm in the ultraviolet
C and 2.9μm in the infra-red C. In the
former, a penetration depth of one to
cfive μm occurs as a result of absorption
of the UV photons by macromolecules,
in particular proteins. In contrast, an
absorption depth of 20-25μm is
observed at 2.9μm and in this case
results from absorption of IR photons
by water molecules. These respective
penetration depths define the maxi-
mum amount of target tissue that will
be directly affected by each pulse of
laser radiation.

There are two theories on the
removal of tissue by absorbed photons.3
The first of these suggests that the
photons cause ultrafast tissue heating,
so-called photon-phonon interactions,
and that the vibration of super-heated
molecules causes them to fall apart.
The second theory asserts that the target
reaction is not thermal but photon-
induced molecular decompensation or
photoablation. The protagonists of this
theory submit that molecules in the
target are released as a direct result of
rupture of intermolecular bonds whose
uncoupling is induced by the absorption
of high energy photons. Such a mecha-

Figure 1—Diagrammatic representation of the molecular events occurring
within a biological matrix after irradiation by high energy ultraviolet photons

nism is possible because in the ultra-
violet at 193nm individual photons have
an energy in excess of six electron volts
and, as this is greater than the binding
voltages of some proteins, the photons
are capable of disruption valency elec-
trons. As the macromolecules break up
the component fragments require a
greater space than the original mole-
cules. Fragment expansion can only be
facilitated by displacement and as these
processes are only occurring at or close
to the target surface, such displace-
ment inevitably results in loss of
material from the exposed surface. This
process is illustrated diagrammatically
in Figure 1.

In practice the depth of the tissue
removed per pulse is determined by the
pulse energy with a maximum set by
the penetration depth. At 193nm,
varying the pulse energy means that
predetermined depths of tissue can be
removed at any level between 1/40 and
1μm per pulse. An example of the
degree of control is seen in the scanning
electron micrograph of excimer
excisions in a human hair (Figure 2).
The unique nature of the photoablation
process becomes even more apparent
when excimers are used to incise soft
tissues such as the cornea (Figure 3). It
is immediately apparent that the walls
of the incisions are perfectly smooth
and coated by a pseudomembrane
rather like a 'shrink-wrap' or 'cling film'
covering of food stuffs.4 This
pseudomembrane is thought to arise
from the somewhat random recombi-
ation of the ruptured bonds of the
molecular fragments that remain
locked in the tissue matrix of the walls
and floor of the excision. Whatever its
origin, it creates an optically smooth
surface and imparts a limited osmotic
integrity to the cut surface. The second
quality of excimer incisions is that no
damage is apparent 100 to 300nm away
from the region of ablation. This lack of
secondary or conductive damage is
unique to the excimer lesion.5

With such precise control of tissue
removal and with such a clean and
highly localised wound, an excimer
seems an ideal instrument to avoid the
procedural limitations incurred during
radial keratotomy procedures carried
out with steel or diamond knives.
However, at a cost in excess of
$100,000 for a clinical excimer laser this
would be a very expensive solution to an
extremely limited surgical problem.

One further attribute of the excimer
laser should be considered. Excimers
usually emit beams of rectangular cross
section typically 20mm by 10mm. The
beam cross section can be made square
by passing it through a cylindrical lens
and then circular by passing it through
an aperture. If an excimer beam of
circular cross section and say 10mm in
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A A biological macromolecule.
B On absorption of a
UV photon (black dot)
the bonds of the
molecule begin to
break up and this
is accompanied by an
increase in volume.
C Complete break-
down of valency bonds
results in molecular
fragmentation and
fragment displacement
with expansion.
D, E, F show the same
process but now
occurring to three
individual macromole-
cules irradiated at the
surface of biological
matrix. The net result
of molecular fragmenta-
tion and expansion is
expulsion of destabil-
ised molecules from
the target surface.

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Optician
Figure 2—Scanning electron micrograph of excimer laser ablations in a human hair. The scales of the hair can be clearly seen in the higher power picture and the slight ridges on the bottom of the excimer excisions have been caused by diffraction of light through the slit aperture used to make these ablations.

Figure 3—Transmission electron micrograph of an excimer laser incision through the stroma of a rabbit cornea. The individual collagen fibres can be seen running diagonally across the photograph. The dark line running vertically is the juxtaposition of two layers of pseudomembrane and outside this an electron dense zone can be seen in relation to excimer laser exposures.

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Diameter is allowed to fall upon a biological surface then at a given pulse energy a 10 mm diameter disc 1 μm deep will be ablated with each laser pulse. If the tissue were the cornea, then a perfectly round, smooth surface excavation would be created to a predetermined depth and this is precisely the configuration desired for preparing the recipient eye in corneal graft procedures. Similarly, if instead of using a beam of circular cross section one was obtained which was an annulus or ring shape, then the corneal button to be grafted could also be cut from the donor eye and the bed and button would match with submicron accuracy. An annular beam cross section can be obtained by using a combination of prisms and lenses called an Axicon.

Circular beams

The facility for producing large beams continued on page 20
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of circular cross section also has profound implications for refractive surgery. If, for example, a beam was produced in which the energy distribution across it was variable in a controlled fashion, then the beam could be used to sculpt or shape the surface of the target. This is shown diagrammatically in Figure 4 where two examples are considered. In Figure 4(a) the highest concentration of energy is located at the centre of the beam and energy per unit area decreases towards the periphery. Such a configuration of energy would result in a concave erosion of the target or in the case of the cornea, the production of a negative lens. Conversely, in Figure 4(b) with the highest concentration of energy at the edges of the beam and the lowest at its centre the resultant erosion would produce a convexed surface or a positive lens.

In practice it is easier to control the number of pulses falling upon a given area of surface rather than varying the energy per unit area. By varying the number of pulses different areas can be ablated to different depths. If for example, an iris diaphragm is placed concentric with the laser beam and then progressively opened or closed with a given number of laser pulses being directed through the aperture in the diaphragm at each aperture size, then the target surface will be ablated to give rise to a series of concentric circular steps (Figure 5). If the aperture is motorised and suitably integrated with the laser control system then the steps could become infinitely small and thus in practice a smooth curve would be generated. This is the principle employed in the two ophthalmic excimer laser systems that are commercially available, one produced by CooperVision, the other by Summit Technology.

Such systems can cut optically smooth curves on to the surface of the cornea and an example of the optical quality of the ablated zone is shown in Figure 6. Computer predictions showed that greater than 90% of all myopia throughout the population of the world could be corrected by ablating curves which maximally removed 25μm or less of stromal material. Subsequent experiments on animals have shown these predictions to be correct in terms of the refractive power of the initially ablated surface.

Figure 5—Scanning electron micrograph of corneal surface showing a series of steps cut into the surface by progressively opening the aperture of an iris diaphragm. Note that each step in this case is not perfectly circular, but has a segmented boundary which is due to the movement of leaves within the iris diaphragm.

Long-term survival experiments are currently being conducted to examine the healing characteristics of these large area ablations. Studies with animals and tissue culture systems indicate that excimer induced ablations do not exhibit a latency in wound healing and that the ablated area is recovered by epithelial cells within 12 hours of exposure. The cells migrate along the pseudomembrane from peripheral unirradiated areas and because the pseudomembrane is so smooth they re-establish a perfectly parallel optically brilliant epithelial system.

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locks both in relation to chemical and radiation hazards. Four further components would be required for photorefractive ablation and these are:
1. A measuring system capable of determining the refractive error and astigmatism axis in the patient's eye.
2. A beam delivery system with optical components that allow programming of the energy distribution across the beam in time or space.
3. A computerised means of inter-relating (1) and (2) such that the required correction is ablated.
4. Some means of locking the laser delivery system to the eye so that the target area remains located throughout the exposure period.

As stated, two commercial systems are addressing these delivery problems but only the Summit system has a purpose-built clinical laser (Figure 7).

As far as the patient is concerned a typical visit for a photorefractive keratectomy procedure should consist of the following. First the patient's refraction is determined by whatever method the practitioner favours, then the procedure is repeated using the integrated refraction system in the excimer laser delivery system. If the surgeon is satisfied there is a good agreement he can lock the refraction into the laser's microcomputer and it will automatically set the laser delivery optics. If the surgeon is dissatisfied he can enter whatever he feels is the required correction manually and again the microcomputer will set up the delivery optics to his specification.

The patient is given a miotic to close the pupil and a local anaesthetic. The delivery system is then locked to the eye by a vacuum ring located on the sclera and the refraction is again checked to ensure that the vacuum coupling has not altered the curvature of the cornea. If satisfied the surgeon fires the laser and for most corrections the laser exposure will last less than 12 seconds. The system is uncoupled from the sclera and, after the instillation of further topical anaesthesia and antibiotics, the eye would be padded overnight. The whole visit as an out patient should be no longer than 20 to 30 minutes. The next morning the site of ablation will have re-epithelialised and the patient should be free of any discomfort and visually active.

We would predict if all goes well with current trials that systems may be in clinical use in two years.

References