Research Academy for Young Scientists

Exploring the Application of High-Power Lasers with Optical Fiber Probes for Cancer Cell Elimination

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Abstract

Cancer is today one of the leading causes of death in the world. Possibilities of using optical fibers to kill cancer cells are currently being studied. The aim of this project was to explore the focusing of a high-power laser to select cancerous cells and killing them. The necessary factors include determining the focal length for a spherical lens and its spot size at the beam waist. Another objective was to position the optical fiber using motors and control the activation of the laser by a script. A 30.9 µm radius of curvature lens on top of a fiber with a 50 µm core was used and the determined focal length was approximately 86 µm. The laser was tested on living onion cells and successfully killed one chosen cell.

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Contents

1 Introduction

Cancer is the second leading cause of death in the world [1]. Every year there is an estimated 10 million deaths and 19 million new cases of cancer [2]. One potential way to treat cancer is to use optical fibers and laser optics to destroy cancerous cells. This method is very effective because it is able to target cancerous cells without harming nearby cells. Additionally, the small size of the fiber allows it to reach many areas in the body which is difficult to reach with other methods. [3]

1.1 Cancer Treatment

Most cancers are quickly discovered with a high chance of survival if treated adequately. The most common cancer treatment is chemotherapy where drugs are inserted into the body to target and kill cancerous cells. Other treatment options are also being developed because chemotherapy is very demanding for the body and can be harmful to weak patients. One method that is being researched today is high-power laser therapy using optical fibers. [3]

1.2 Optical Fibers

Optical fibers are tiny silica tubes used to transmit light. Optical fibers have a core which is surrounded with a cladding. The core has a higher refractive index than the cladding. Combining this with a large incident angle achieves total internal reflection. This lets light travel through the optical fiber with little loss of energy.

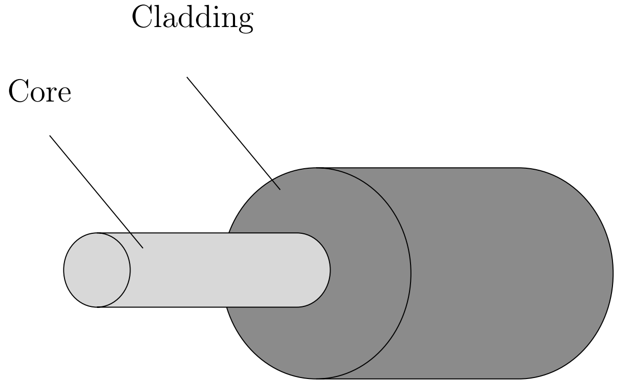

Figure 1: Optical fiber with a core and a cladding.

The core size of the optical fiber determines if the beam will be single-mode or multi-modal. Single-mode fibers often have a core diameter of around 8–10 µm while multi-modal fibers have a core diameter are around 50–62.5 µm. Multi-modal fibers make combining and launching light into the core easier because of their larger size. Additionally, multi-mode fibers are preferred to work with as they are more tolerant to poor laser beam quality. [4] Multi-modal beams are light beams that consist of an input beam profile that distributes into multiple different modes and therefore have an uneven energy distribution, usually in a granular pattern. The exact amount of modes depend on the wavelength, optical frequency and refractive index. [5]

1.3 Laser Beam

Most laser sources emit a beam in the form of a Gaussian beam. A Gaussian beam is a transverse laser beam with energy modes that follow the Gaussian energy distribution, a distribution with a "bell curve" shape. [6] Laser beams need to be focused on an area with high energy density to do substantial damage to a cell. In cancer treatment it is important to focus to the size of one cell in order to not damage healthy cells. To concentrate laser energy into a small focal spot, a lens is formed on the end of an optical fiber.

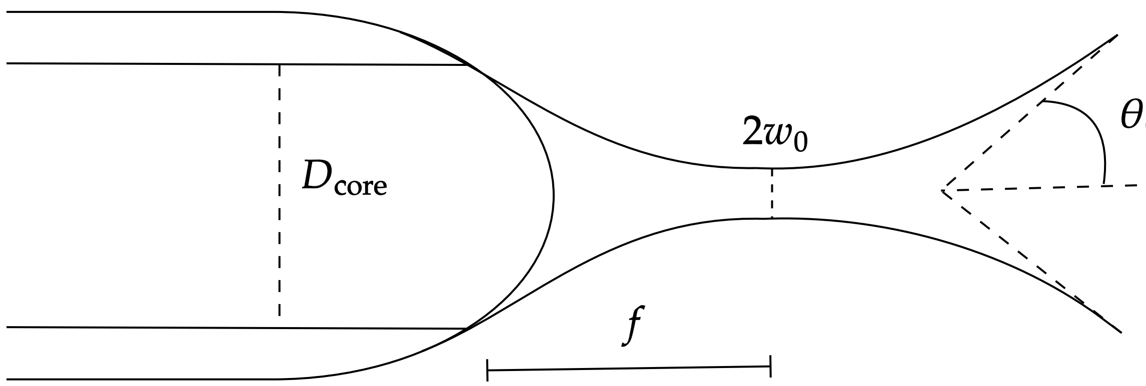

Figure 2: Beam divergence of a Gaussian beam from an optical fiber. D_{core} represents the core diameter, w_0 is the spot radius and θ_0 is half-divergence angle.

The lens will converge the beam to the beam waist which is where the beam is the narrowest, and then start diverging. The beam will diverge linearly far from the lens and the divergence angle can be calculated using far field approximation. The radius of curvature of the lens tip decides the focal length. The distance from the fiber tip to the focal spot is called the focal length f and the beam waist is the diameter at the focal spot.

1.4 Theory

One way to experimentally determine the focal length and spot size of a laser is to use the far field approximation and look at the divergence angle.

The divergence half-angle θ_0 can be calculated by

$$\theta_0 = \arctan\left(\frac{D_2 - D_1}{2\Delta d}\right) = \arctan\left(\frac{\Delta D}{2\Delta d}\right) \tag{1}$$

where D_2 and D_1 are beam diameters at different distances away from the plane. Δd is the difference in distance between the two points. [7]

The spot size of a Gaussian beam can be calculated from the focal length by using the equation

$$w_0 = \frac{\lambda}{\pi\theta_0} \tag{2}$$

where λ is the wavelength, w_0 is the radius of the spot size and θ_0 is the divergence half-angle. From equation (2) it can be inferred that a larger wavelength results in a larger spot size. A larger spot size means that the power density is lower at the targeted cell. [6]

Using this, the focal length can be determined by rearranging an equation for the spot size dependant on the focal length f and diameter of the optical fiber D_{core} instead of the divergence angle. The equation

$$2w_0 = \frac{4f\lambda}{\pi D_{\text{core}}} \tag{3}$$

is rearranged into the equation

$$f = \frac{w_0 \pi D_{\text{core}}}{2\lambda} \tag{4}$$

where D_{core} is the diameter of the fiber and f is the focal length.[8]

The beam diameter of a beam is defined by the $\frac{1}{e^2}$ definition, the distance where about 86.5 % of all energy is gathered. [6]

In order to determine the beam diameter of a beam at a certain distance, the full width at half maximum can be analyzed where you find the distance of the beam when the intensity is half of its max. The full width at half maximum, FWHM, can be converted into the beam diameter, the equation

$$2w_0 = \sqrt{\frac{2}{\ln 2}} \times \text{FWHM} \tag{5}$$

is used. [9]

1.5 Aim of Study

The aim of this study is to develop better treatment possibilities for cancer using fiber optic technology. This specific project is an extensive investigation of laser focusing of optical fibers with lens tips, and its effects on living cells. The project focuses on finding the spot size with an energy density high enough to do lethal damage to cells. The aim was also to further develop the equipment around the optical fiber to easily control the position and exact firing of the laser. This study will experiment using onion cells instead of human cells.

2 Method

The usage of high-power lasers on cancer cells requires certain steps to ensure that a high energy density is concentrated on the cancerous cells without damaging surrounding healthy cells. Precise movement, laser focusing and precise laser activation are important factors for this research.

2.1 Far Field Divergence

An experiment was performed by shooting an arbitrarily chosen 632 nm red laser from a multi-mode fiber with a 50 µm core diameter and a lens tip that had a radius of curvature of 30.9 µm. The laser output was displayed on a paper plane at different distances from the fiber cable. The resulting beam spread was captured by a stationary camera and the beam was plotted by converting the image into a grayscale. The plotted beam was fitted according to a Gaussian model and the full width at half maximum was measured for all distances. The full width at half maximum length was converted into beam diameter for all distances using equation (5). The FWHM diameters were plotted against distance with a trend line, the gradient of the trend line was used to calculate the divergence half-angle according to equation (1).

2.2 Refractive Indexes

The analyzed optical fiber had a spherical lens with a radius of curvature of 30.9 µm. The measured divergence and focal length for the lens will depend on what medium the light enters after the fiber. This is because of the difference in refractive index when traveling from the lens to the outer medium, the refraction angle is dependant on the refractive indexes of the two mediums according to Snell's law.

2.3 Instrumentation Development

The optical fiber was mounted on a 3D-Stage that was controlled by 3 motors and could be viewed with a 100x microscope. The 3D-Stage was programmed to have a three dimensional coordinate system x, y, z by using the absolute value parameter from the motors, that is the total length the motors are extended. Using this, the fiber could be moved anywhere in a 2.5x2.5 cm cube with micrometer precision. To test the capabilities of the 3D-Stage an 100x upscale simulation was run where a precise pump was activated at certain coordinates and released a small amount of liquid. This was a simplified version of chemotherapy delivery to some cancerous cells. The laser diode was being controlled by a laser diode controller that was controlled via a python script, which resulted in complete control over movement, activation and power of the laser.

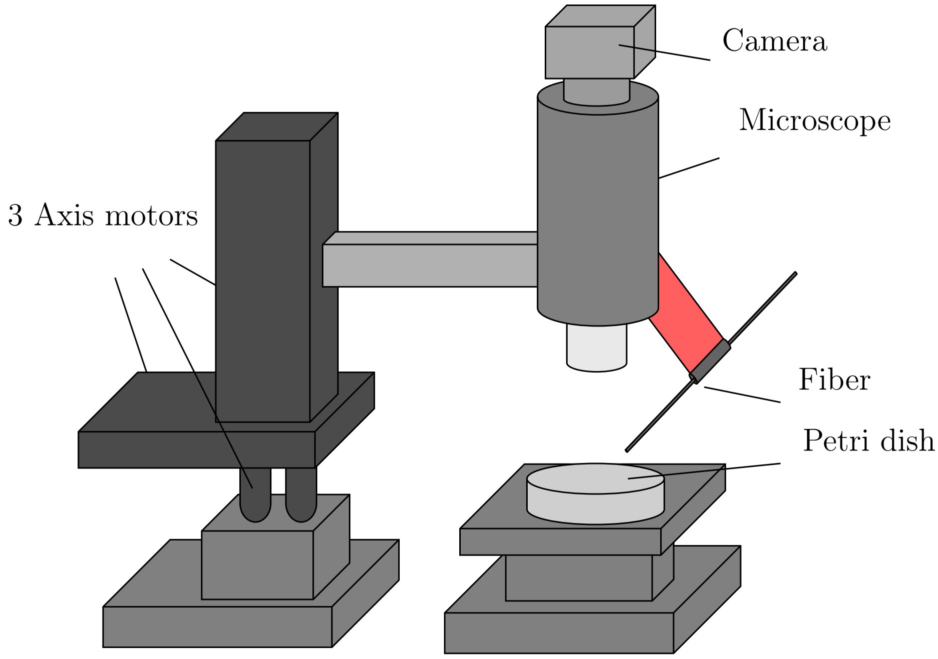

Figure 3: 3D-Stage with 3 motors on different axises, a camera connected with a microscope to view the cells and a fiber connected to the microscope.

2.4 Onion Experiment

The 980 nm high-power laser was used on onion cells because they offer easy access, large cell size and easily seen cell structure in a microscope. An onion cell is approximately 200 µm in size which is around 10 times larger than a cancer cell of approximately 15–25 µm in size [10][11]. As a proof of concept, if the laser is able to damage a larger cell then it should be able to damage real cancer cells in further studies. Thus, the onion experiment will test if any cellular damage is possible with the laser. The optical fiber probe used had a lens with a radius of curvature of 30.9 µm. The experiment was performed with the onion piece inside of a water droplet, this resulted in a different laser focal length than in air. The focal length was then not determined but the distance was experimentally tested on the onion cell. The experiment was performed multiple times at different focusing distances.

2.4.1 Laser Coupling

An infrared single-frequency laser with a wavelength of 980 nm was used as a primary source of power to destroy cells because of its high-power. The output power compared to the current was measured with a power and energy meter console.

A blue LED at 430 nm was added in order to show a marker of where the high-power beam was focused. Using the blue marking laser as guidance the high-power laser was activated when the energy spread was appropriate for the cell size. A laser coupler which combines multiple beams into one was used to combine the two lasers. The coupler had a perceived efficiency of at least 90% kept output energy from the high-power laser.

2.4.2 Power Output

The laser was controlled by the laser controller ILX Lightwave LDC-3742. The input current was adjustable and the power output was measured for different values of current by a ThorLabs PM100D power meter. The power was measured in intervals of 20 mA between 400–1000 mA. The data points were plotted and the setting for maximum power was chosen for the onion experiment in order to test if the laser could harm the cell. The diode laser temperature was controlled using TEC and kept constant at 25 °C because it was the preferred temperature for the laser.

3 Results

The measured data is the angle of divergence, the focal length and the spot size of the laser beam.

3.1 Angle of Divergence

The divergence of a 30.9 µm radius of curvature lens tip was examined because it was shown to converge.

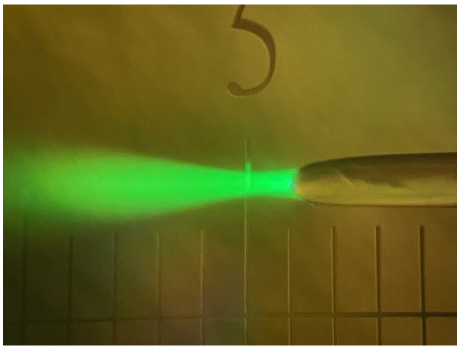

Figure 4: Lens tip with radius of curvature of 30.9 µm and a blue LED source in fluorescing water-like material shining a green beam. Every notch is 100 µm wide.

As seen in figure (4) the beam converges to a focal spot. However, the LED used does not have the same divergence as a Gaussian beam and can not be used as experimentally measured data.

A ball tip lens was also examined, however its divergence angle was smaller than the fiber without a lens, thus it was ruled inefficient for our purpose. The measured divergence image was analyzed on a gray scale and plotted. The data was fitted to a Gaussian model and the full width half max points were noted.

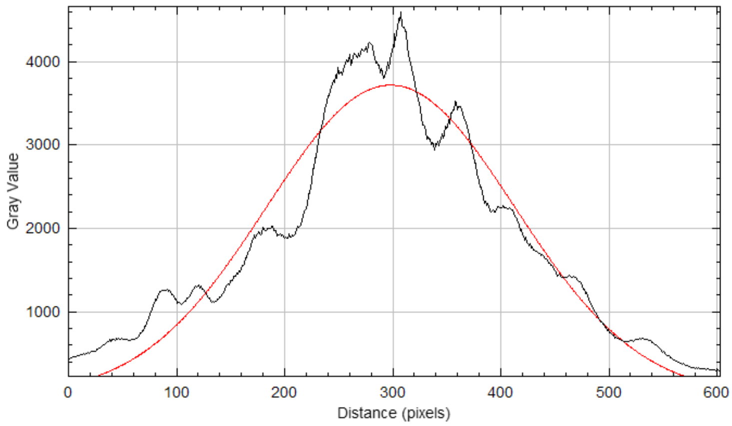

Figure 5: Gaussian model fitting for a distance of 16 cm

An image was taken of a ruler on the output plane with the same camera and the measurement for the amount of pixels of 1 cm was taken by averaging the amount of pixels from 10 cm. The result was approximately $45.5\,\mathrm{px\,cm^{-1}}$. The difference in pixels between the full width half maximum points were converted to cm for all distances using equation (5).

Table 1: This table shows the beam diameter of the laser compared to the distance from the fiber.

Distance (cm)	Beam Diameter (cm)
6.0	3.84
8.0	4.94
10.0	6.36
12.0	7.02
14.0	7.79
16.0	9.87
18.0	10.7
20.0	12.4

The beam diameter was plotted against the distance from table 1 and a linear trend line was fitted.

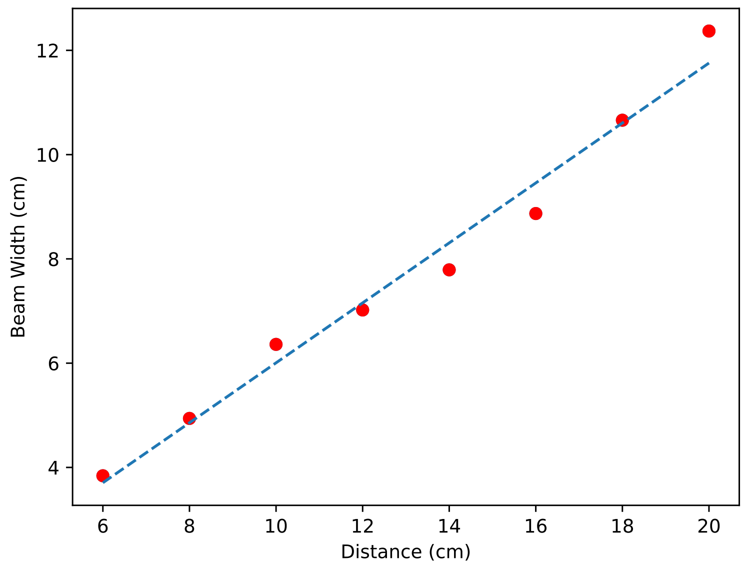

Figure 6: The measured beam diameter at different distances away from the lens tip.

The slope of the trend line is approximately 0.59 which was used to calculate the divergence half-angle using equation (1). The resulting half-angle was calculated to be approximately 0.29 rad. Additionally, using this value in equation (2) and (4) resulted in a spot size of approximately 2.16 µm and a focal length of approximately 86 µm for a

30.9 µm radius of curvature lens in air.

3.2 Onion Experiment

The measured power output plotted against the current and can be seen in figure 7.

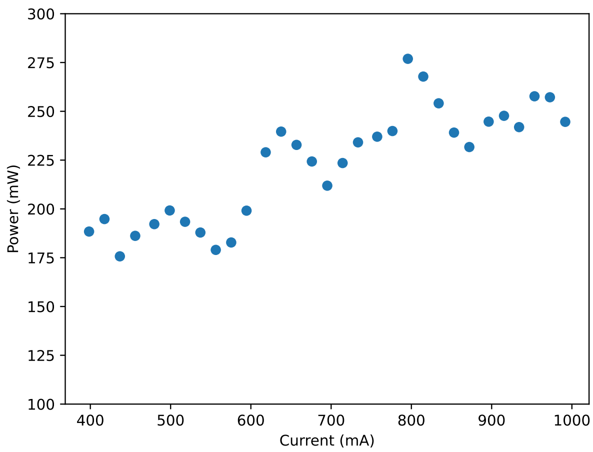

Figure 7: Power output against input current in intervals of 20 mA

The maximum power of approximately 280 mW was measured at a current of 800 mA. This maximum input setting was chosen for the entire duration of the onion experiment in order to determine if any harm was possible.

Using the spot size value, the cross-sectional area for the focal spot is approximately 3.64 μm^2. This resulted in an average surface power density of approximately 76 mW μm^{-2}.

There was visible damage made to one onion cell after the high-power laser had been activated for a total of 10 s.

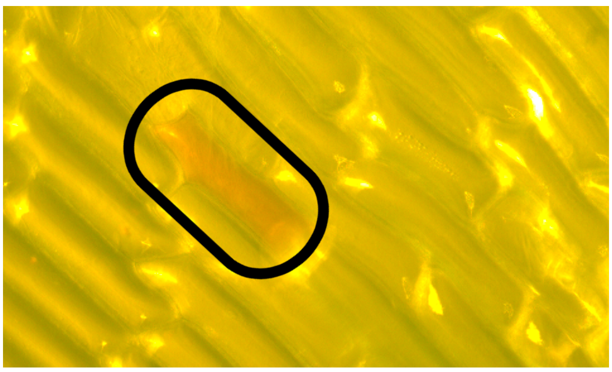

Figure 8: Discoloured onion cell, presumably dead.

The specific dead onion cell seen in figure 8 shows that it was possible to selectively eliminate one cell by using a high-power laser.

3.3 Experimental Uncertainties

The distance estimation had an uncertainty of about ± 1 mm. However the FWHM model curve fit had a substantially lower maximum values which could lead to an unusual model fit, a maximum uncertainty of ± 10% is estimated. These values were used for further calculations and therefore an estimated total uncertainty in focal length, spot size and energy density is approximately ± 10%. The R^2 value for the diameter against distance graph is 0.986 which is a strong correlation.

4 Discussion

Many attempts were made with firing the laser at similar distances away from the onion cell but only one attempt had any visible success. This would show that the precise measurement and spot size is very important for usage on cancerous cells. The current setup with the 3D-Stage lacked an easy way to determine the distance to the cell which led to imprecise positioning. It was shown that the optimal focal length in order to focus with maximum energy density was approximately 86 µm, using a 30.9 µm radius of curvature lens on a fiber with a 50 µm core. The marking laser originated from an LED and does not have the same divergence angle as the high-power laser and is therefore not very reliable. Additionally, the optical fiber had an angle of 35° at which some energy was reflected away from the onion cells.

4.1 Further Studies

This experiment was focused around focusing a laser and ability to eliminate a cell using a high-power laser. In further studies with more experimental information the laser could be tested on smaller cells which require more precise focusing. Eventually, this method may be used to eliminate human cancer cells and cure patients. In future experiments there should be a marking laser with the same beam and divergence as the infrared laser which therefore makes manual laser focusing more precise. Additionally, with further development the 3D-Stage the positioning will be automated by moving directly to cancerous cells which can be detected using the microscope and fluorescent lasers.

4.2 Conclusion

The experiments showed that an optical fiber with a core of 50 µm and a radius of curvature of 30.9 µm and a 980 nm high-power laser has a half-angle of divergence of approximately 0.29 rad, and converges with a focal length of approximately 86 µm and a spot size of 2.16 µm in air. The focusing of the laser was examined by firing at onion cells with different distances and approximately 280 mA of average power. The results showed that one focused cell was discoloured and presumably dead.

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