LASER LITHOTRIPSY OF KIDNEY CALCULI
WITH A Nd:YAG LASER

Diploma paper

by

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1 ABSTRACT

This paper describes *in vitro* laser lithotripsy (stone fragmentation) studies of urinary calculi with a Q-switched Nd:YAG laser, oscillating at 1064 nm.

A fibre is intended to be the laser energy delivery tool through the urethra, although it was found to be difficult to transmit enough energy and power from laser to stone. The 10 ns long pulses from the laser easily damaged the fibre itself. A step index fibre with a diameter of 600 μm could transmit 20 mJ/pulse. This corresponds to a fluence of about 0.7 GW/cm^2.

At a pulse energy level limited to 20 mJ/pulse a piece of metal wire must be placed between the fibre exit surface and the stone, in order to damage the stone. The metal piece encourages plasma initiation.

Plasma emission and fluorescence spectra from a kidney stone, induced by a XeCl excimer laser at 308 nm, can easily be distinguished from spectra obtained from the urethra. Fluorescence spectra from stones using nitrogen laser excitation at 337 nm and dye laser excitation at 405 nm are also presented.

2 INTRODUCTION AND THEORY

2.1 SURGICAL TREATMENT OF URINARY CALCULI

Urinary calculi frequently result in painful and serious medical conditions. During a person's lifetime the probability of formation of stones somewhere in the renal tract may be as high as 10-20% (1). It is the precipitation of dissolved salts in urine which results in the formation of urinary calculi, but it is not well established exactly which factors lead to calculi formation. Urine concentration is, of course, important. Correlations with occupation, geographical location and state of industrial developement have also been established (2),(3).

All urinary calculi are crystalline. Most of the stones in the adult population in industrial countries consist predominantly of calcium oxalate. Stones found in children have a different composition.

<u>Calculus in the kidney</u>.

A few years ago calculi in the kidney were removed by open surgery. The kidney was laid bare by a long incision in the flank. The stone was then removed through a hole in the kidney or the kidney pelvis.

This open surgery was replaced in the beginning of the 1980's by so-called percutaneous stone extraction. A narrow tube is inserted through the wall of the abdomen into the kidney, the so-called nephrostomy technique. This is done with the help of X-ray monitoring. The tube is left for a while to drain the kidney. The channel is then widened by replacing the narrow tube with a larger one of 1 cm diameter. Calculi with a diameter smaller than 1 cm can hence be removed. Bigger calculi are fragmented into smaller pieces and collected with a special instrument, nephroscope.

In 1985 the Extracorpueral Shock Wave Lithotripsy, ESWL, technique came into use. A shock wave is produced outside the patient, led through the body and focused on the stone. The stone is fragmented into small pieces, which usually disappear the natural way, with the excretion of urea..

ESWL has many advantages compared with open surgery and percutaneous stone extraction: There are fewer complications, usually no anaesthesia is needed, it usually involves less pain and other discomfort to the patient, the patient does not have to remain in hospital afterwards and can usually start working again the next day. So even if ESWL involves expensive instruments, in the long run, money is saved.

When the stones are big or hidden behind the skeleton, ESWL has to be combined with percutaneous stone extraction. 80% of patients with calculi can be treated with ESWL only, while 10%-15% need the combined treatment of ESWL and percutaneous stone extraction and 5%-10% still need open surgery.

Calculi in the urethra

Stones sometimes leave the kidney and pass into the urethra. If they are small enough (< 6 mm) they usually spontaneously disappear through the bladder. Bigger stones may become trapped and block the urethra and/or cause a great deal of pain.

Until 1985 these stones had to be removed by open surgery. Only if they were less than 6 mm in diameter and were trapped in the lower third of the urethra, could transurethral stone extraction be used. A stainless steal basket is led into the urethra, the stone is caught and pulled out.

At hospitals with access to ESWL, this can be used. Hopefully, most hospitals will soon have access to this technique, meanwhile, other techniques will have to be used. Some stones that are in the upper part of urethra can be removed by percutaneous extraction (a tube through the abdomen) through the kidney. Some can be removed with an urethrascope. This is an instrument that is led through the bladder and into the urethra. Stones are caught in the stainless steel basket, while looking through the instrument. The urethrascope has a diameter of 6 mm and is rigid. Bigger stones are first fragmented with ultrasound or electrohydraulically by a spark at the stone. There are also smaller, flexible urethrascopes with a diameter of 3 mm. These are today only used for diagnosis.

2.2 LITHOTRIPSY WITH LASERS

There are several disadvantages with the methods described above. Even ESWL involves some risks. If the shock wave is not focused exactly on the stone, damage will occur to the surrounding tissue. There is also a risk of developing high blood pressure, due to disruptions in the blood circulation in the kidney.

Laser lithotripsy is the fragmentation of stones using a laser. Laser lithotripsy is intended to be a complement to ESWL, but with a more advanced and developed technique perhaps the laser will even replace ESWL. The energy needed to destroy a stone by leading laser light, by means of an optical fibre, <u>into</u> the body is about 100 times less than the energy needed for stone destruction with ESWL (4). With ESWL the energy has to be led <u>through</u> the body. With laser lithotripsy it only takes a few minutes to destroy a stone.

Quite a few experiments have been performed *in vitro* on the destruction of calculi. During the last year *in vivo* experiments have also been performed (5),(6). The treatments have mainly been performed in the urethra. A light guide is led through a stiff or flexible urethrascope and positioned by looking through the scope. It would be even better if the surgeon could position the fibre tip with the aid of X-ray or ultrasound techniques.

One way to be sure that the fibre is located at the correct position is to take a spectrum at this location. The spectrum can either be a fluorescence spectrum or an opto-acoustic spectrum (a spectrum of the shock waves emitted when laser energy hits a tissue). To be sure no tissue is damaged the laser must be used at a sufficiently low energy. A higher laser energy is then used to fragment the stone.

In the performance of laser lithotripsy, Nd:YAG lasers (1),(5),(6),(7),(8) and flashlamp-pumped dye lasers (9),(10),(11),(12) have been used. Pulsed lasers are used because a sudden temperature rise at the stone surface creates a shock wave which fragments the stone into smaller pieces. Pulsed lasers also avoid heating of the surrounding tissue. This paper describes *in vitro* laser lithotripsy experiments using a Nd:YAG laser at 1064 nm.

A disadvantage with lasers is that they are relatively complex tools to work with. A person familiar with lasers is needed for maintenance and urgent reparations.

2.3 THE FIBRE

The fibre is an important instrumental part in laser lithotripsy. It is the laser power delivery tool, and there are a great number of demands, placed on the fibre.

Above all, it must be able to transmit the high energy and power from the laser without being damaged. To destroy a stone a high laser intensity is needed, but also high energy transmission per pulse is important. A calculus is a hard, compact stone and the fibre must have a higher threshold for laser power damage than calculi. Experiments have shown that the fibre damage threshold is proportional to the fibre cross-sectional area (13). Thus a fibre with a larger diameter can transmit more energy.

It also has to be flexible, so that the surgeon can insert and position it as easily as possible. This means it has to withstand mechanical stress such as bending, pulling and torsion. The smaller diameter of the fibre the more flexible it is. This is because the stress on the fibre increase proportionally to the radius at a given curvature (14).

In conjunction with the Nd:YAG laser, fibres of 600 μm or 1000 μm are usually used. Smaller fibres are easily damaged by the high energy and short pulses from Nd:Yag lasers. Larger fibres do not fit into the endoscope and are less flexible.

Other important factors that affect the damage threshold are focal length of the coupling lens, fibre type and the nature of the fibre surface preparation. Special attention must be paid to these factors, especially if a small fibre is chosen.

Sterilization and moist environment affects the solidity of the fibre negatively (14). This ,of course, has to be considered when fibres are used for medical purposes.

When considering the fibre damage threshold one has to be aware that overlapping spikes may occur in the intensity distribution of the laser light (7). These intensity spikes may damage the fibre, although the mean energy level is below the damage threshold.

2.4 WHAT HAPPENS UPON STONE FRAGMENTATION?

When the laser energy hits the surface of the calculus, which is immersed in liquid in the body, laser-induced breakdown (LIB) occurs and a plasma is formed. The plasma expands and emits a shock wave which propagates into the stone. This conversion of light energy into mechanical stress gradually destroys the stone.

A plasma is defined as a medium consisting of neutral atoms, electrons, ions and quanta emitted from atoms or ions. The plasma is formed due to an avalanche effect (8). Looking at it quantum mechanically, the laser beam constitutes a photon flux. Electrons are accelerated by inverse Bremsstrahlung. A free electron collides with an ion or an atom and absorbs photons in doing so. The electron gains energy and is accelerated. At a high photon flux there is a considerable acceleration of the electrons. When their energy is great enough, additional electrons are stripped off when the electrons collide with atoms. The new electrons are also accelerated and the number of free electrons increases in an avalanche fashion.

To trigger an electron avalanche, either free electrons or conducting electrons must be present, or else the first electrons have to be produced by photoionization. However, the photon energy in a Nd:YAG laser is 1.2 eV, far below the necessary ionization energy (8). So several photons are needed simultaneously, i.e.multiphoton ionization. This process is chiefly dependent on the magnitude of the photon flux.

Upon plasma production, the temperature rises rapidly. The plasma shields the surface from laser light by absorbing the laser energy. The plasma becomes very hot, reaching several 1000 K (8).

The interface between plasma and adjacent medium represents a discontinuity surface in terms of density, pressure and temperature. This discontinuity surface is called a shock wave and is identical to the plasma boundary during the expansion phase. In this phase, the shock wave is propagated due to energy absorption, and can be described as a detonation wave.

The expanding plasma acts as a piston on the surrounding environment. The plasma-filled bubble propagates with a maximum velocity of about 8000 m/s (15). This rapid expansion prohibits heat conduction from inside the plasma into the surrounding tissue. Therefore, only that tissue which lies in the path of the detonation wave is affected thermally and is fully evaporated. A laser which is not Q-switched (Appendix B), with μs-long pulses creates a lower pressure and velocities around 1500 m/s. So plasma generation with Q-switched lasers can only be compared to breakdown with μs-long pulses in the limit of strongly absorbing targets, such as graphite (16).

After laser emission, plasma motion slows down and the shock wave propagates at supersonic speed. The cooling plasma left behind causes cavitation to occur in liquids. The cavity is compressed so much by the hydrostatic pressure of the surrounding liquid that the internal pressure ultimately overcomes the external pressure. As a result of the two opposing forces the cavity begins to oscillate, and after passing through the minimum volume another shock wave of considerable amplitude is emitted. Due to emission of shock waves and associated energy losses the oscillation of the bubble rapidly attenuates.

Fig. 1 shows how the pressure in a liquid changes upon plasma creation. It also shows how the pressure changes becomes smaller and smaller during cavitation oscillation.

Fig. 2 shows photographs of cavitation growth. Notice the stainless steel basket enclosing the stone.

The calculus is struck by the shock waves travelling through the liquid medium. Mechanical stress occurs at the interface, and the calculus is destroyed. If the LIB occurs only at the stone surface, the destruction is effectively promoted by cavitation effects (8).

Fig. 3 shows the plasma creation as a function of time.

The pressure is linearly dependent on the mean electric field strength from the laser (12),(17). However, there is a minimum fluence (energy/area) required to initiate plasma formation. This threshold is reproducible for the same stone but varies as much as a factor of ten between different stones (8). Fig. 4 shows breakdown frequency in water as a function of electric field strength. According to Ref. (8) a field strength of 60 MV/m will destroy any calculi in water.

It has been shown that when the stone is immersed in water, the destruction is ten times more effective than when the stone is surrounded by air (12). This is probably due to improved coupling of the plasma to the stone and not because of differences in plasma initiation. This conclusion has been drawn as the fluence requiredto initiate the plasma for a given delivery pulse energy is insensitive to the immersion (19).

The amount of energy that is coupled from an acoustic wave into the stone depends on the difference in acoustic impedance between the stone and surrounding medium. Acoustic impedance is the product of density and sonic speed .through the bulk material. Reflection losses of a plane wave travelling through materials of different densities is given by the Rayleigh formula:

$$I_r/I_t = [\ (Z-Z')\ /\ (Z+Z')\ ]^2$$

Where I_r and I_t are reflected and transmitted acoustic intensities, Z and Z' are acoustic impedance. According to Ref. (12) I_r/I_t (air stone) = 0.999 and I_r/I_t (water stone) = 0.36.

Furthermore, the ability to support a high-pressure stress wave is important. Acoustic waves formed in water can be of higher intensities than in air due to the higher density of water and the higher sound velocity in water.

In Ref. (12) it has also been found that the stone has to be immersed to at least a depth of 0.3 cm for maximal pressure. Immersion beyond this does not result in an increase in stress wave amplitude. This suggests that the plasma has to be built up against a critical static pressure before the surrounding medium can effectively confine it.

Fig. 5 shows laser lithotripsy of a gallstone, which follows the same path as laser lithotripsy of kidney stones.

2.5 THE PURPOSE OF THIS PAPER

The Department of Atomic Physics has not previously performed any research on laser lithotripsy. This is the introduction to, hopefully continued, research within this area and continued collaboration between the Department of Urology at Lund University Hospital and the Lund Institute of Technology.

This paper is essentially focused on three subjects:

1) Light transmission from laser to stone

Investigation of experimental geometry and fibre tip position, for maximum transmission of energy from laser to stone. For example:

* What focal length shall the lens that focus light on the fibre have.
* How far from lens focus shall the fibre entrance be positioned.
* How much of the entrance energy does the fibre transmit.
* How much energy can the fibre transmit without getting damaged.

2) Fluorescence

Obtaining fluorescence spectra (Appendix A) of kidney stones and urethra. The spectra are intended to be used for the identification of calculi, to ensure thet other tissues in the body are not injured by the laser energy. It is interesting to have spectra of both the plasma emission and the fluorescense of the kidney stones/urethra.

3) Fracturing kidney stones

3 MATERIALS AND METHODS

3.1 LIGHT TRANSMISSION FROM LASER TO STONE

a) Fibre transmission
The energy at the fibre exit can be measured, but it is interesting to know the energy at the fibre input. The set-up for this experiment is shown in Fig. 6.

The laser is a pulsed, Q-switched neodynium YAG laser (Appendix B) from Quanta-Ray. It oscillates at 1064 nm and in the Q-switching mode it has a pulse duration of 10 ns. Without the Q-switch the pulse has a duration of 200 µs. The pulse frequency is variable but during these investigations it was kept at 10 Hz. The energy/pulse is variable from 0 to 400 mJ/pulse.

The laser light is first led through an aperture, and then a lens with a focal length of 300 mm focuses the beam onto the fibre entrance surface.

The fibre, PCS 600, has a diameter of 600±24 µm and is manufactured by Fibre Optiques Industries. It is a step index multimode silica fibre with a plastic cladding.

The fibre entrance surface has to be perfectly polished and plane, otherwise energy is reflected and/or absorbed in an unwanted way at the surface. The fibre strength is also diminished if the entrance surface is not smooth. A smooth surface is obtained by grinding the surface on paper covered with aluminium oxide. The paper is placed on a flat piece of glass to ensure a plane fibre surface. The fibre is ground on three papers with different grain sizes. First the paper with the largest grain size, 40 µm, is used and then the smaller sizes 12 and 3 µm. The smoothness and flatness of the surface are controlled with a microscope.

The entrance tip of the fibre is positioned with a holder that is movable in the x, y and z directions. The fibre entrance is correctly positioned when the output energy from the fibre is maximized, at constant energy from the laser. The energy is measured with a power meter sensitive in the 0.001 to 10 W range.

Fibre transmission is measured by first placing the power meter in front of the laser, as the arrow in Fig. 6 indicates. Then the power meter is moved to measure the fibre output energy at this laser energy.

b) Laser beam distribution

The beam intensity distribution on the fibre surface should be as constant as possible for maximal energy reception. If the beam has a larger or smaller diameter than the fibre it is also easier to damage the fibre entrance. This is why one has to study the beam intensity distribution. The set-up is shown in Fig. 7. The same laser, aperture, lens and power meter as used in the above (3.1 a) investigation are used.

At the position where the fibre entrance is assumed to be positioned, a razor-blade, mounted on a micrometer positioner, is placed. The razor-blade cuts off parts of the beam depending on its position. By gradually cutting off more and more of the laser beam the distribution of the beam can be measured.

3.2 FLUORESCENCE

The stones were made to fluorescence (Appendix A) with three different light energy sources:

a) Excimer laser

b) Nitrogen (N_2) laser and

c) Nitrogen-laser-pumped dye laser

(More about these lasers can be found in Appendix B)

a) The excimer-laser-induced fluorescence

The Excimer laser is made by Lambda Physik and emits light with a wavelength of 308 nm. The experimental set-up is shown in Fig. 8.

The laser light is focused onto the sample by a lens with a focal length of 100 mm. To record the sample fluorescence, the sample is placed a small distance out of focus. In this position the intensity threshold for plasma formation is not reached and pure sample fluorescence is emitted. If the sample is placed in the focus of the lens, the excimer laser emits enough light energy to produce a plasma (see section 2.4 What happens upon stone fragmentation) on the sample surface. In this way both sample fluorescence spectra and plasma emission spectra can be obtained

The light emitted is led through a plastic clad silica fibre PCS 600 from Fibres Optiques Industries with a diameter of 600 μm.

In front of the polychromator the light passes through a WG345 filter. This filter does not transmit light with wavelengths shorter than 345 nm. A sample fluorescences at longer wavelengths (corresponds to lower energy, see Appendix A formula (1)) than the absorbed light. In this case the absorbed light is of 308 nm so wavelengths less than about 345 nm are not interesting.

A lens focuses the light on a polychromator with a 25 mm wide diode array of 1024 diodes. A 150 grooves/mm grating in the 275 mm polychromator gives a wavelength separation of 25 nm/mm at the detector. The resolution obtained with the 1024 diodes is thus 0.6 mm/channel in a wavelenght region from 200 to 800 nm. An Optical

Multichannel Analyser, OMA III, from EG&G Princeton Applied Research receives the information and makes it possible to analyse the results.

Firstly, the background light is measured and stored in the OMA, and the background is subtracted from each spectrum. The wavelength calibration of the OMA is obtained by taking a spectrum from a Hg light source with lines of known wavelengths.

A trigger signal is led from the laser to the OMA. On the OMA one specifies how long after the triggering pulse a gate at the detector will be opened and how long it will remain open. For a sample fluorescence spectrum no delay time is used and the gate was open for 500 ns.

When a plasma emission spectrum is recorded, the possibility of obtaining several spectra at various time delays is utilized. This is done in order to see how the plasma behaves as a function of time. The gate was open for 500 ns, with an initial time delay of 0 ns and a time increment delay of 500 ns on sequential laser shots. The OMA was programmed to receive 10 spectra in one sequence.

Spectra were taken of 6 kidney calculi received from the Department of Urology at the Lund University Hospital and on a pig urethra bought from the Scan slaughter-house in Kävlinge, southern Sweden.

The resulting spectra were printed out on paper for evaluation.

b) Nitrogen-laser-induced fluorescence and

c) Nitrogen-laser-pumped dye-laser-induced fluorescence

Almost the same experimental set-up and equipment was used for these two laser excitations as in the excimer-laser-induced fluorescence recordings. The arrangement is shown in Fig. 9.. In these cases no fibre is used and, of course, different filters are placed in front of the polychromator.

Since the nitrogen laser (LN 250, PRA) emits light of 337 nm, wavelengths shorter than about 375 nm are not interesting and a WG375 filter that does not transmit wavelengths shorter than 375 nm was used. In the nitrogen-laser-pumped dye-laser (Laser Science) excitation at 405 nm, a GG435 filter was used.

These two lasers do not emit enough energy to induce plasma at the stone surface. Due to problems with keeping the urethra fresh no urethra fluorescence spectra were obtained with these lasers..

3.3 FRACTURING KIDNEY STONES

The set-up used for the *in vitro* calculi destruction is shown in Fig. 10. The same Nd:YAG laser as described in section 3.1 a) was used. The light was led through an aperture, and a lens with a focal length of 300 mm focused the light onto the fibre entrance (PCS 600, diameter 600 μm from Fibres Optiques Ind). The fibre was about 1.5 m long. In *in vivo* applications the fibre is brought through the urethra and up to the calculus. The fibre exit is placed at the stone surface.

The stone was kept in a stainless steel basket, obtained from the

Department of Urology. They use the basket in their transurethral stone extraction operations (see 2.1 "Surgical treatment of urinary calculi"). The basket with stone was placed in a water-filled one-litre jar.

4. RESULTS

4.1 LIGHT TRANSMISSION FROM LASER TO STONE

If the goal is to transmit as much energy as possible through the fibre, it did not seem to matter which lens was used to focus the light onto the fibre entrance. At the focus of the lens, laser induced breakdown, LIB, occurred in the air for some pulses. A plasma is created from the air molecules (see section 2.4: "What happens upon stone fragmentation") which absorb laser energy. LIB in air is desirable because it absorbs some of the unavoidable overlapping spikes in the laser intensity distribution. However if this happens too often, not enough energy reaches the fibre entrance. The smaller focal length of the lens the easier LIB occurs, due to the smaller spot at the focus. A lens with a focal length of 300 mm was found to be convenient to work with during these investigations.

With Q-switching the fibre entrance damage threshold was reached at 900 MW/cm^2. This corresponds to a pulse energy of 25 mJ. If 25 mJ/pulse hit the fibre entrance, 20 mJ/pulse are transmitted through the fibre.

If the laser is not Q-switched all energy that the laser can emit can be transmitted through the fibre. The maximum output energy from the laser is 400 mJ/pulse. This means a fluence that is below the damage threshold of the fibre. (The Q-switching has to be used to obtain enough power to damage the stones).

a) Fibre transmission

A fibre transmission curve is plotted in Fig. 11. Up to 25 mJ/pulse, Q-switching and non-Q-switching give the same transmission results. At 25 mJ/pulse the fibre damage threshold is reached for Q-switching and the rest of the curve is only valid for non-Q-switching conditions.

For pulse energies up to 100 mJ about 78% of the energy is transmitted through the fibre. Then the transmission is about 70%.

b) Laser beam distribution

Results from these measurements can be seen in Fig. 12 and Fig. 13. In Fig. 12 beam intensity distribution under Q-switching and non-Q-switching various conditions are compared. In Fig. 13 the intensity distribution at various distances from the lens focus is shown when the laser is not Q-switched. The Q-switching destroys the razor-blade easily and non-Q-switching measurements are more reliable. The slope of the curve corresponds to the intensity at that spot.

A curve of an ideal "top-hat" beam intensity distribution is plotted in Fig. 12. For this distribution all energy hits the 600 μm fibre surface and the energy is evenly spread out on the surface.

When the Q-switch is operating, the beam profile is smoother and is also spread out over a bigger area. Thus the fibre can be closer to the lens focus during Q-switching.

In Fig. 13 one can see the trivial result that the further away from the lens focus the bigger the area of the beam cross section. A larger distance from the focus also gives a smaller and more even slope of the distribution curve, which is preferred. The fibre should be placed as far away from the focus as possible, but at a place where not too much energy misses the fibre surface. Since Q-switching evens out the curve, 10 mm from focus is a suitable distance.

4.2 FLUORESCENCE

a) Excimer-laser-induced fluorescence

In Fig. 14 typical stone plasma fluorescence spectra can be seen. In Fig. 14a the initial spectrum without any delay is seen. In part b of Fig. 14, a spectrum of the plasma 1 μs later is shown. In the latter figure the atomic and ionic lines appear more clearly. The peaks then become smaller and smaller, and after another 1 μs no plasma emission can be detected.

The identified peaks are as follows, denoted as in figure b:

1.	CaI	363 nm
2.	CaII	371 nm
3.	CaII	374 nm
4.	CaII	393 nm
5.	CaII	397 nm
6.	CaI	423 nm
7.	CaI	430 nm
8.	CaI	445 nm
9.	CaI	453 nm
10.	CaI	459 nm
11.	CaI	488 nm
12.	CaI	504 nm
13.	CaI	519 nm
14.	CaI	527 nm
15.	CaI	535 nm
16.	CaI	551 nm
17.	CaI	559 nm
18.	CaI	586 nm
19.	Na	589 nm

Some of the stones did not show all the lines as clearly as the spectra of this stone. However, no extra lines could be observed in the plasma fluorescence spectrum of any stone. The following lines always appear very clearly (denoted as above and in Fig. 14b): 1,2,3,4,5,6,7,8,14,16 and 17.

Fig. 15 shows plasma emission from the pig urethra. This is the initial emission without any delay. With a delay the emission intensity is too low to be detected and disappears. The arrow in the figure points at the easily detectable Na line at 589 nm.

Comparing Fig. 14 and 15, it is easy to separate a urethra plasma emission spectrum from a kidney stone spectrum.

The fluorescence spectra can be seen in Fig. 16. The two upper curves are typical fluorescence spectra from stones. The uppermost curve is from a stone that is lighter in appearance than the stone that gives the middle spectrum. The stone spectra are similar. Darker stones fluorescence slightly more in the 350 nm region and a little less in the 450-500 nm region.

The lower curve in Fig. 16 is a urethra fluorescence spectrum. Also in this case, one can easily distinguish between a kidney stone and the urethra wall by means of their fluorescence spectra.

b) Nitrogen-laser-induced fluorescence and
c) Nitrogen-laser-pumped dye-laser-induced fluorescence

The results from these investigations can be seen in Fig. 17 and 18. In Fig. 17 the upper curve is the spectrum obtained from N_2 laser excitation of kidney calculi and the lower curve is the spectrum obtained from N_2-laser-pumped dye laser excitation.

In Fig. 18 two spectra from N_2-laser-pumped dye-laser (405 nm) excitation are shown. The upper curve is the same as the lower curve in Fig. 17, a typical stone fluorescence spectrum. But sometimes one obtains a spectrum such as the lower curve in Fig. 18. This spectrum has a lower intensity than the typical spectrum and three spectral lines start to appear at about 580, 630 and 690 nm. These spectra seem to occure at random, and are not correlated with stone colour or stone surface roughness. The same spectrum sometimes appears with N_2 laser excitation of stones.

4.3 FRACTURING KIDNEY STONES

A piece of copper wire has to be placed between the exit of the fibre and the stone in order to induce any damage to the stone. With Q-switching we were able to transmit only 20 mJ/pulse through the fibre. Even when a piece of copper wire was inserted, the stone was fragmented into small pieces very, very slowly. However only a moderate increase in the output power should be sufficient to more effectively destroy the stones.

5. DISCUSSION

5.1 LIGHT TRANSMISSION FROM LASER TO STONE

During the investigation no difference in performance was observed when changing the lens used to focus the laser light onto the fibre. However in Ref. (13) it is stated that it is important to use a lens with a short focal length if one whiches to increase the fibre damage threshold. Apparently, the energy distribution at a given axial position is more uniform in the cross section of the fibre for a diverging source than for a more collimated source (before a steady-state distribution is reached further down the fibre). This is also the reason that the fibre was placed behind the lens focus and not in front of it.

Grinding the fibre surface is a tedious work, but is necessary in order to achive good fibre performance. It was sometimes difficult to judge whether the results of an experiment were due to something that had been changed, or to the fact that the fibre had not been polished in exactly the same way.

The main problem encountered during the project was to obtain a high enough energy transmission through the fibre without destroying it. It is very important that the fibre is well polished, that the laser beam is perpendicular to the fibre entrance and it seems to help to increase the intensity at the fibre entrance slowly to condition the fibre for the energy. A small scratch or a speck of dust on the fibre surface can lower the damage theshold enormously. However, no significant improvement was observed when flowing nitrogen gas or air in front of the fibre entrance to keep dust particles away.

An aperture is believed to make the beam intensity distribution more even by allowing only a part of the beam that looks uniform through the hole.

By changing the surrounding medium of the fibre entrance tip, to a medium with a refractive index that is closer to the refractive index of the fibre, it was hypothesised that the shock at the surface of the fibre would be reduced. The fibre was thought to accept more energy in this way. The fibre entrance was placed in a piece of copper tube with a quartz plate in one end and an opening in the other. The pipe was first filled with water and then silicon oil. But in both cases absorption, SBS, Stimulated Brillouin Scattering, and LIB, Laser Induced Breakdown, diminished the amount of energy that reached the fibre entrance. SBS is a scattering of light by light and acoustic wave coupling. (This is described in more detail in Ref.18). LIB is described in section 2.4 "What happens upon stone fragmentation". A liquid column of 10 cm scatters and absorbs so much energy that when the laser emitted 400 mJ/pulse only 20 mJ/pulse were transmitted through the water. Equipment such as the lens may be damaged if the laser energy is kept at such a high value as 400 mJ/pulse. SBS and LIB do not occure as often if a lens with a longer focal length is used, and LIB is less frequent with a lower pulse repetition rate of the laser, but sufficient energy does not get through the water.

Another idea was to focus the light at the fibre exit, and thereby increase the fluence at the stone surface, by forming the fibre tip sperically. The fibre tip would then act as a lens. The fibre tip was melted with a CO_2 laser and then formed. But due to lens abberations as well as the very small object distance the focusing effect was not very good. Also the fibre strength was altered during heating so the fibre tip was more easily damaged after the treatment.

5.2 FLUORESCENCE

Looking at Fig. 14a, at first the plasma fluorescence spectra is a continuum with a superimposed emission spectrum. The emission lines then evolve into a well-resolved line spectrum with a weakened continuum. This can be observed in Fig. 14b. The continuum observed initially is due to collisions of electrons (e^-) with ions (M^+) and neutral atoms (M), Bremsstrahlung emission (see section 2.4 "What happens upon stone fragmentation"). Two types of Bremstrahlung emission can occur (18):

$$e^- + M^+/M \longrightarrow e^- + M^+/M + h\nu$$

and

$$e- + M^+ \longrightarrow M^* + h\nu$$

where M^* is an excited atom, h is Planck's constant and ν is the frequency of the emitted radiation. The decay of the continuum is caused by plasma expansion and cooling and collisional deactivation of the emitting species.

The Na line at 589 nm appears both in the kidney calculus spectrum and in the urethra spectrum. It is interesting to note that no emission from trace metals such as Fe, which is known to be a component of the calculi, is evident. This is probably due to the high concentration of calcium deposits within the calculi and the relatively low ionization potential of calcium (6.1 eV) (18). Furthermore, the manifold of excited electronic states of calcium begins just 1.8 eV above the ground state, so collisions between relatively low-energy electrons and ground state calcium atoms can result in emission from excited electronic states (18).

It is also interesting to note that spectra from a calculi and a urethra differ so much that the fluorescence technique can almost certainly be used for identification purposes.

5.3 FRACTURING KIDNEY STONES

In section 2.4 "What happens upon stone fragmentation" the need for free or conducting electrons to start the electron avalanche for plasma formation was mentioned. In the case of a stone multiphoton ionization is needed to obtain free electrons. In a metal an initial electron density is present in the conduction band. If a metal is placed in front of the stone, the electron avalanche is led from the metal to the stone, and a plasma is formed (8).

5.4 GENERAL COMMENTS

According to Ref. (5) 35 to 50 mJ/pulse are needed to create a plasma at the stone. In Ref. (7) it is stated that 40mJ/pulse are required. In both cases a Nd:YAG laser with the same specifications as the one used in this project has been used. With the help of copper, the stone starts to show signs of damage at 20 mJ/pulse. With copper 30 mJ/pulse should be sufficient for efficient stone destruction. The following things should be investigated in order to transmit more energy through the fibre:

*Trying other kinds of fibre. A smaller numerical aperture of the fibre would give a smaller energy spot on the stone and thus higher fluence. In Ref. (7) a hard cladded silica (HCS) fibre from Ensign-Bickford Optics Company is suggested.

*LIB in air at the lens focus absorbs some of the overlapping spikes in the laser distribution. This can be used as a non-linear filter, which absorbs all energy higher than a certain value. This threshold can probably be controlled by keeping a gas in a chamber at a specific pressure. In this way, one is sure that no unwanted spikes destroy the fibre (7).

* Instead of spherically forming the fibre tip at the exit, perhaps a lens system could be used.

Fluorescence can be used as an identification technique. Another way of identifying the stones is to record an optoacoustic spectrum. This can be done by placing a microphone, coupled to an oscilloscope, at the fibre exit. But to be able to record such a spectrum no metal can be used, as the characteristics of the metal would always be obtained.

By using both fluorescence and optoacoustic spectra for identification, there should be no doubt as to whether the fibre is correctly located at the stone and not at the surrounding tissue.

6. CONCLUSIONS

For laser lithotripsy both a great deal of energy and high intensity are required to destroy a stone.

The Nd:YAG laser emits a great deal of energy and enough power is obtained by Q-switching. However the equipment between the laser and the stone limit the performance. The fibre, which is the laser energy delivery tool through the urethra, is fragile. To avoid damaging the fibre the laser light must be orthogonal to to the fibre entrance surface. The surface must be plane and very smooth, which can be obtained by carefully grinding it. 20 mJ/pulse at a 10 ns pulse duration can be transmitted through the PCS 600 fibre, from Fibres Optiques Ind. The energy impinging on the entrance surface of the fibre is then 25 mJ/pulse.

The stones can be identified by making them fluorescence at low laser energy irradiation. Both fluorescence and plasma fluorescence spectra of stones and urethra can easily be identified. Most stones are made up essentially of calcium oxalate and it is the calcium emission lines that appear in the plasma emission spectra.

Upon fragmentation of the stone an acoustic wave is emitted. Recording an optoacoustic spectrum is providesanother way of identifying the stones. With these two identification possibilities, doubts about leading higher energy through the fibre and into the patient should can be dispelled.

About 45 mJ/pulse at a pulse duration of 20 ns destroys a calculus effectively in a few minutes (5). With a fibre diameter of 600 µm this corresponds to an intensity of 0.8 GW/cm^2. By placing an absorber of metal between the fibre exit and the stone surface, the threshold can be reduced. At 20 mJ/pulse (0.7 GW/cm^2), with a 10 ns pulse duration, the stone is slowly fragmented into pieces.

7. ACKNOWLEDGEMENTS

I would like to thank everyone that somehow has been involved in this project.

Eric Lindstedt at the Department of Urology has shown a lot of interest by telling me about kidney operations and allowing me to be present during one. He has also supplied the stones that I have tried to destroy.

I am grateful to Stig Borgström, Hans Hallstadius and Jonas Johansson at the Department of Physics for good advice and help on various occasions

I would like to thank Sune Svanberg for good ideas and making this project possible.

Above all I would like to thank my supervisor Stefan Andersson-Engels who has constantly encouraged, supported and helped me.

8. FIGURES

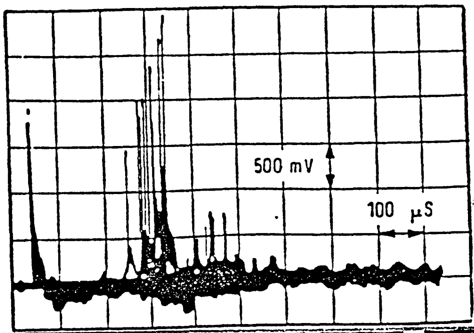


Fig. 1 (Ref. 8)
Pressure amplitude for seven laser-induced breakdowns in a liquid. The first peak originates in the initial plasma expansion. Notice the lower pressure peaks of the subsequent cavitation bubble.

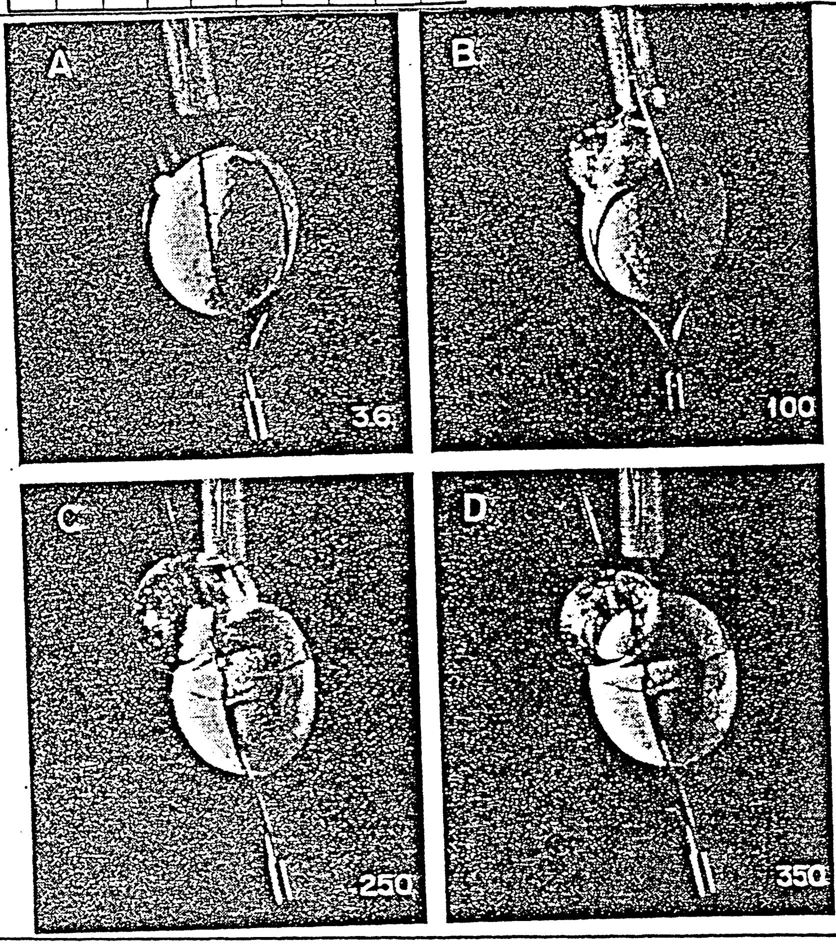


Fig. 2 (Ref. 12)
A sequence of microsecond-flash photographs showing cavity (bubble) growth at various delay times relative to the start of the pump pulse. Delay times are given in microseconds.

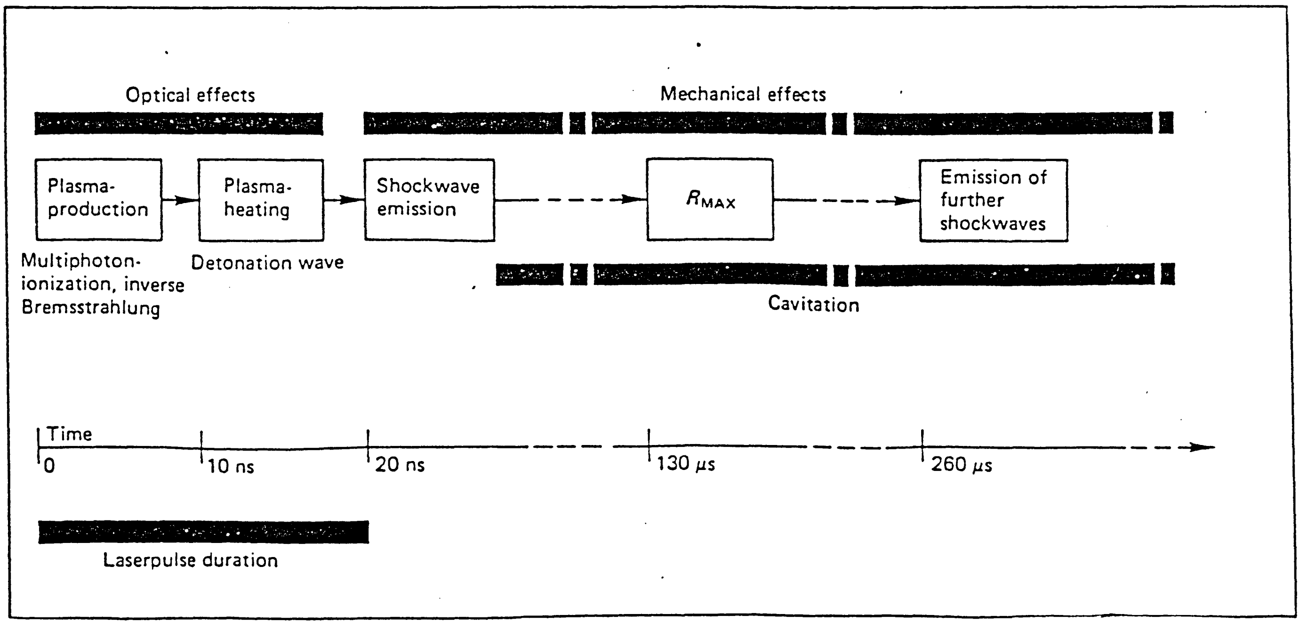


Fig. 3 (Ref. 15)
Phases of the plasma creation. R_{MAX}=maximum radius of the cavitation bubble. The times shown are mean values from experiments.

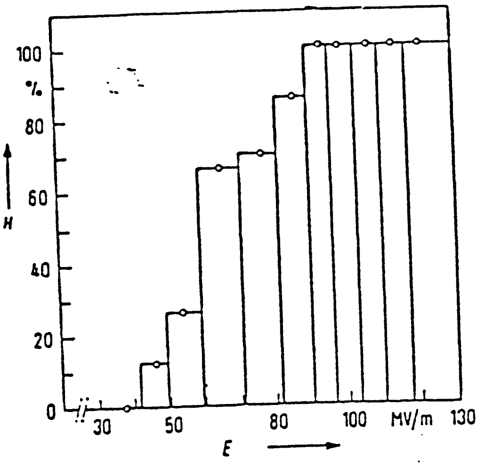


Fig. 4 (Ref. 8)
Breakdown frequency in water as a function of the electrical field strength. Notice the threshold around 40-50 MV/m.

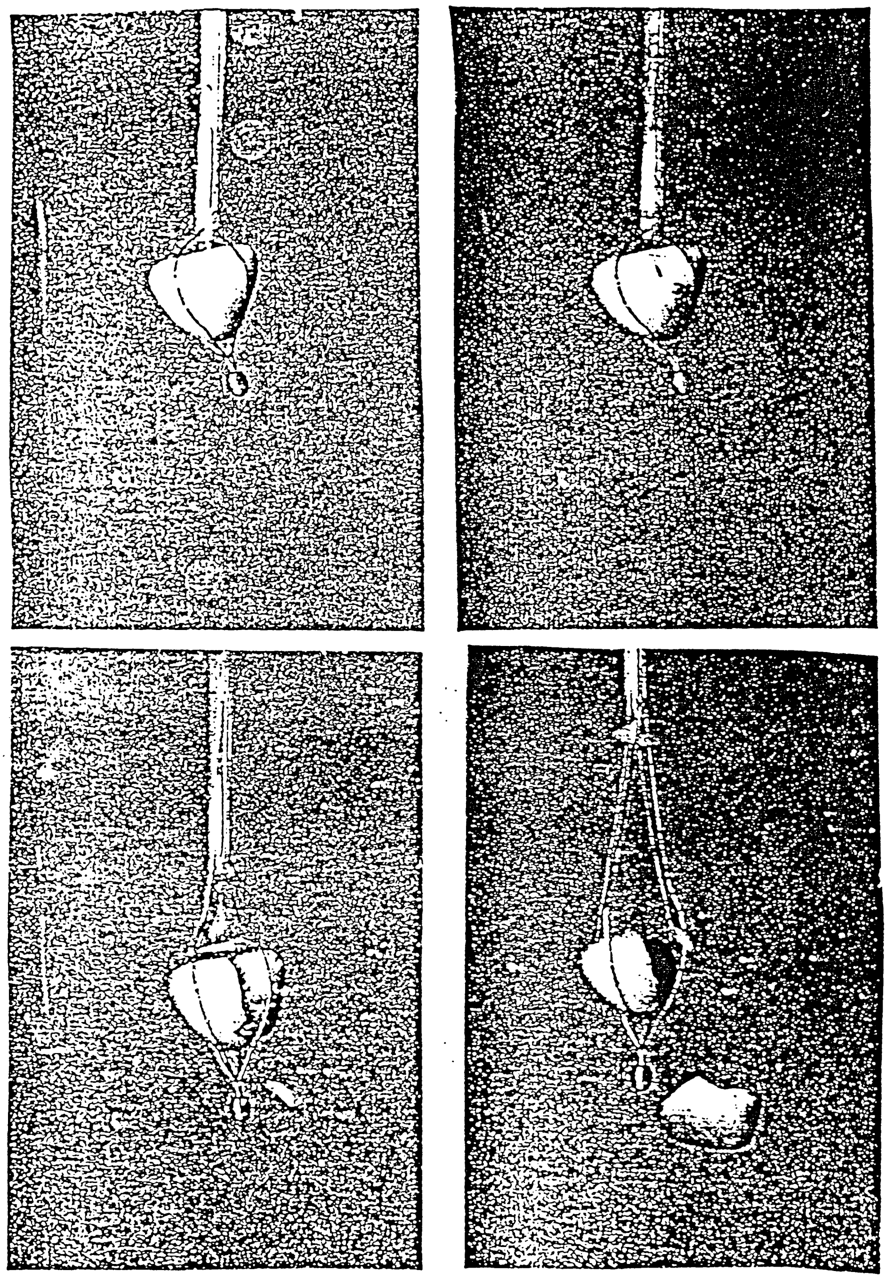


Fig. 5 (Ref. 20)
Laser litothripsy of gallstones.

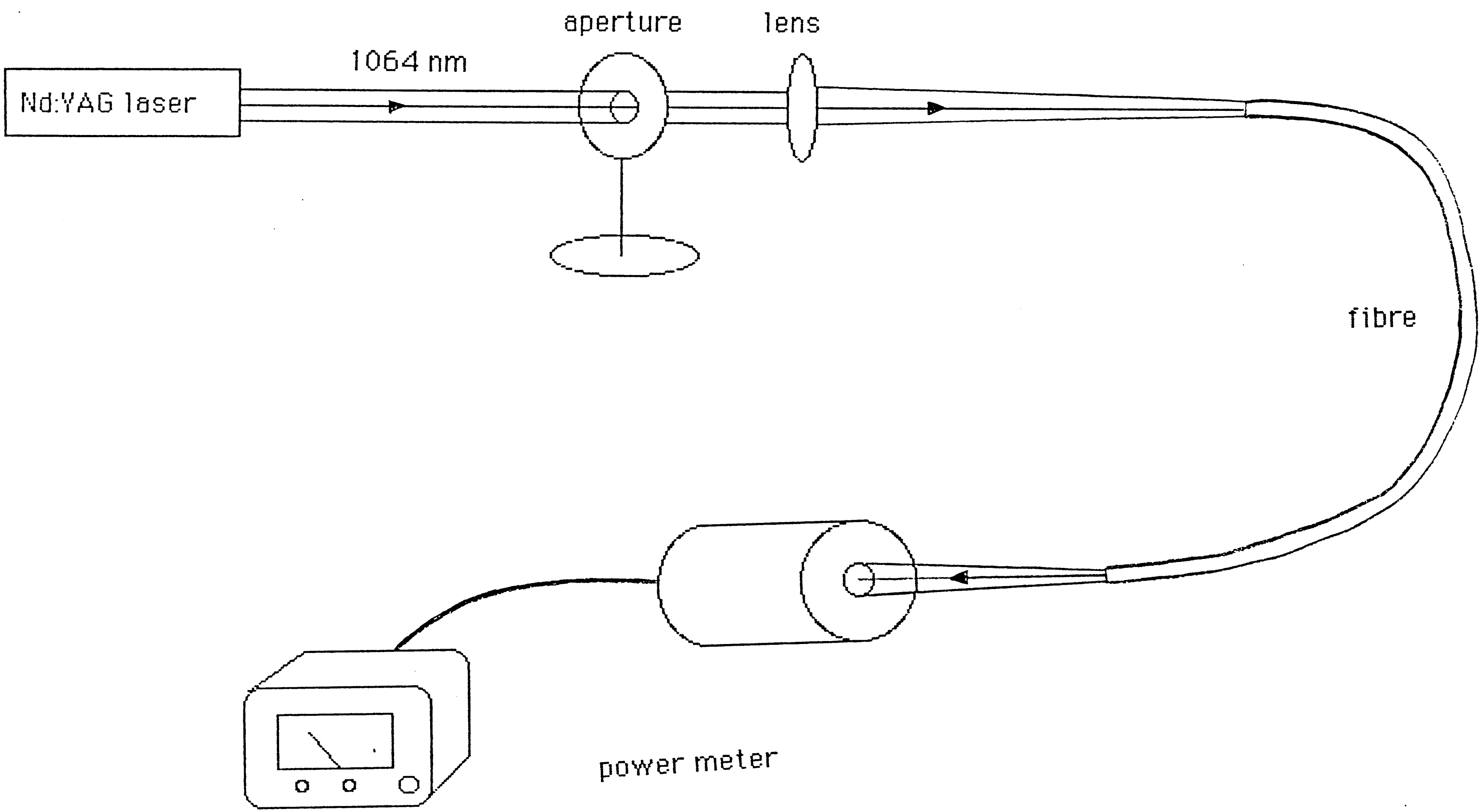


Fig. 6
Set-up for fibre transmission experiments.

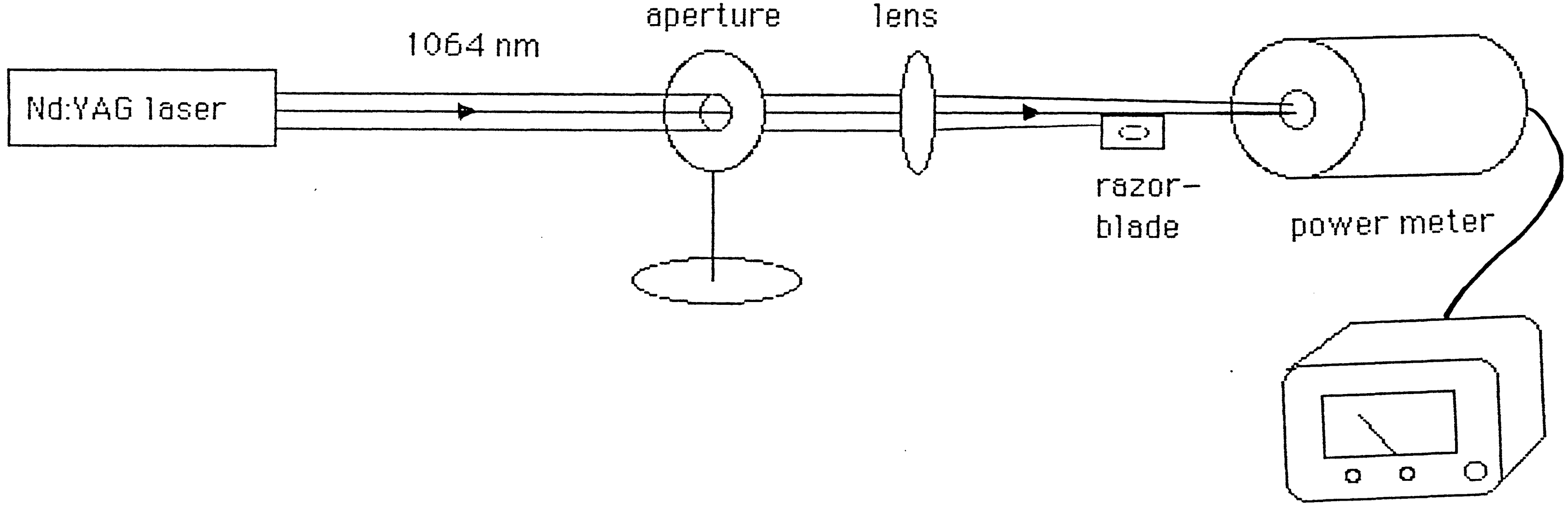
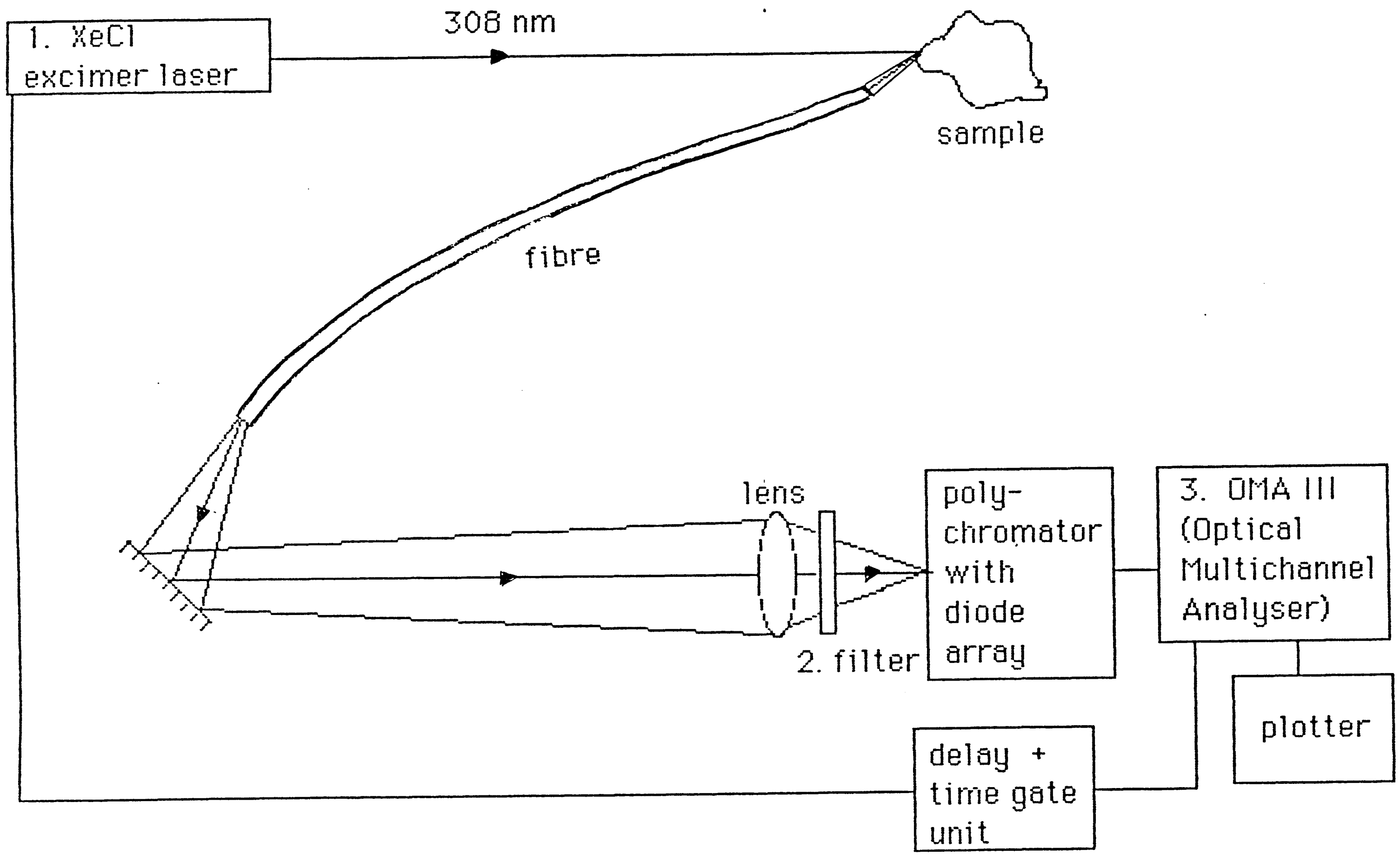


Fig. 7
Set-up for beam intensity
distribution investigation.

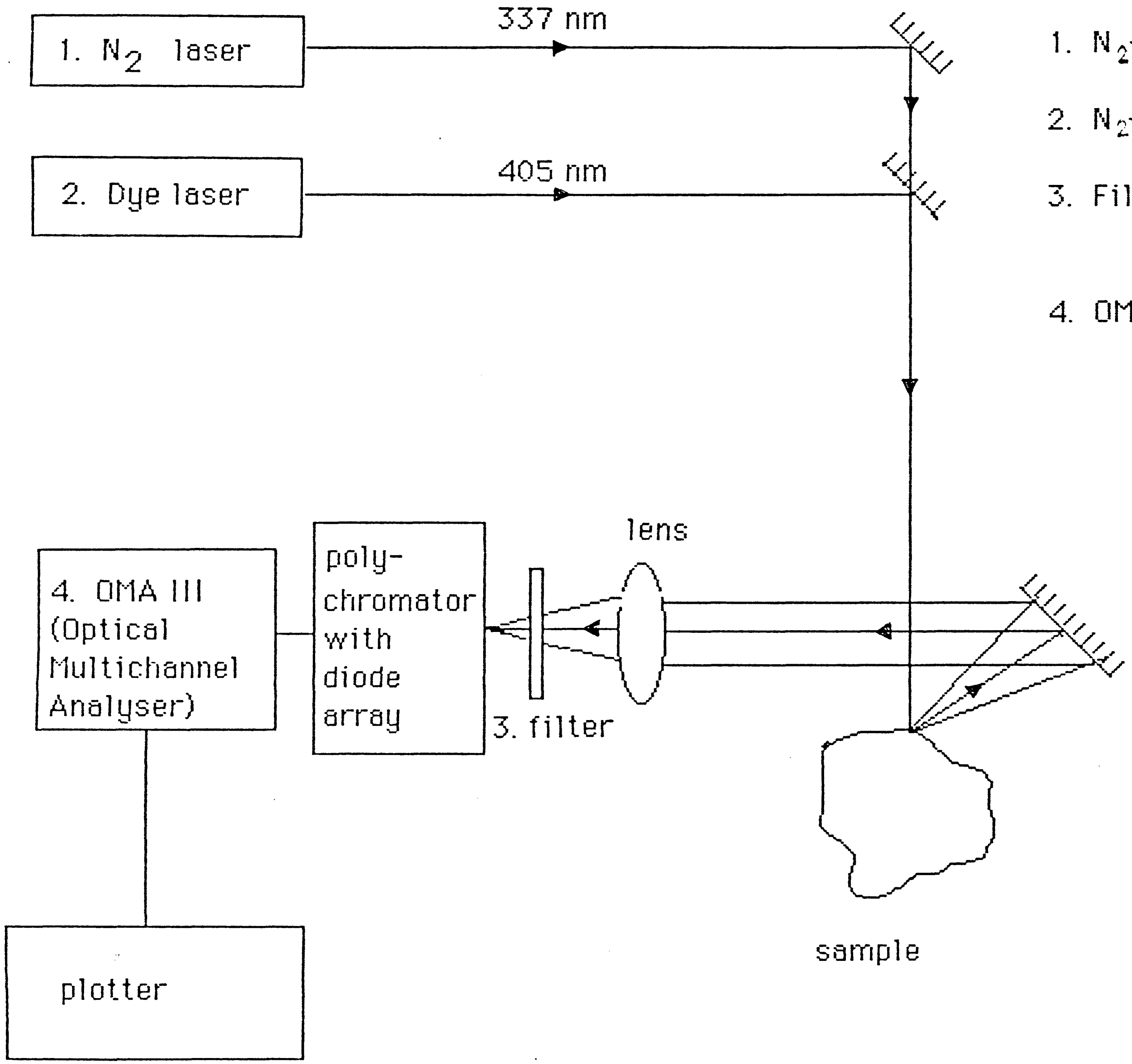


1. XeCl excimer laser (308 nm) from Lambda Physik

2. WG345 filter

3. OMA III from EG&G Princeton Applied Research

Fig. 8
Set-up for recording of fluorescence spectra, induced with a XeCl excimer laser.



1. N_2-laser (337 nm), LN 250, PRA

2. N_2-laser-pumped dye-laser (405 nm), Laser Science

3. Filter: WG375 when N_2 laser was used
   GG435 when dye laser was used

4. OMA III, EG&G Princeton Applied Research

Fig. 9
Set-up for recording of fluorescence spectra, induced with a N_2 laser and a dye laser.

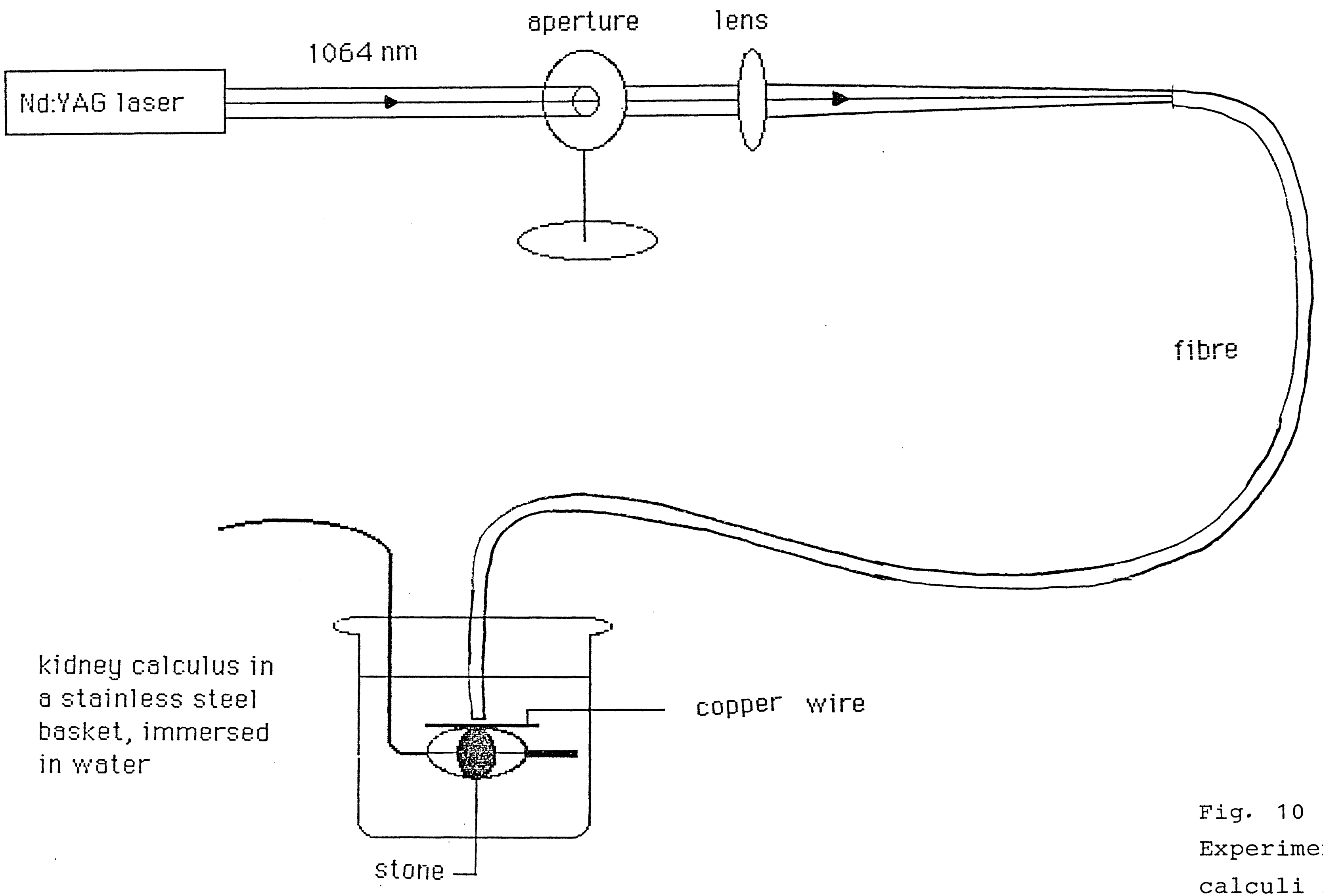


Fig. 10
Experimental set-up for
calculi fracturing.

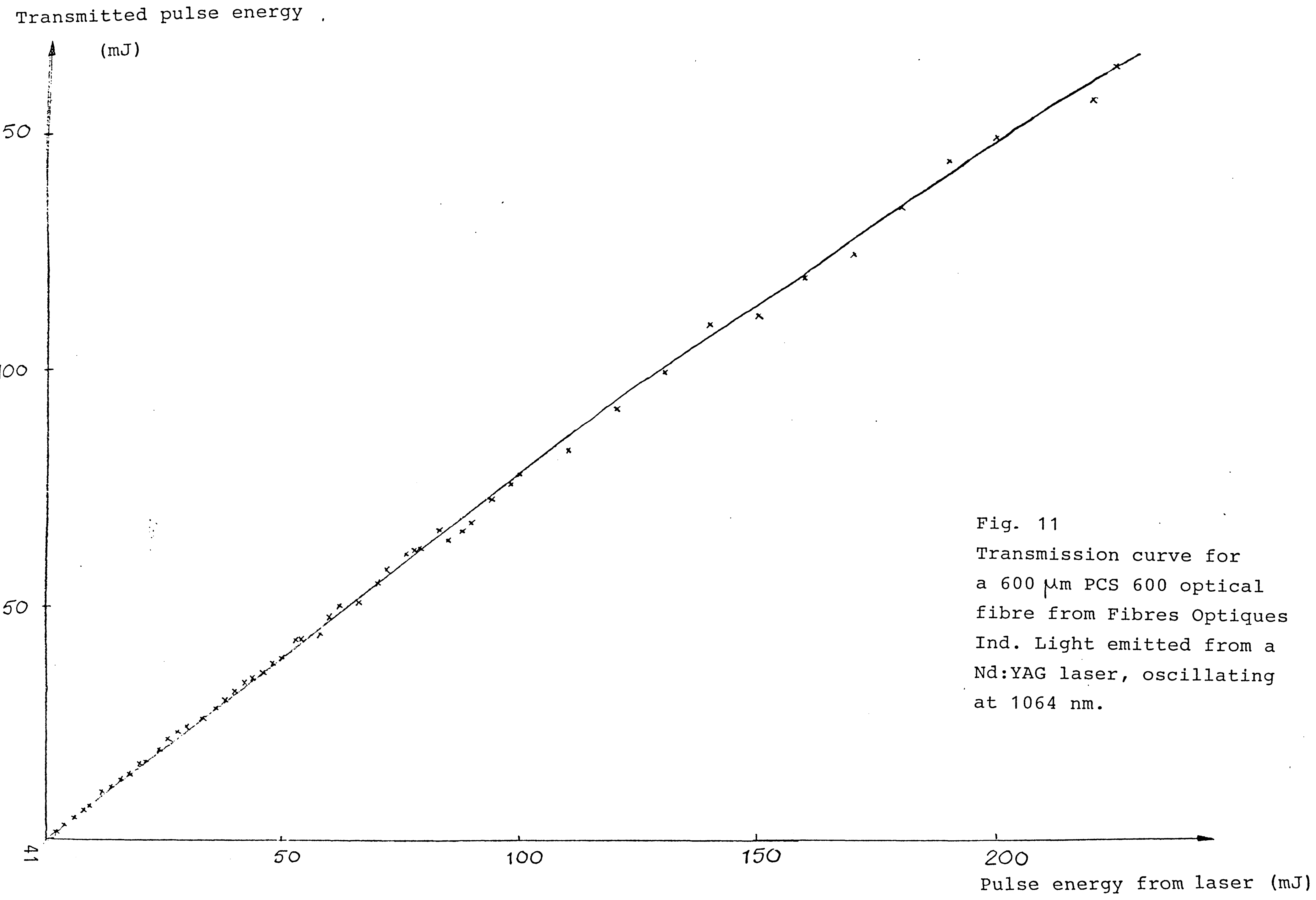
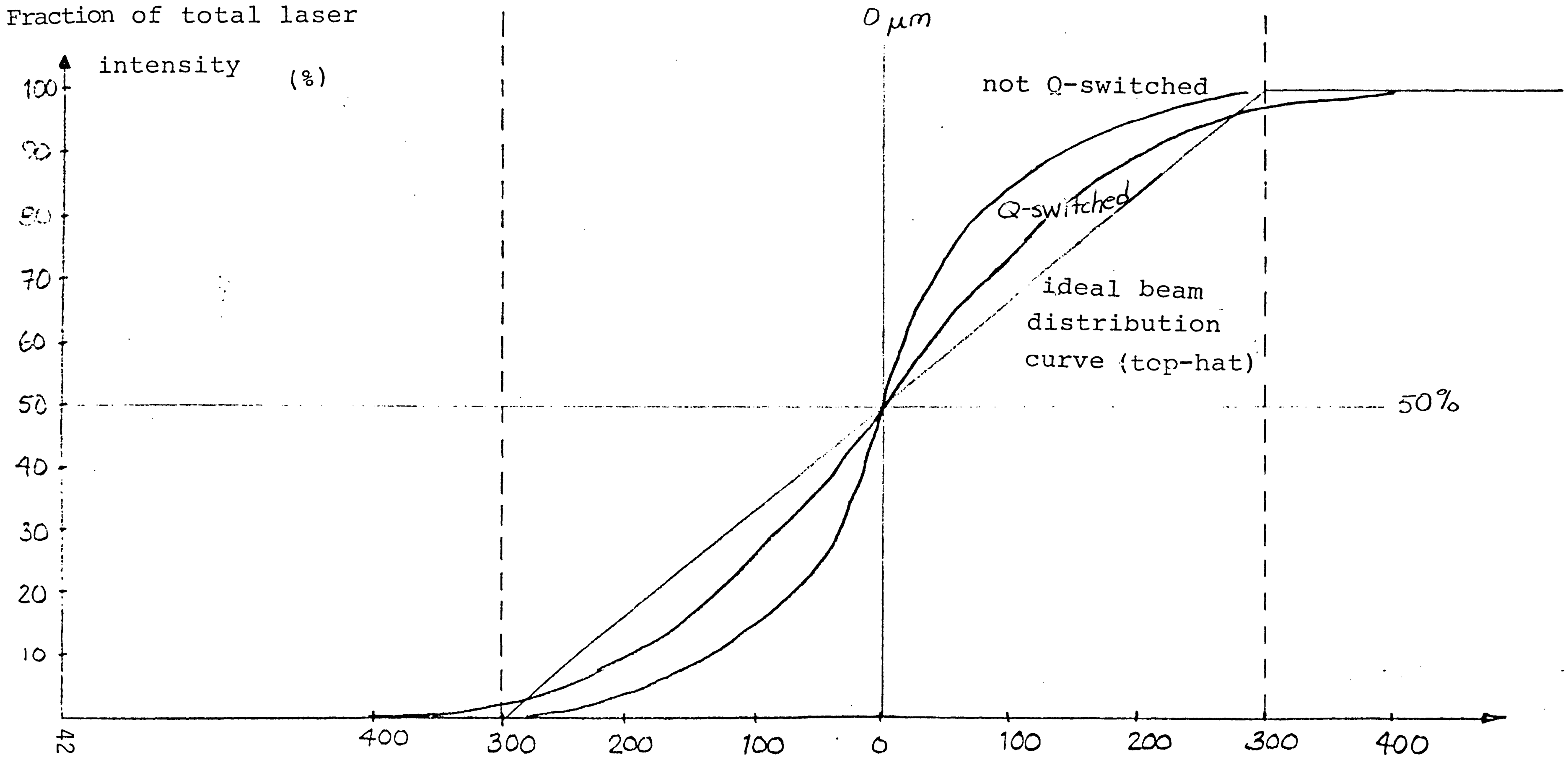


Fig. 11
Transmission curve for a 600 μm PCS 600 optical fibre from Fibres Optiques Ind. Light emitted from a Nd:YAG laser, oscillating at 1064 nm.

Fig. 12
Beam distribution curve
for a Nd:YAG laser emitting
5 mJ/pulse.



1. Intensity distribution 0 mm from lens focus
2. ——— " ——— 6 ——— " ———
3. ——— " ——— 10 ——— " ———
4. ——— " ——— 14 ——— " ———
5. ——— " ——— 18 ——— " ———

Fig.13
Beam distribution curve for a Nd:YAG laser emitting at 1064 nm - lens is placed in the beam. Different curves represent the beam intensity distribution at different distances from lens focus.

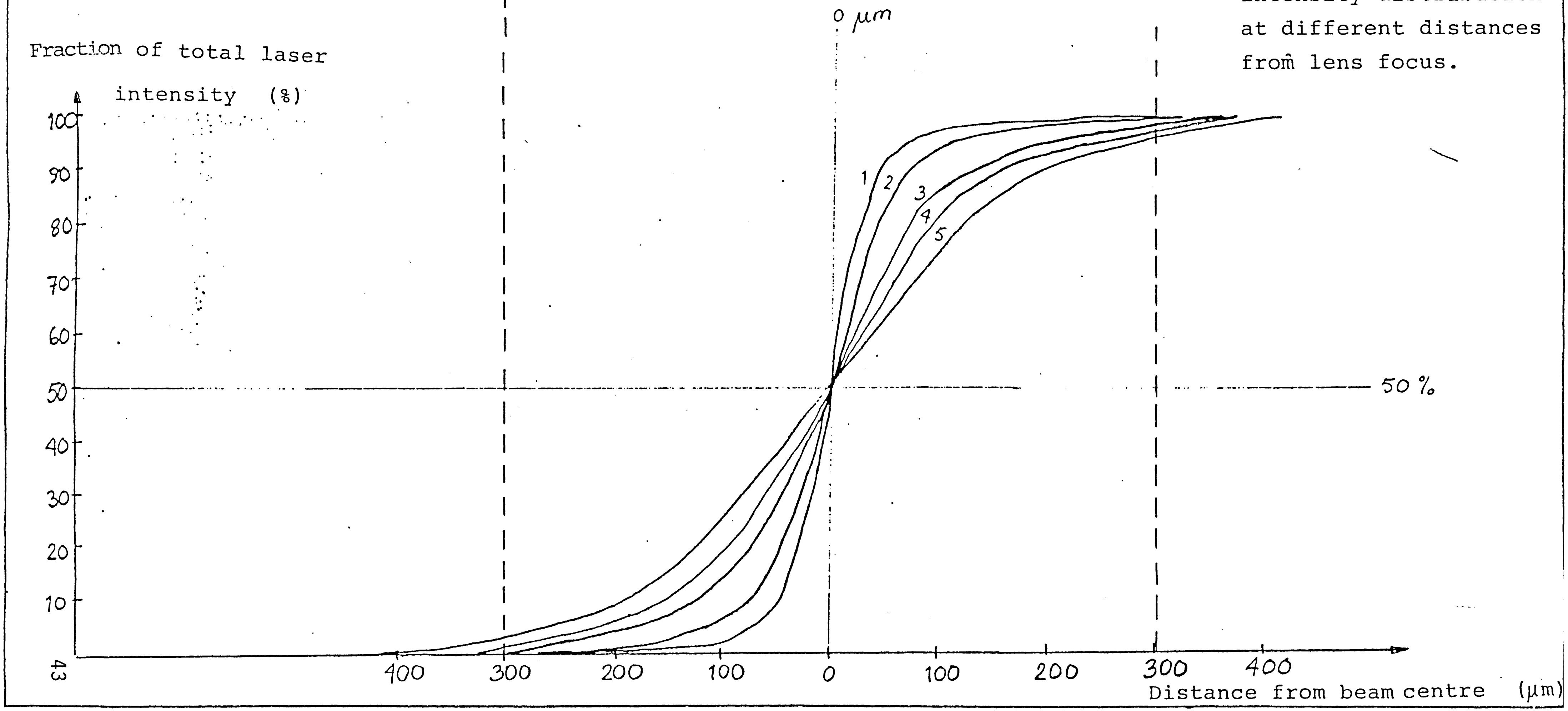


Fig. 14a
Typical plasma fluorescence spectrum from a kidney stone at the initiation of the plasma. A XeCl laser is the energy source.

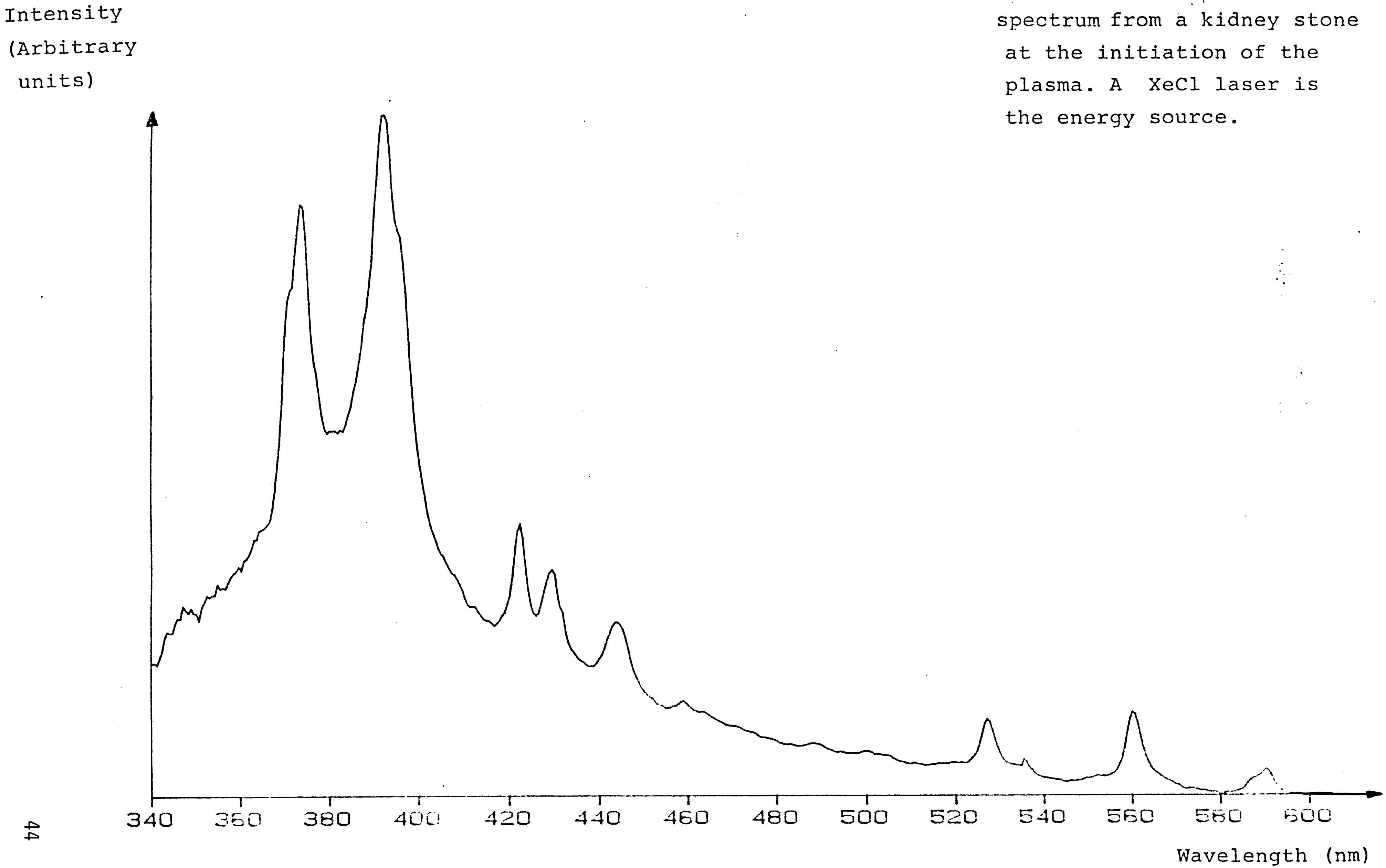
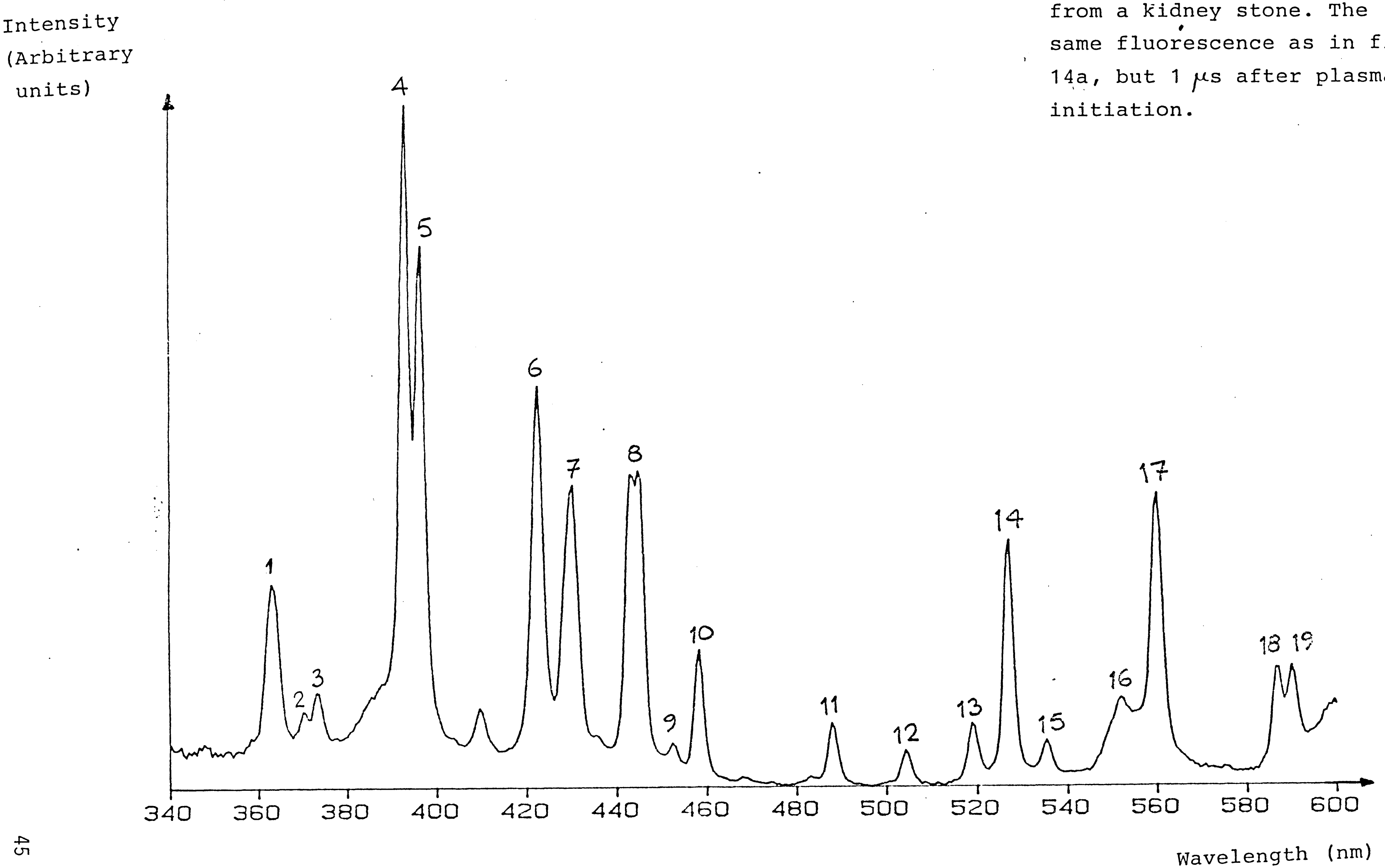


Fig. 14b
Plasma fluorescence spectrum from a kidney stone. The same fluorescence as in fig 14a, but 1 μs after plasma initiation.



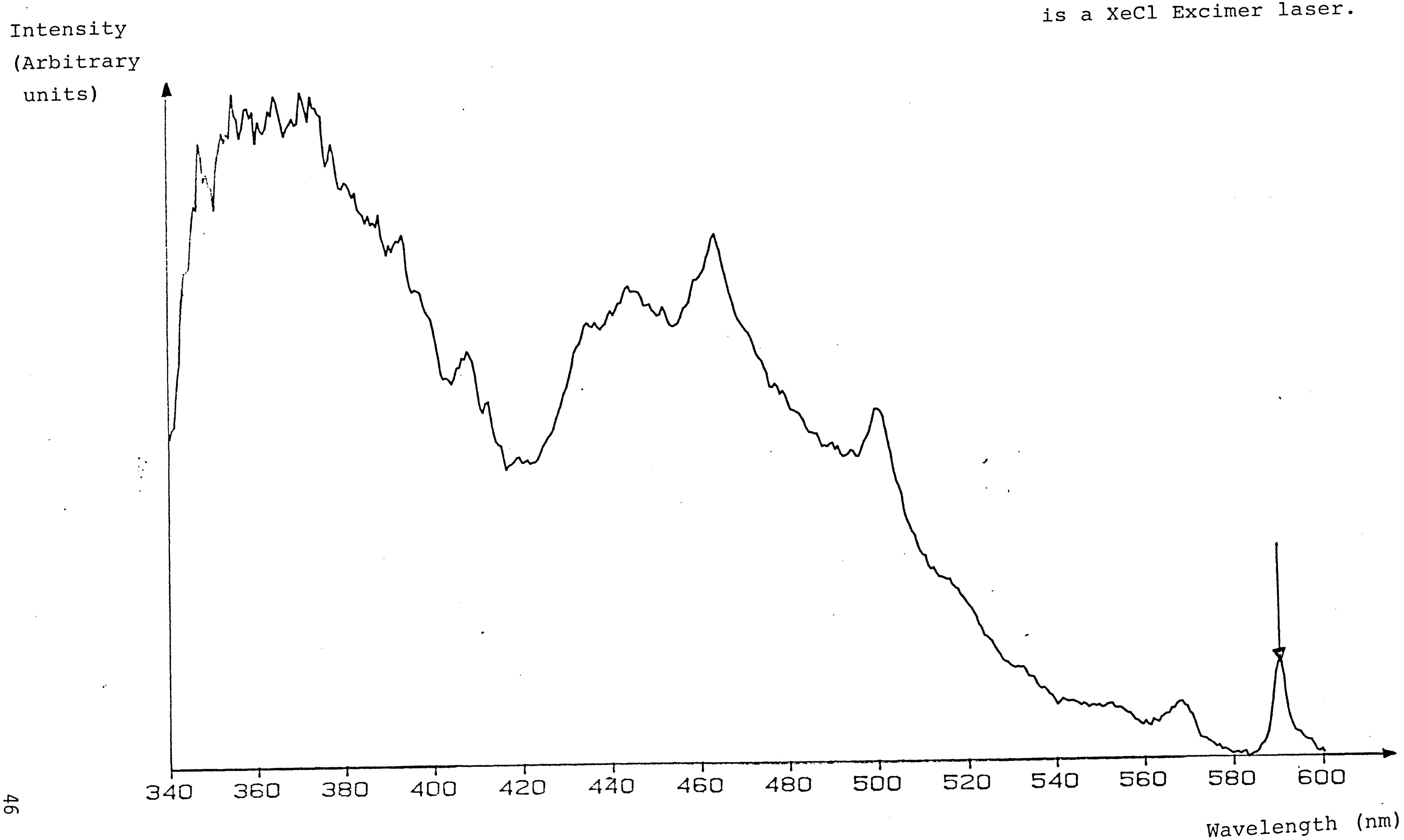


Fig. 15
Plasma fluorescence from a pig urethra. Energy source is a XeCl Excimer laser.

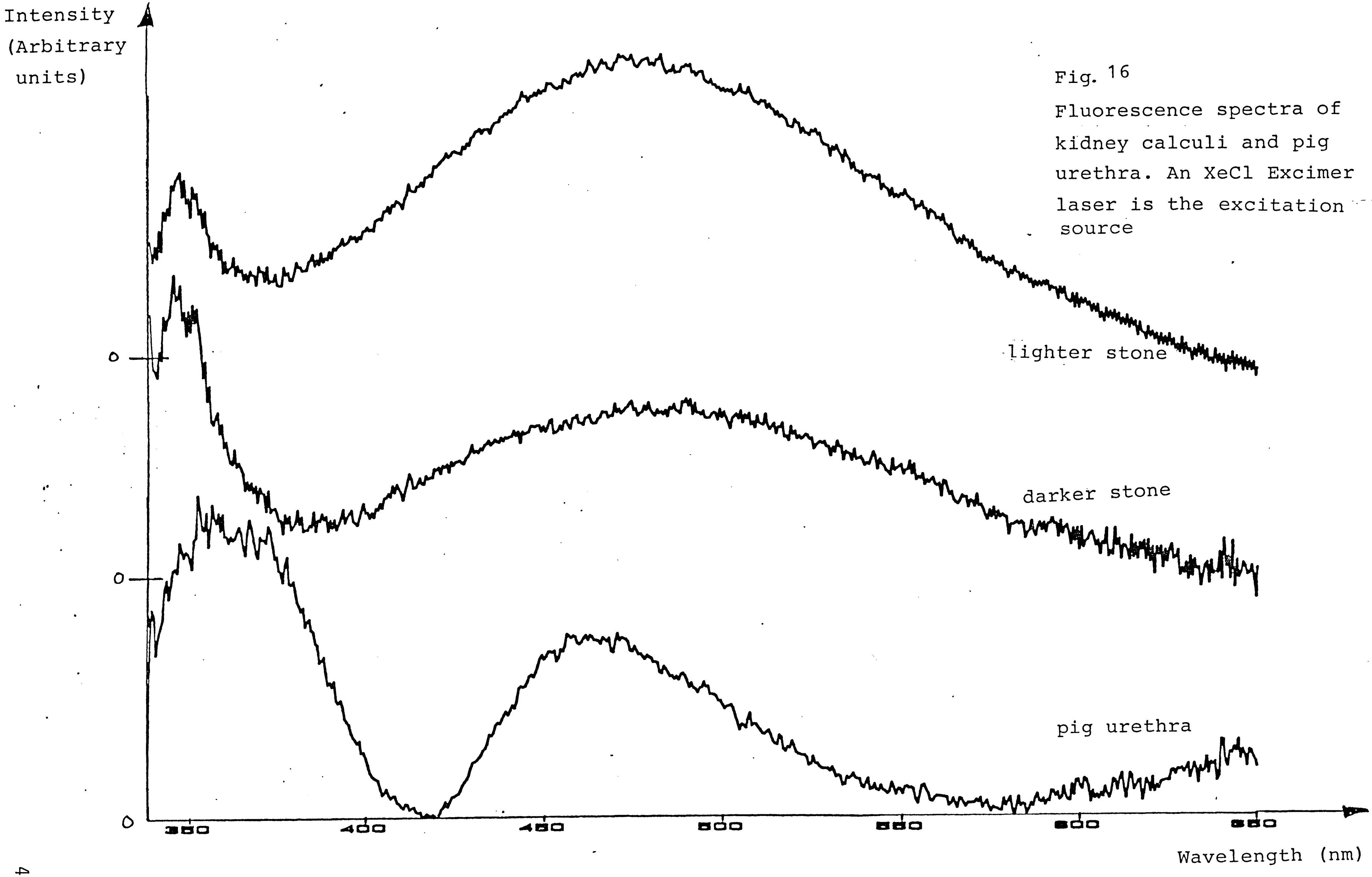
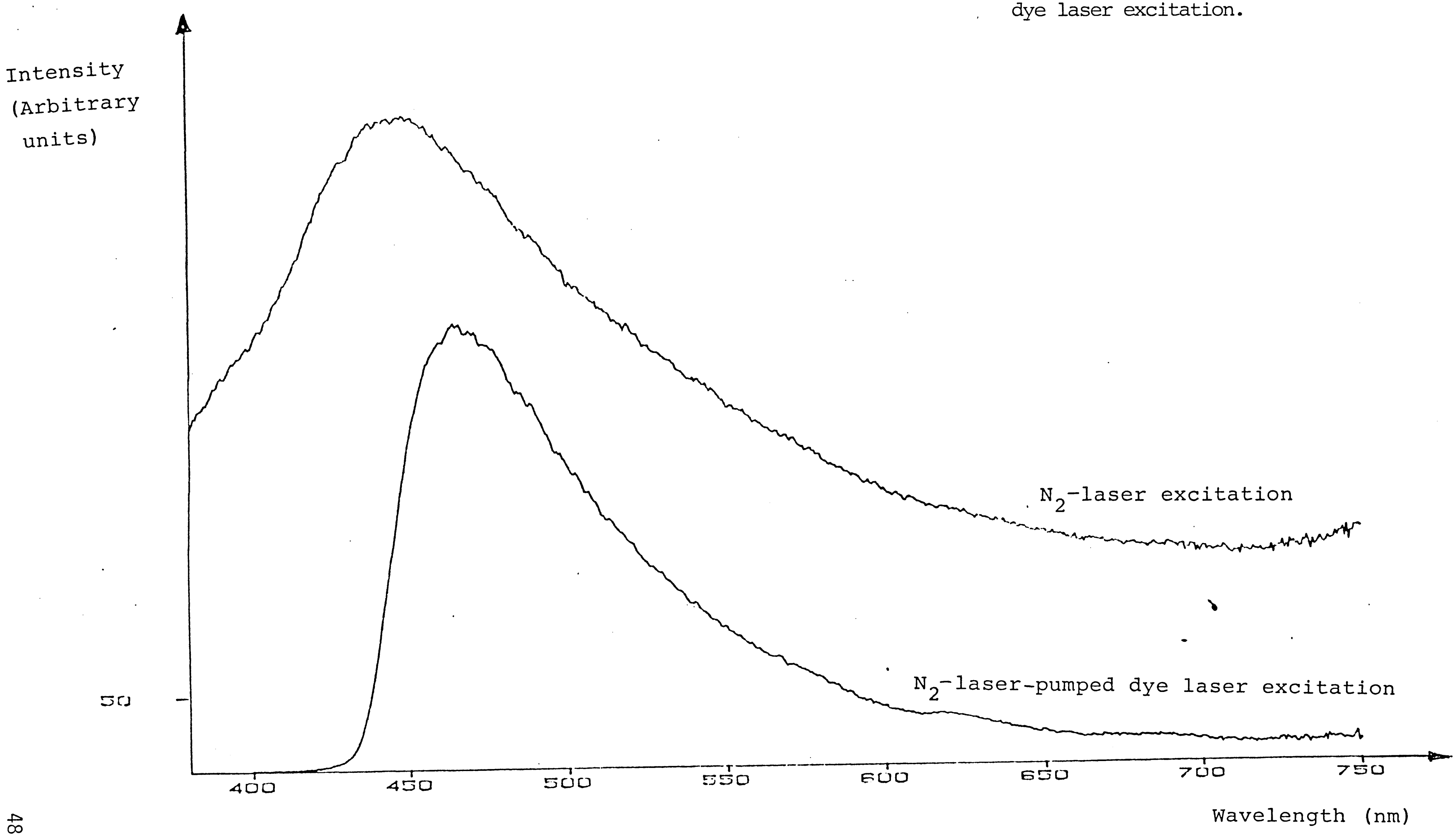


Fig. 16
Fluorescence spectra of kidney calculi and pig urethra. An XeCl Excimer laser is the excitation source

Fig. 17
Fluorescence spectra of kidney calculi resulting from N_2 and N_2-laser-pumped dye laser excitation.



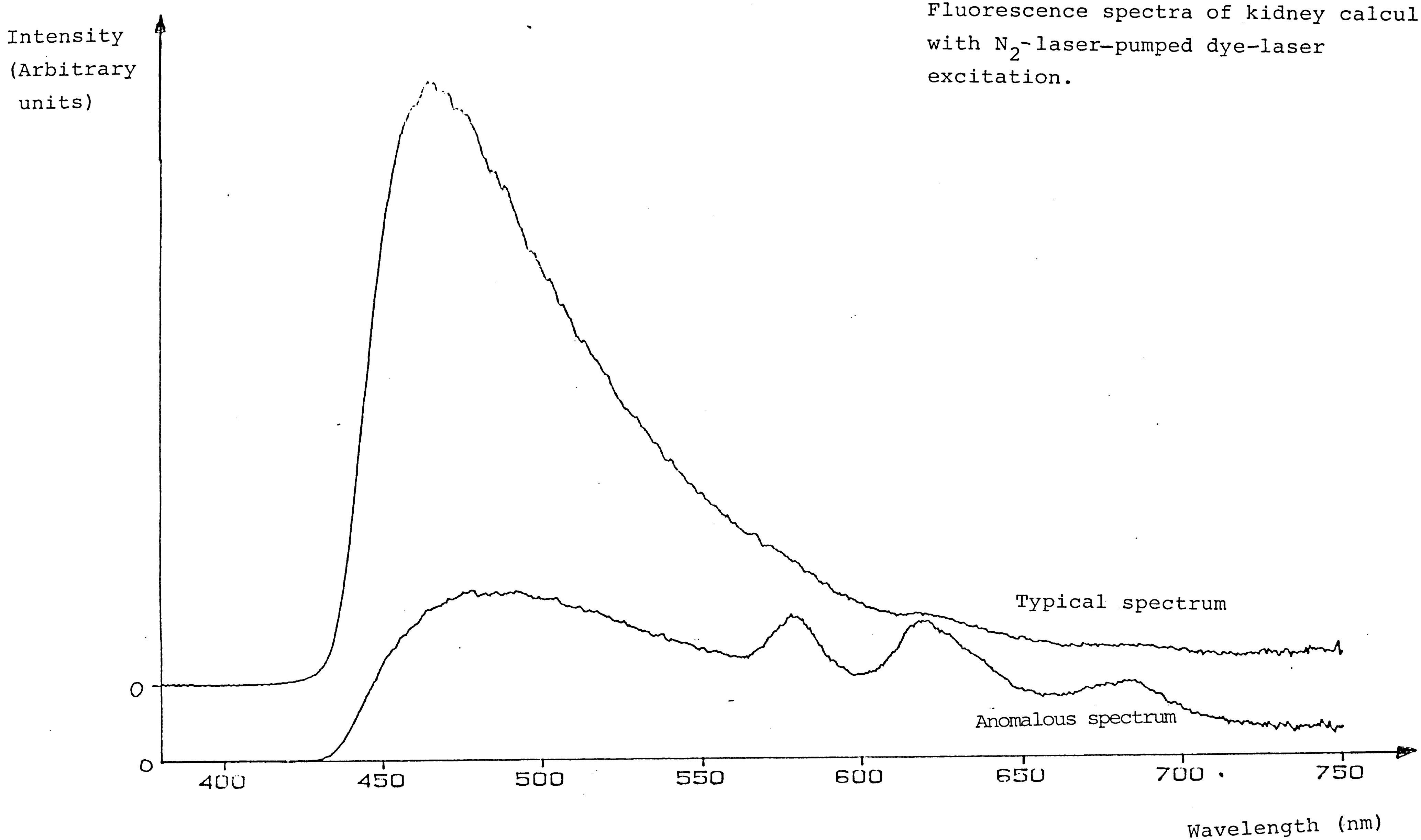


Fig. 18
Fluorescence spectra of kidney calculi with N_2-laser-pumped dye-laser excitation.

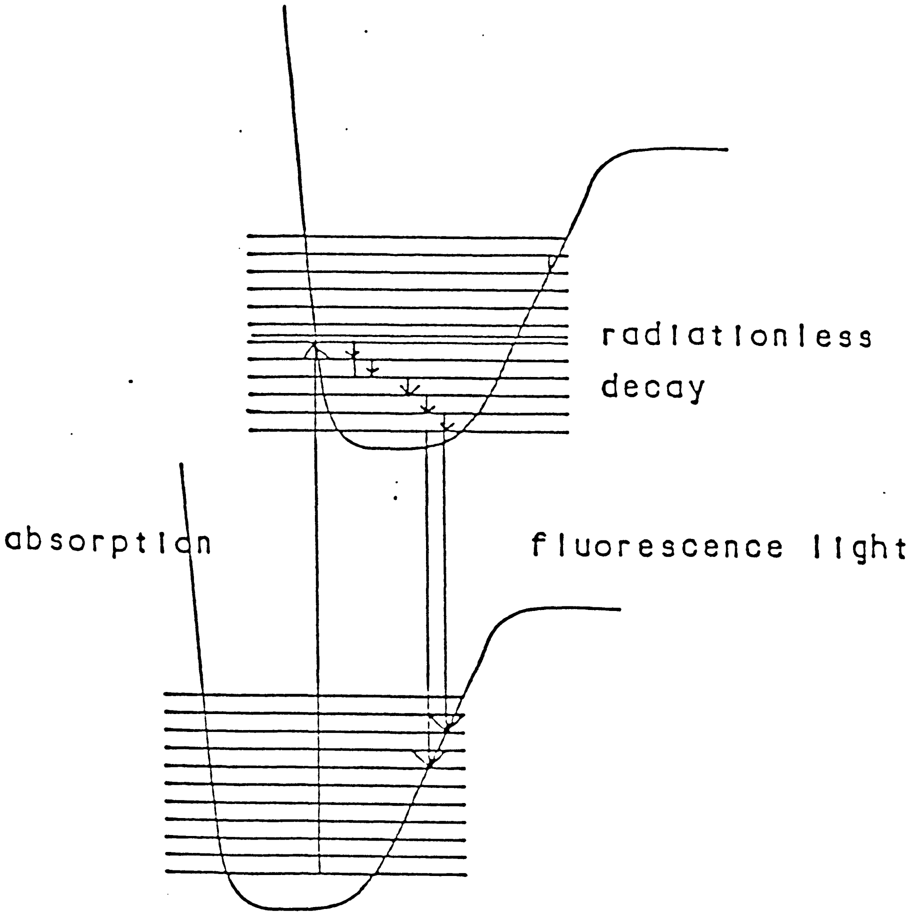


Fig. 19
Fluorescence of a molecule.

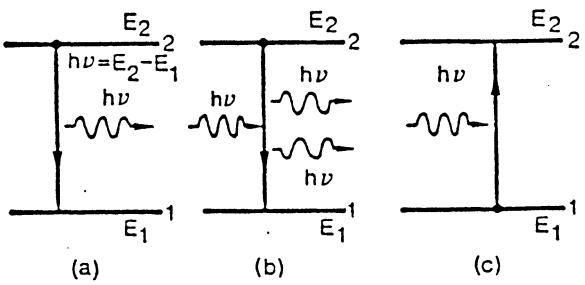


Fig. 20 (Ref. 22)
Schematic illustration of the three processes:
a) spontaneous emission
b) stimulated emission and
c) absorption

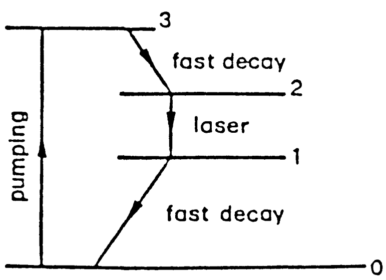


Fig. 21 (Ref. 22)
A four-level laser scheme.

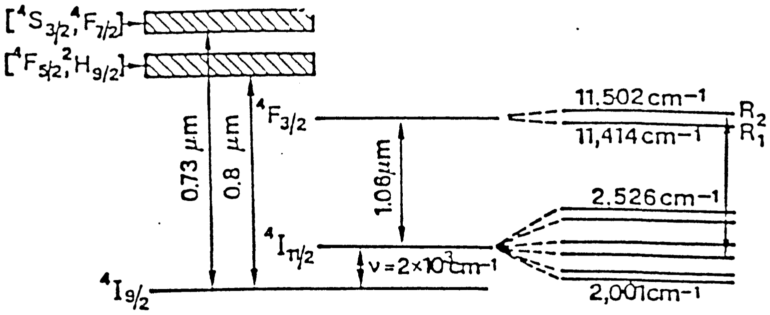


Fig. 22 (Ref. 22)
Simplified energy levels of a Nd:YAG laser.

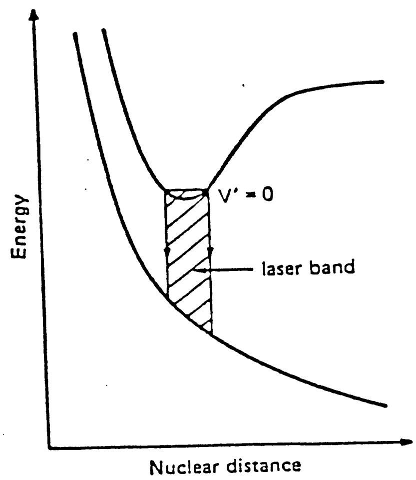
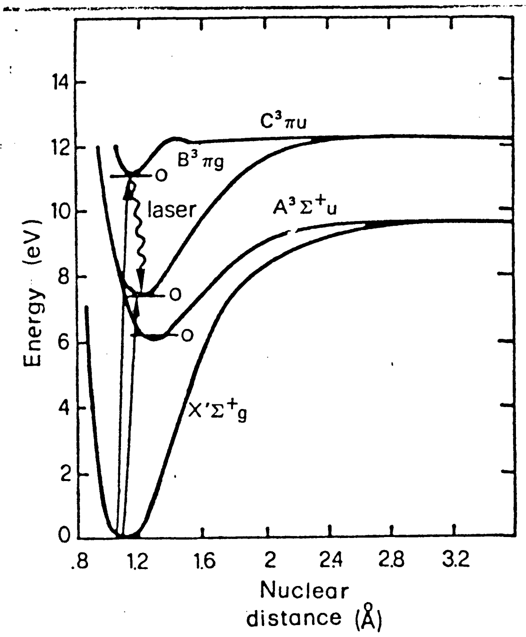


Fig. 23 (Ref. 22)
Energy levels of an excimer laser.

Fig. 24 (Ref. 22)
Energy levels of N_2 molecules. For simplicity only the lowest vibrational level (v=0) is shown for the electronic state.



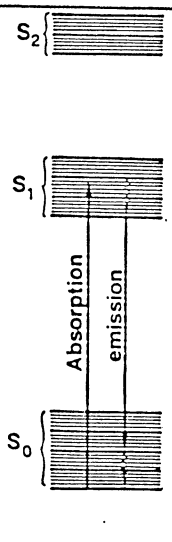


Fig. 25 (Ref. 22)
Typical energy levels for a dye in solution.

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10 APPENDICES

A. EMISSIONAL FLUORESCENCE SPECTRUM

One can make a gas, liquid or solid material emit light by transferring energy to the atoms or molecules in the material. The energy can be transferred by e.g. heating the sample, sending an electrical discharge through it or by illuminating it. The atoms or molecules absorb the energy and are transferred to higher energy states. Usually, they move back quickly to their ground states and "return" the energy by sending out light. This process is called resonance fluorescence.

There is the following relation between the difference in energy of the two states the atoms/molecules move between and the emitted wavelength:

$$(E_2 - E_1) = h * c / \lambda \qquad \text{Formula (1)}$$

$(E_2 - E_1)$ is the energy difference, h is Planck's constant, c is the velocity of light and λ is the wavelength emitted.

Different atoms/molecules have different energy states. So the light emitted is characteristic of the atom/molecule. Atoms have different electronically excited energy states. Molecules also have rotational and vibrational energy states. (See Fig. 19).If a substance is made to emit light and one analyses the wavelengths contained within the emitted light, then a spectrum is said to be made of the substance.

B. LASERS AND Q-SWITCHING

Most of the information in this Appendix was obtained from Ref. 22.

a) The LASER (Light Amplification by Stimulated Emission of Radiation) idea

A laser exploits three fundamental phenomena which occur when an electromagnetic wave interacts with a material. These processes are spontaneous and stimulated emission, and absorption. Atoms or molecules in a material can move between different energy levels or states by absorbing or emitting light. Consider two energy levels E_1 and E_2. E_2 is the higher energy level.

Spontaneous emission

The atoms/molecules are initially in level E_2 and will tend to decay to level E_1. This is done by emitting an electromagnetic radiation (light). (See Fig. 20a)

Stimulated emission

The atoms/molecules are in E_2. An electromagnetic wave, with a wavelength equal to that emitted during spontaneous emission, is incident on the material. There is then a finite probability that this incomming wave will force the particles to undergo a transition from E_2 to E_1. In this process, where the emission is forced by an incident electromagnetic wave, the emission adds, in phase, to that of the incoming wave and the incoming wave also determines the direction of the emission. (See Fig. 20b).

Absorption

The atoms/molecules are initially in E_1 and need external stimulation to move to the higher energy state E_2. An electromagnetic wave with a wavelength corresponding to the energy difference can give this stimulation. (See Fig. 20c).

Under normal circumstances, i.e. thermal equilibrium, the lower energy level is more populated than the higher. This is given by the Boltzmann distribution:

$$N_2/N_1 = \exp\ (-\ (E_2-E_1)/(k*T)\ )$$

N_2 and N_1 are the populations of level E_2 and E_1 respectively. The population of a level is the number of atoms/molecules per unit volume in that level. k is Boltzmann's constant and T is the absolute temperature of the material. So under normal circumstances, the material must act as an absorber if it is irradiated with light. If, however, a nonequilibrium situation is achieved where $N_2 > N_1$, the material will act as an amplifier. Then a <u>population inversion</u> exists in the material. A material with a population inversion is called an <u>active material</u>.

To make an oscillator which continuously emitts light, the active material needs feedback. In a laser this is obtained by placing the active material between two highly reflecting mirrors. A plane wave travelling in a direction orthogonal to the mirrors will bounce back and forth between the mirrors and be amplified on each passage through the active material. If one of the mirrors is made partially transparent an output beam can be extracted. A certain threshold condition must be fulfilled before the laser starts to oscillate. Oscillation starts when the gain of active material compensates the losses in the outgoing beam.

After some consideration one realizes that a population inversion can not occur between <u>two</u> energy levels. At thermal equilibrium $N_1 > N_2$ and an incomming wave would produce more transitions from E_2 to E_1 than from E_1 to E_2. But after a while when $N_2 = N_1$ is reached, the absorbing and stimulating processes will compensate each other and the $N_2 > N_1$ state will never be reached. More than two energy levels are needed.

b) Nd:YAG lasers

The Nd:YAG laser is a neodynium (Nd) laser. It uses a crystal of $Y_3Al_5O_{12}$ as active material. YAG stands for Yttrium Aluminum Garnet. Some of the Y(3+) ions in the crystal are replaced by Nd(3+) ions. The strongest oscillating line is 1064 nm.

It is a so-called four-level laser. Fig. 21 shows how it basically works. The atoms are raised from the ground level E_0 to level E_3. Atoms in level E_3 decay rapidly to level E_2 and a population inversion between E_2 and E_1 can be obtained if the E_2 to E_1 decay is slow and the E_1 to E_0 decay is fast.

Fig. 22 is a more detailed energy level diagram, but still somewhat simplified.

c) Excimer lasers

This type of laser works in a very complex way. Consider a diatomic molecule A_2 with a potential energy curve, as shown in Fig. 23. The ground state is repulsive and the molecules cannot exist in this state. They can only exist in the ground state in the monomer form A. But the molecule A_2 can exist in the excited state, that is the species A exists in the dimer form A_2 in the excited state. A_2 is called an "excimer" from contraction of excited dimer.

If a large number of excimers have been created laser action can be produced between the upper (bound) state and the lower (free) state. As the ground state is repulsive, once the molecules reach the ground state they immediately dissociate.

In most excimer lasers a rare gas, such as Xe, is combined in the excited state with a halogen atom as Cl. The XeCl excimer laser oscillates at 308 nm.

d) N_2 lasers

These are so-called vibronic lasers. These lasers use transitions between vibrational levels of different electronic states as the oscillating transition. The N_2 laser oscillates at 337 nm. The word vibronic is a contraction from the words vibrational and electronic. An energy level scheme is shown in Fig. 24.

e) Dye lasers

Organic dyes are large, complicated molecular systems. Usually they have strong absorption bands in the UV or visible region of the electromagnetic spectrum, and when excited by light of the appropriate wavelength, they display intense broad-band fluorescence spectra.

A typical energy level scheme is shown in Fig. 25. Note that each electronic state is made up of a set of vibrational levels (the heavier lines in the figure) and rotational levels (the lighter lines)

If a molecule is excited to the upper state it decays in a very short time (nonradiative decay) to the lowest vibrational state of the S_1 level. From there it decays radiatively to one of the vibrational level of S_0 (fluorescence), and the fluorescent emission will take the form of a broad band. Having dropped to an excited rotational-vibrational state of the ground level S_0, the molecule will then return to the lowest vibrational level by another very fast nonradiative decay.

These materials can exhibit laser action at the fluorescence wavelengths. The fast nonradiative decay within the excited single state, S_1, populates the upper laser level very efficiently, while the fast nonradiative decay within the ground state is efficient in depopulating the lower laser level.

Pulsed laser action can be obtained by e.g. a short light pulse from another laser. The N_2 laser, in particular is frequently used for this application. Its UV output is suitable for pumping many dyes that oscillate in the visible range.

f) The Q-switch

The technique of Q-switching allows the generation of laser pulses of short duration and high peak power. The principle is as follows. A shutter is introduced into the laser cavity. If the shutter is closed, laser action cannot occur and the population inversion can reach very high values. Then the shutter is opened suddenly. A single, giant, short pulse results if the opening of the shutter only takes a short time compared with the build-up time of the laser pulse.