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INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
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Second Training College on Physics and Technology of Lasers and Optical Fibres

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Lasers in Medicine

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Lasers in Medicine

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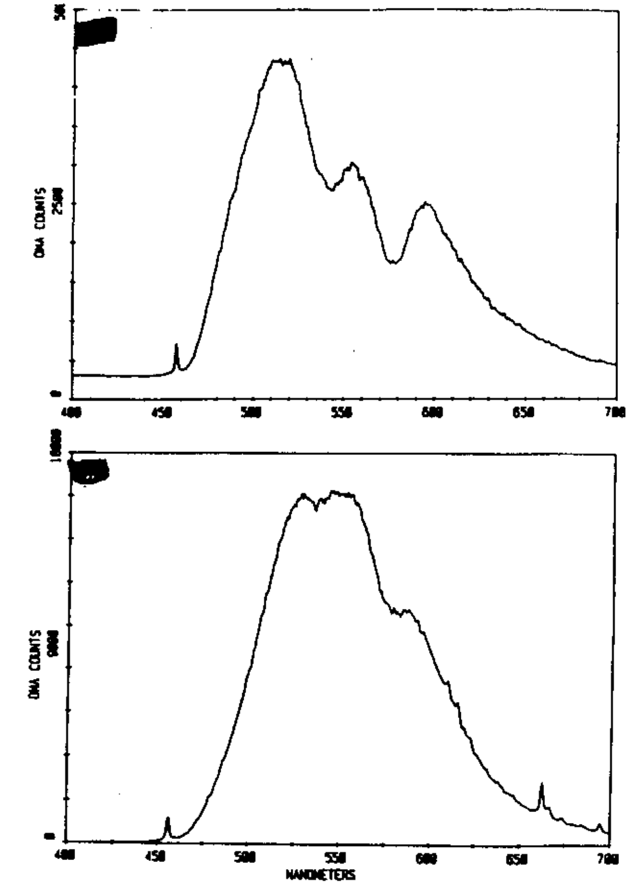


Figure 2 : Autofluorescence spectra from human arteries. [redacted] Normal section of tissue. It shows the characteristic three peaks. [redacted] Calcified section of tissue. The spectrum shows almost no structure but is more than four times more intense that the autofluorescence intensity from normal tissue.

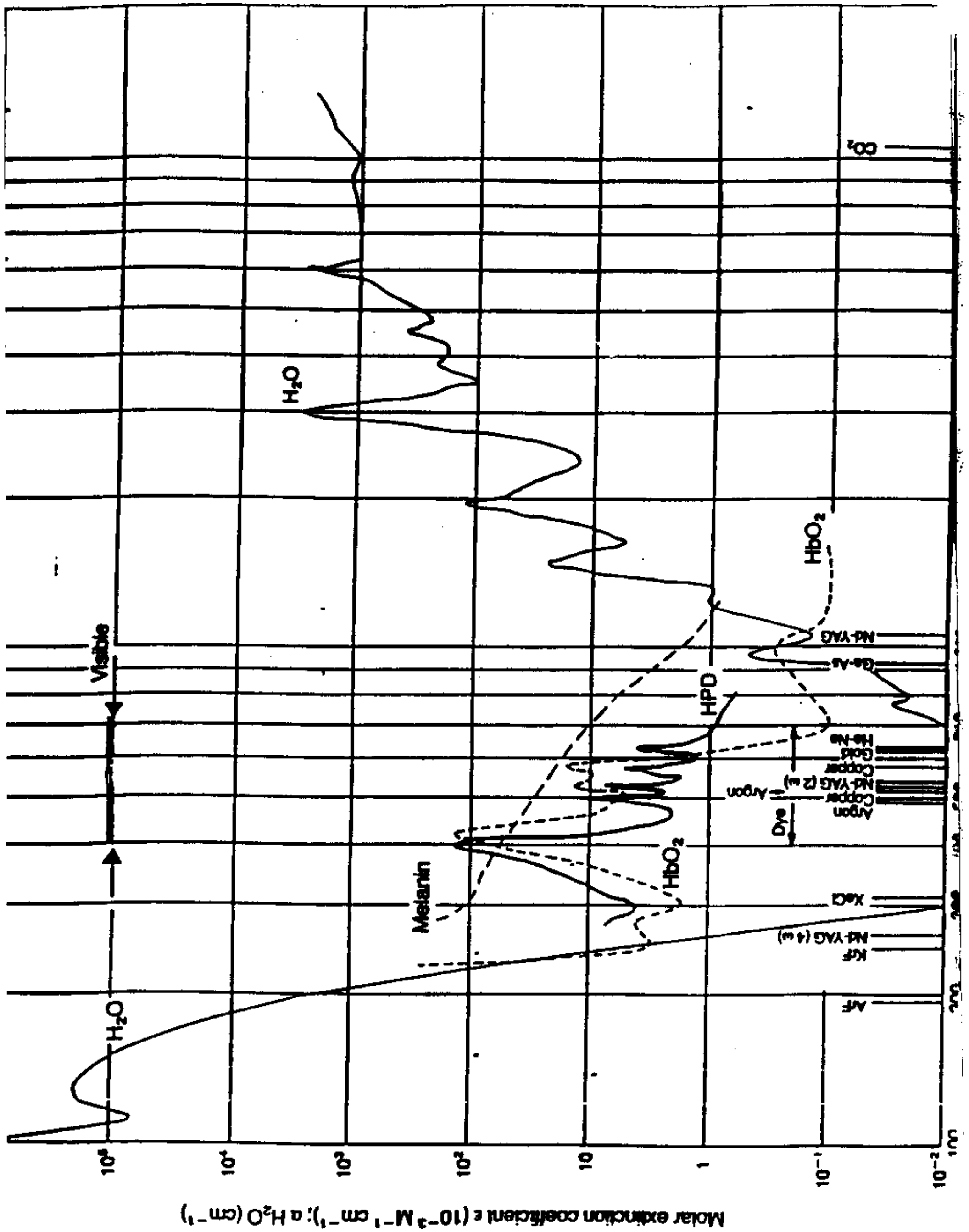


FIG. 11

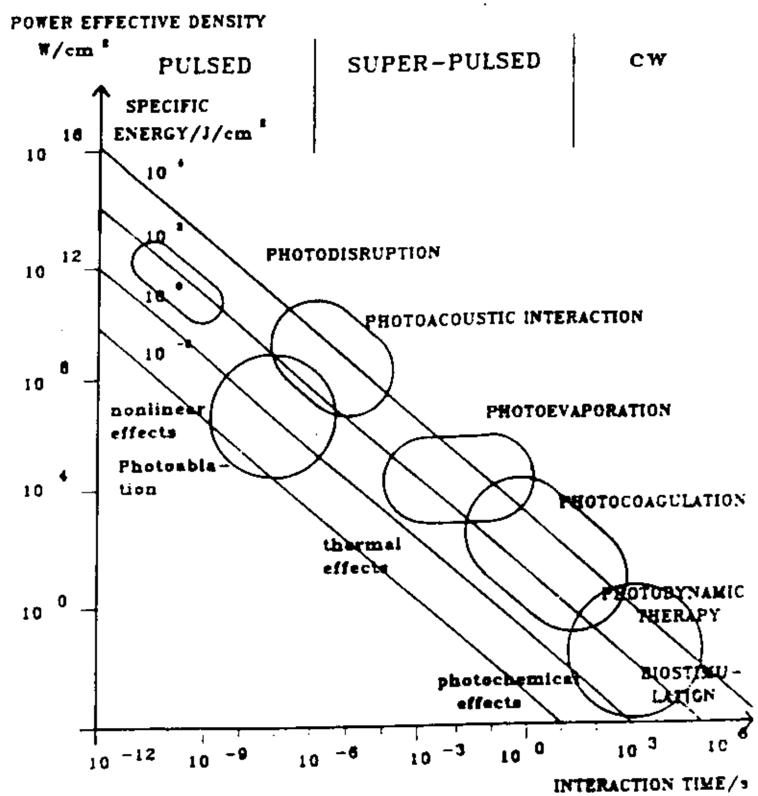


Fig. 10 Different laser tissue interactions as a function of interaction time and power density. The specific energy is the field parameter.

THERMAL INTERACTION

The surgical applications of LIGHT rely on the conversion of light energy into thermal energy.

At the microscopic level, the photothermal process consists of a two-step reaction:

- the excitation of the target molecule A :

$$h\nu + A \longrightarrow A^*$$

- the deactivation of A^* through an inelastic scattering with a collisional partner M of the surrounding medium, with an increase ΔE of kinetic energy of M :

$$A^* + M(E) \longrightarrow A + M(E+\Delta E)$$

The photophysical parameter of interest is the absorption coefficient α of the medium, and its reciprocal $1/\alpha$, which measures the characteristic absorption length of the biological system.

Another important parameter of interest is represented by the THERMAL DIFFUSION LENGTH, L, of the sample, defined as :

$$L^2 \sim 4\varkappa t$$

where :

t = [redacted] time

$\varkappa$ = thermal diffusivity (which depends on thermal conductivity, specific heat, and density)

In the CLINICAL procedure COAGULATION and/or VAPORIZATION of the tissue must be obtained with minimum thermal damage to the non-irradiated healthy tissues.

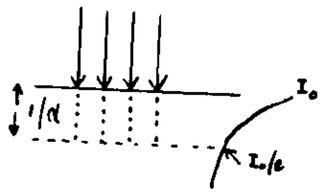
This requires a PRECISE control of the temperature rise in the irradiated volume and in the surrounding zones: the temperature in the irradiated volume must reach the COAGULATION or VAPORIZATION limit, while it must remain below the irreversible damage limit in the untreated tissue.

By adjusting the duration of the exposure to the light beam, its energy content, and the repetition rate, the temperature RISE in the irradiated volume and in the adjacent zones con be controlled in a sufficiently precise way.

If the pulse duration is much shorter than the characteristic time τ that the heat needs to diffuse along a length nearly equal to the penetration depth $1/\alpha$ of the optical radiation, the optical energy of the pulse remains trapped in a volume S/α (S=beam cross-section), where it produces a high temperature increase.

The expression of τ is given by

$$\tau = 1 / 4\varkappa\alpha^2$$



For water : $\varkappa = 1.4\ 10^{-3}\ cm^2/s$ (heat diffuses 0.8 cm in 1 s)

heat of vaporization : 2530 J/g

At $\lambda = 10.6\ \mu m$ (CO_2 laser) : $\alpha = 10^3\ cm^{-1}$; $1/\alpha = 10\ \mu m$

and $\tau = 200\ \mu s$

Consequently, by pulsing the laser with pulses shorter than 200 μs it should be possible to vaporize tissue directly and still obtain an extremely small amount of necrosis.

Typical pulses of 10 mJ/50 μs from a CO_2 laser operating at 50 Hz would vaporize 300 μm spots, and would cut with a velocity larger than 10 mm/s.

The **first mechanism** by which tissue is thermally effected is by **MOLECULAR DENATURATION** :

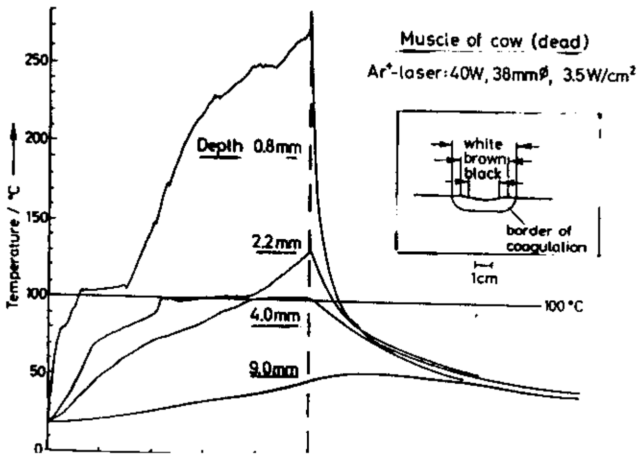
macromolecular conformational changes, bond destruction, and membrane alterations occurs aroud 45°C, with consequent tissue retraction (shrinkage).

Protein denaturation is observed beyond 60°C, and the macroscopic result is the COAGULATION of the tissue.

Vaporization occurs beyond 100°C, predominantly from heated free water; the excess heat is carried away by the steam and the temperature remains constant untill all the water is evaporated.
From this point the temperature increases rapidly, leading to carbonization and final decomposition of the tissue architecture.

Physical principles of photothermal processes: Conversion of electromagnetic radiation into heat increases the tissue temperature

Temperature	Effects on tissue
43-45°C	Conformational changes Retraction Hyperthermia (cell mortality)
50°C	Reduction of enzyme activity
60°C	Protein denaturation Coagulation
80°C	Collagen denaturation Membrane permeabilization
100°C	Vaporization and ablation Carbonization

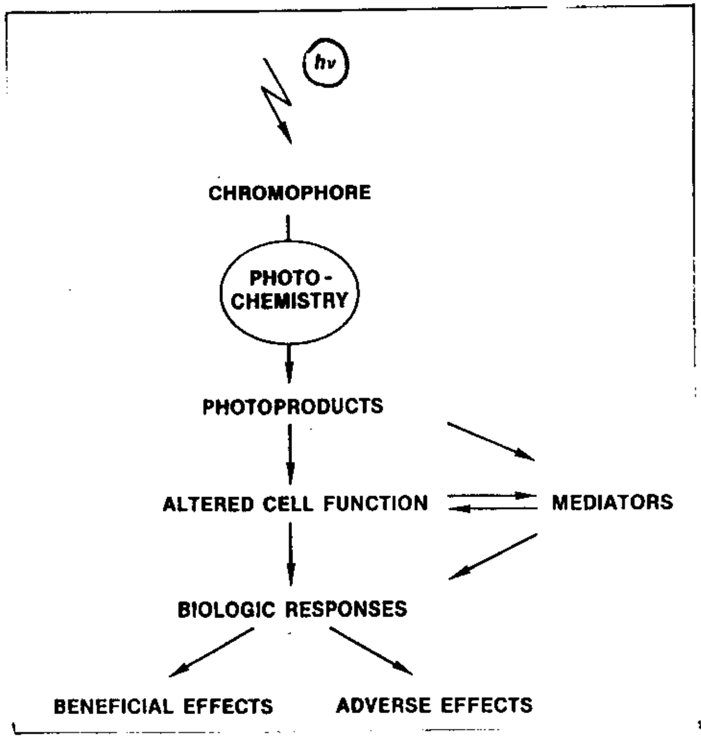


PHOTOCHEMICAL INTERACTION

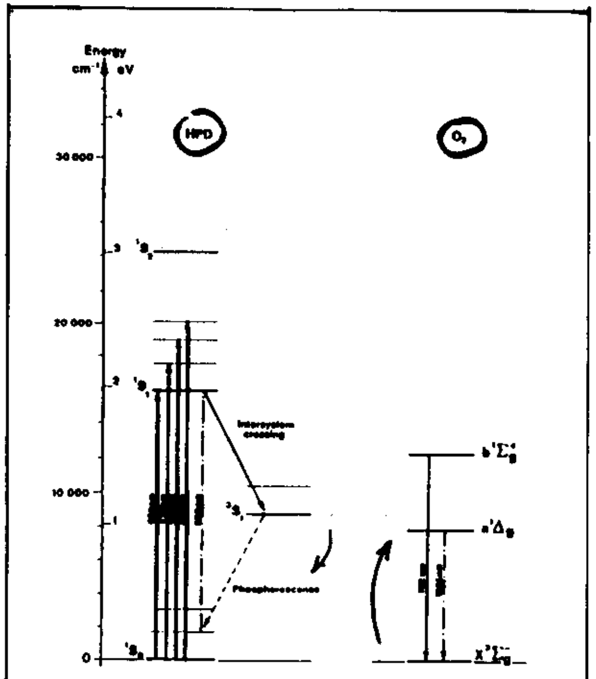
Light may act as a REACTANT in a photochemical reaction. In this case the photon energy is used to excite a particular CHROMOFORE that in turn initiates a complex biological process whose final products have a THERAPEUTICAL relevance.

A Chromofore capable of causing light-induced reactions in molecules that do not absorb light is called a "PHOTOSENSITIZER".

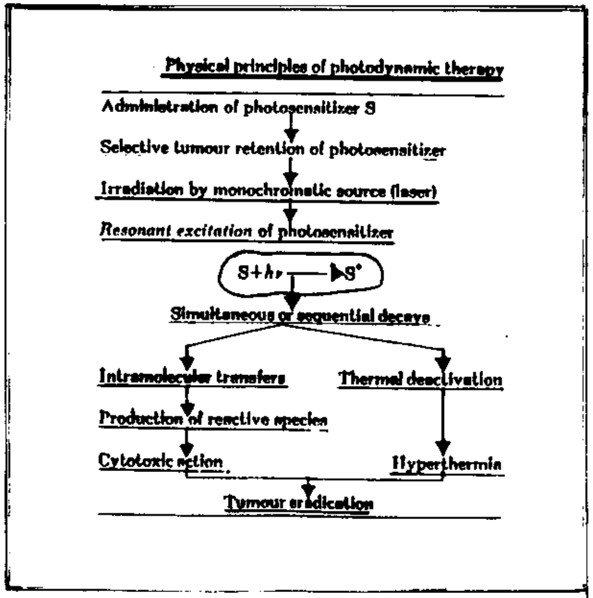
The photosensinsitizer, once excited, undergoes a sequence of simultaneous or sequential decays, which result in intramolecular transfer reactions and ultimately culminate in the release of highly reactive CYTOTOXIC species, which cause irreversible oxidation of some essential cellular component and destroy the affected host tissues.



Possible sequence of events following exposure of skin to nonionizing radiation (hv) leading to beneficial and/or adverse effects.



Energy level diagrams of haematoporphyrin derivative (HPD) and molecular oxygen.



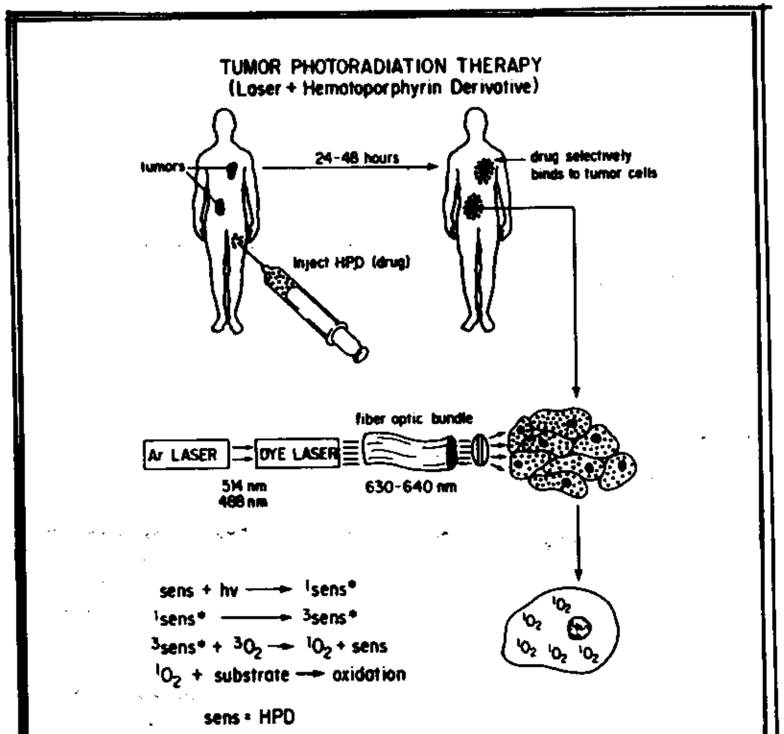


Fig. 1. Summary diagram of hematoporphyrin-laser photoradiation therapy. The generation of singlet oxygen ($^1O_2$) is proposed to be the cytotoxic species. The HPD (or one of its subcompartments) is selectively retained by the tumor tissue, rather than "selectively bound" to tumors as suggested by the diagram.

ELECTRO-MECHANICAL INTERACTION

In a transparent dielectric medium absorption of a light pulse may occur if the peak power is sufficiently high to induce the BREAK-DOWN of the dielectric itself (light-induced optical break-down).

The initial ionization mechanism depends on the pulse duration :

1-10 ns (Q-switched laser) : ionization is caused by THERMOIONIC EMISSION resulting from focal heating of the target ($T>10^4$ °K)

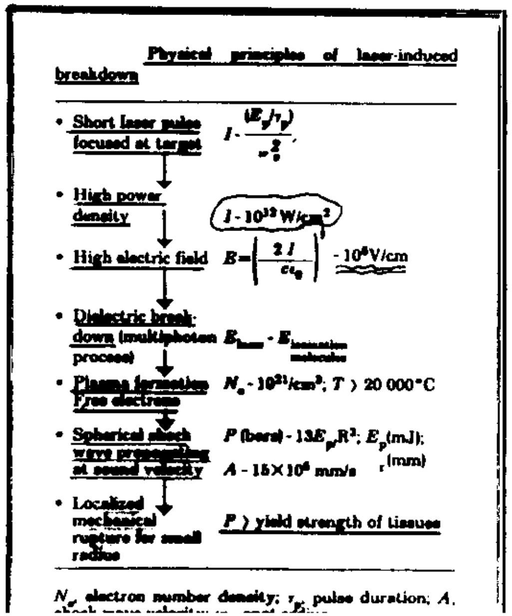
1-10 ps (mode-locked laser) : ionization is produced by multi-photon absorption.

The initial ionization is followed by an ELECTRON AVALANCHE growth produced by the acceleration of free electrons and subsequent energetic free electron-atom or molecule collisional ionization.

The absorption of photons is basically a FREE-FREE transition, and must necessarily occur in the field of an ion or in that of a neutral atom (INVERSE BREMMSTRAHLUNG) :

$$h\nu + e(E) + A^+ \longrightarrow e(E+\Delta E) + A^+$$

The breakdown of the dielectric produces a MICROPLASMA, whose rapid expansion generates a SHOCK WAVE, with consequent localized mechanical rupture of the tissue when the pressure rise is superior to the yield strength of the tissue.



2.4 Photodecomposition

Ablative photodecomposition is a new technique to make incisions of controlled depth and shape in defined areas of specific tissues or body structures, and to remove any amount of tissue by ablating that tissue to a predetermined depth, with no apparent thermal damages to adjacent tissues. True ablative photodecomposition needs the employment of lasers emitting high-peak-power far UV radiation. In this spectral region, laser ablation produces a trench with sharp and clearly defined boundaries by light microscopy. Among the various ophthalmological applications the application for refractive keratoplasty would seem to be of great interest due to the fact that the cornea can be reshaped in such a manner as the correct most moderate degrees of hyperopia, myopia, and astigmatic defects.

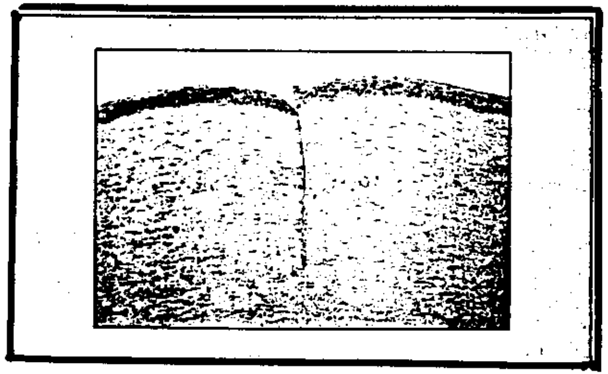
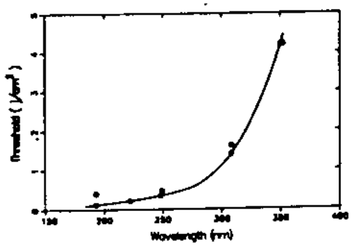


FIGURE 2. Experimental excimer-laser incision in the cornea is approximately 20-μm wide and hundreds of micrometers deep. Note the absence of alteration in tissue adjacent to the incision. Such spatial confinement of tissue effects is not possible with other laser therapeutic tools. The incision was made with a Questek Series 2000 excimer laser. Magnification is 16 X. (Photo: courtesy of Carmen A. Puliafito, Massachusetts Eye and Ear Infirmary.)

Excimer laser systems for angioplasty

* Electric discharge excitation of a gas mixture
* ArF , KrF , XeCl , XeF
* Low ablation threshold   0.05 - 4 J/cm^2



TUA3 Fig. 3. Threshold fluences for different excimer laser wavelengths: O, calculated by combining the threshold (KrF line) for formation of low molecular weight hydrocarbons in the ablation of normal artery wall and the photoacoustic spectrum of Fig. 2; ●, experimentally determined upper limits for removal of tissue determined by light microscopy.

* "cold" photochemical decomposition

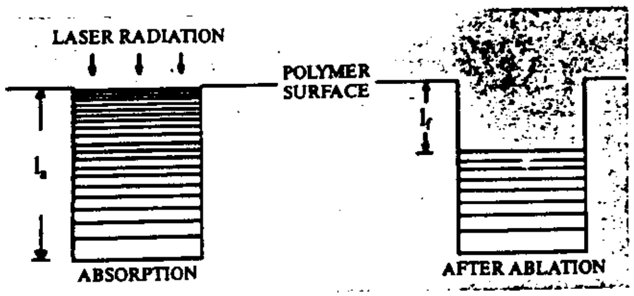


Fig.2 Schematic representation of impact of laser pulse on polymer surface

Material ejection

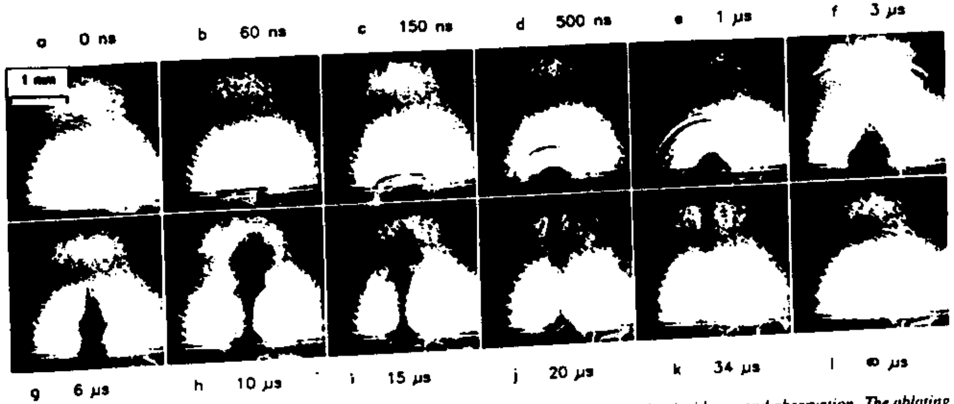


Fig. 3 Ablation plume and precursing shock wave in profile, seen at different delays in grazing incidence and observation. The ablating laser pulse is directed vertically downward onto the surface which is at the bottom of each frame.

Small scale particulates and gaseous products

TABLE I. Amounts of products formed by laser ablation of healthy artery wall using a KrF laser.[a]

	Fluence (J/cm^2)			
	0.61	1.1	2.5	3.2
CH_4	0.20	0.50	1.3	1.7
C_2H_4	0.29	0.97	2.8	3.3
C_2H_6	0.038	0.072	0.14	0.18
C_3H_6	0.065	0.18	0.42	0.51
C_3H_8	[b]	[b]	0.066	0.081
c-C_3H_6	[b]	[b]	0.22	0.26
C_4H_8's	0.056	0.13	0.30	0.31
CH_3CHO	0.029	0.080	0.098	0.11

[a] The amounts are 10^{-8} moles. 500 laser pulses.
[b] Analysis was prevented by the presence of an impurity.