Research Academy for Young Scientists

Towards Cancer Cell Termination Using Optical Fiber Probe and High-Powered Laser

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Abstract

Cancer is a disease affecting millions worldwide. Different types of cancer require different approaches. In this paper, the focus is on cancers that are inaccessible without invasive procedures, such as pancreatic cancer. Therefore, the aim of this study is to create an optical fiber probe capable of moving to a specific location and targeting a cell with a laser powerful enough to kill it. This was tested on epithelial onion cells using a laser of wavelength 980 nm. It was found that the precision needed to be improved in order for the maximum amount of power to hit the cell. However, through further research, this method could prove successful.

Acknowledgements

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Contents

1 Introduction

Cancer is a common disease that touches people worldwide and accounts for 10 million deaths every year. It can occur anywhere in the body and spreads in different stages. Often, there are treatment options available and it is not always fatal. However, certain cancers can be hard to diagnose and treat without invasive procedures. [1]

For instance, pancreatic cancer is a rare but particularly fatal type of cancer, where most patients die within five years of getting sick [2]. Early diagnosis is uncommon as the pancreas is located underneath the liver which makes it difficult to detect tumors or abnormalities during routine checks. Often patients exhibit symptoms after the cancer has progressed to the metastatic stage, at which point the survival rate is 1% [3]. Current pancreatic cancer treatments are invasive and rarely successful.

In recent years the search for new treatments has sparked new research into the use of laser physics. Fiber optics has historically been used as an alternative to invasive surgical procedures and could potentially be used as a cancer treatment as well.

In fact, fibers have been used in medicine since the 1950s when they were first implemented in endoscopes and used to visualize inaccessible organs. Over the past 20 years, in an effort to make preventative action more affordable and accessible, the lab-on-a-fiber field has been introduced [4]. Based on the widely successful lab-on-a-chip format, lab-on-fiber allows for various diagnoses that are facilitated by the microscopic dimensions of the fiber. Capable of analyzing, collecting and in the case of this study, potentially terminating, lab-on-fiber has various uses within cancer research.

1.1 Aim of Study

The aim of this study is to develop a new treatment method for cancers like pancreatic cancer that are in inaccessible areas. This is done by focusing a laser using a lensed fiber optic probe to target and terminate cells whilst controlling a 3D-stage in order to move the fiber to the desired point.

2 Theory

When developing this probe, the particular characteristics of fibers must be considered as well as the behavior of light travelling through them and out.

2.1 Optical Fibers

Optical fibers are usually made out of silica glass and have a diameter ranging from 50 µm to 1 mm. They are made up of an innermost layer known as the core, which light travels through, a middle layer called cladding which prevents light from spreading through the fiber in unintended directions and an outer layer known as the coating, which is usually acrylic, and surrounds the fiber to protect it from humidity and other environmental factors that could damage it, see Figure 1. The core of an optical fiber has a higher refractive index than the cladding, meaning that light travels slower through the core, thus refracting at an angle greater than the critical angle when coming into contact with the cladding, resulting in total internal reflection. All of the light passing through the fiber rebounds at the boundary between the core and the cladding, thus guiding it through the core with minimal energy loss.

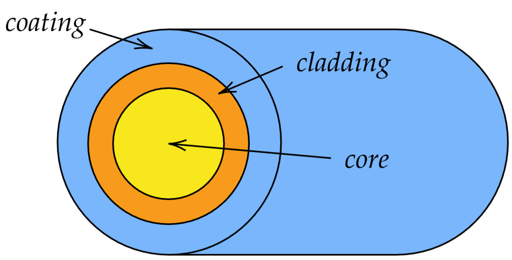


Figure 1: Structure of an optical fiber

The fiber used in this project is the LFM100 from ThorLabs and has a core diameter of 50 µm and a cladding diameter of 125 µm, see Figure 2. Additionally, it has a lensed tip with a radius of curvature of 30.90 µm allowing for light to be focused at the focal point, see Figure 3b. The fiber is multi-mode, allowing it to propagate multiple modes at once.

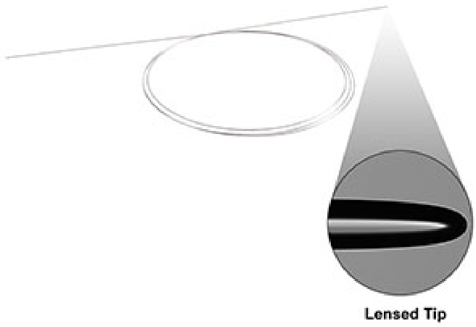
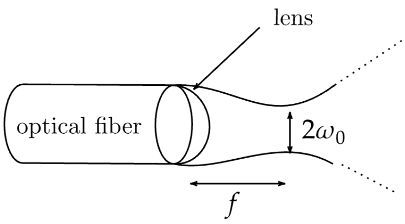
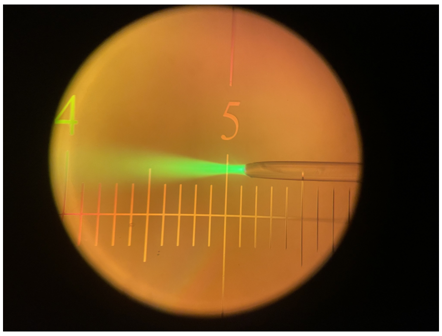


Figure 2: ThorLabs LFM100 fiber used in this study [5]



(a) Diagram of a lensed optical fiber



(b) Lensed fiber seen through microscope with LED propagating

Figure 3: Light propagation through lensed fibers

By using a lensed optical fiber, it is possible to focus the beam of the terminating laser at the desired cell, in this case, a cancer cell with a diameter ranging from 15 µm to 25 µm.

The focal length f can be described as the distance from the tip of the lens to the beam waist w_0, which is the radius of the smallest spot of light called focal point, see figure 3a. At the focal point, the energy concentration is the greatest. As the aim is to terminate cells, it is extremely important to find the focal point of the laser. By adjusting the focal length of a laser it is possible to adjust the spot-size, and thus the concentration of light at the focal point. The focal length is described as

$$f = \frac{2\omega_0 \pi D_0}{4\lambda} \tag{1}$$

where f is the focal length, D_0 is the diameter of the core of the fiber or 50 µm and λ is the wavelength, see figure 4. The beam waist of a Gaussian beam with a lens can be written as

$$\omega_0 = \frac{2\lambda}{\pi\theta} \tag{2}$$

where ω_0 is the radius of the beam waist, λ is the wavelength of the laser,and θ is the divergence half-angle.

Gaussian beams converge into the focal point before diverging meaning light does not travel in a straight line. Once the beam enters the far-field, the beam waist increases in a linear fashion and a formula used in geometrical optics can be applied in order to find the focal length [6]. This method involves looking at the angle formed between the middle of the divergence and the edge of the beam, see Figure 4.

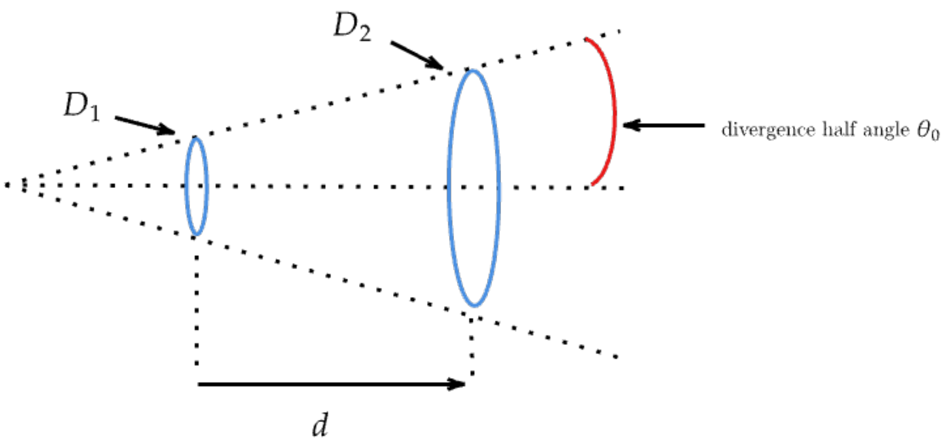


Figure 4: Beam Divergence

The divergence half-angle in Figure 4 can be described by the equation

$$\theta_0 = \arctan\left(\frac{D_2 - D_1}{2d}\right) \tag{3}$$

where θ_0 is the divergence half-angle of the beam, D_2 is the final diameter of the beam D_1 is the initial diameter of the beam and d is the distance between diameters. [7]

The Full Width at Half-Maximum or FWHM is defined as the distance between the two points from a measurement of light intensity that are 50% of the maximum intensity and are closest to the peak. This definition is used to find the beam diameter 2ω, where ω is the beam radius. by determining the beam diameter it is possible to find the focal length through equation 1. It can be described as

$$2\omega = \sqrt{\frac{2}{ln2}}FWHM \tag{4}$$

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3 Method

In order to develop the probe, several separate parts needed to work in unison. Firstly, the laser needed to focus on a cell with enough power to kill it. Because of this, determining the focal length of the laser was crucial. Secondly, the fiber needed to move to the desired cell. Using a 3D-stage which held the fiber, it could be guided to a specific spot with precise movement from the motors.

3.1 Positioning 3D-stage

As part of the instrumentation development part of this project, it was necessary to control the 3D-stage, seen in Figure 5, on which the optical fiber probe rests. The stage is composed of Zaber X-LSM025A motors in the x, y and z planes which are controlled through the PySerial library in Python. By adjusting the speed and position of the motors, it was possible to divide the search area of the probe into a grid allowing it to move to a specific coordinate. The range on each motor is 25.4 mm and the precision is 1 µm.

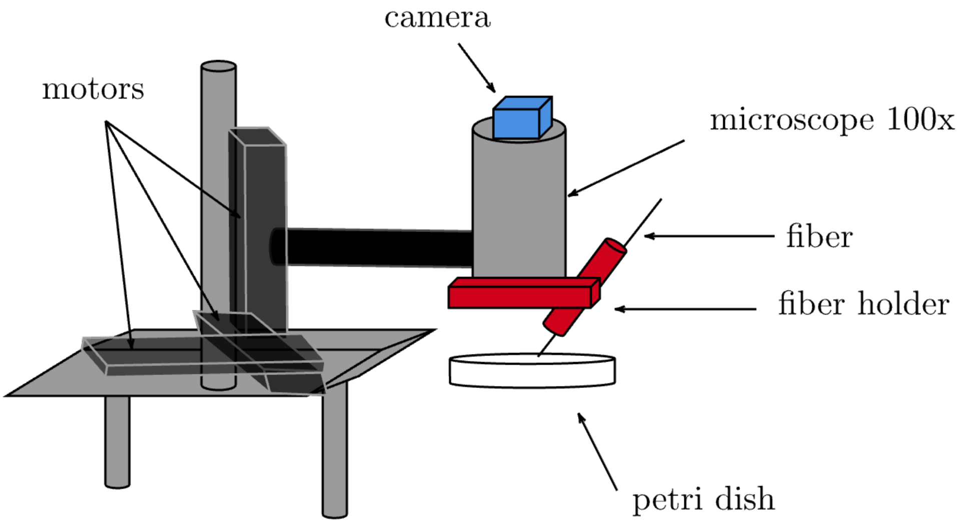

Figure 5: Schematic of 3D-stage

3.2 Determining Focal Length

The focal length of a lensed fiber is extremely important as there are big power discrepancies between the focal spot and the diverging beam of the laser. In order for this treatment to be as effective as possible, a high concentration of power is desired to ensure the death of the cancer cell.

Using a red laser with wavelength 632 nm and a lensed multi-mode fiber with radius of curvature 30.9 µm and core diameter of 50 µm, it was possible to approximate how the light emitted by the laser propagated in the far-field. This was done by measuring the intensity of the light against a piece of paper, see Figure 6. A camera was fixed 27 cm from the paper. The fiber was placed on a stand and moved in increments of 2 cm between 4 cm and 20 cm away from the piece of graduated white paper. Based on the intensity experiment, see Figure 7, a Gaussian distribution was plotted for each distance within the interval described in the previous section and the FWHM of the function was then estimated based on the Gaussian fit.

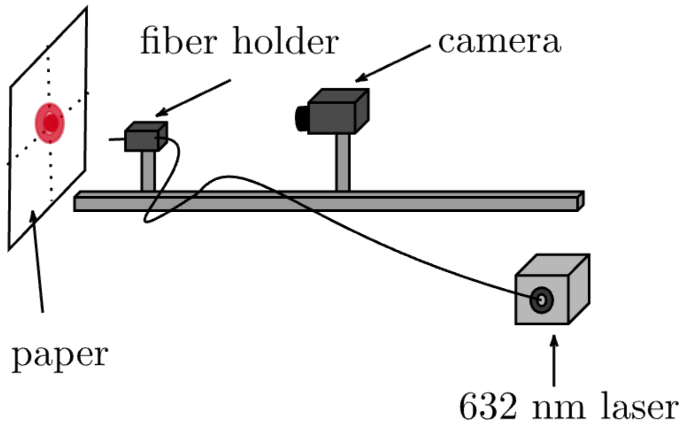

Figure 6: Experimental setup

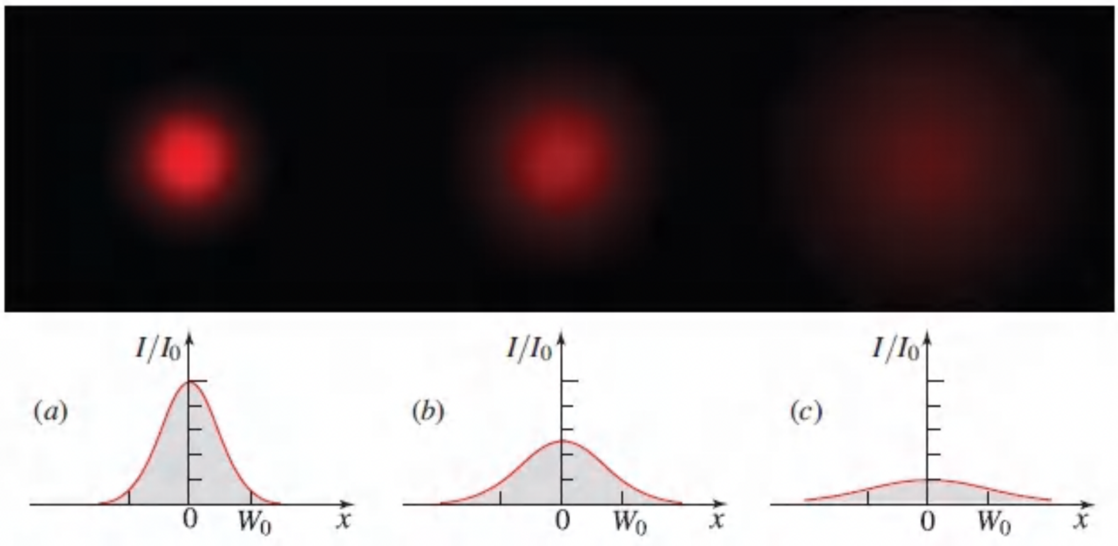

Figure 7: Intensity profile of a Gaussian beam from different distances [8]

Once the gray scale photos were analyzed, it was possible to fit a Gaussian curve to the data so as to estimate the Full Width at Half-Maximum, or FWHM.

3.3 Killing of Onion Epithelial Cells

In order to test the findings of this study in a practical way, epithelial onion cells were used to simulate human cancer cells since most cancer cells are found in the epithelium [9] and onions are easy to procure. Additionally the average size of an epithelial onion cell is 250 µm and the size of pancreatic cancer cells is around 25 µm. Since the onion cell is scaled by a factor of 10, it is easier to estimate the true proportions. The epithelial sample was collected from the onion membrane, placed on a petri dish and covered in a fluorosceine, a fluorescent dye with excitation at 498 nm and emission at 517 nm. An analyzing laser of wavelength 450 nm made the cells fluoresce in a neon green nuance and allowed for the fiber to focus on a cell before switching to the infrared killing laser of wavelength 980 nm.

4 Results

Based on the intensity experiment, the beam widths obtained can be seen in Table 1.

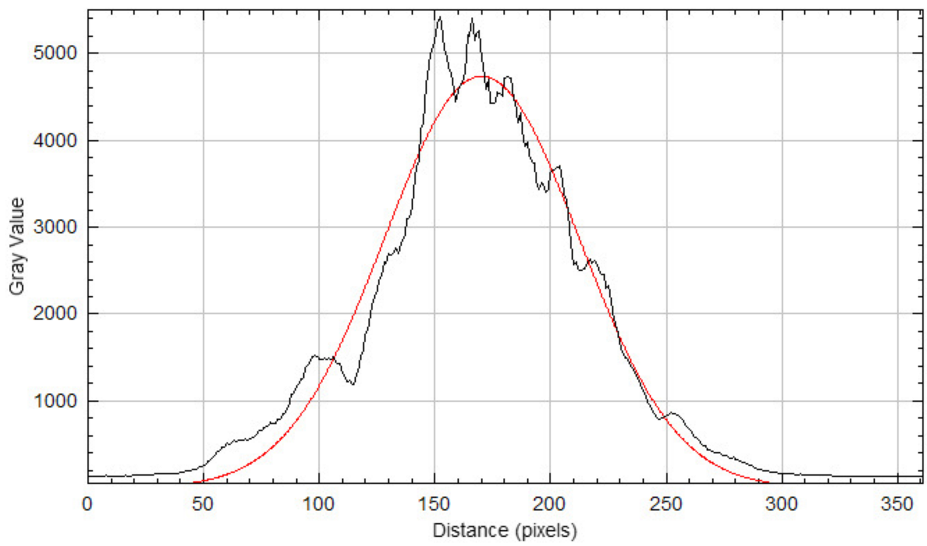

Figure 8: Example of a Gaussian distribution of the intensity profile at 6 cm

Figure 8 shows a Gaussian curve fitted to the intensity profile of a 632 nm red laser at a distance of 6 cm from an object. The Gaussian distribution can be seen in red.

Table 1: FWHM and beam width based on the distance from fiber lens

Distance (cm)	**FWHM (cm)**	**Beam Width (cm)**
6	2.26	3.84
8	2.91	4.94
10	3.75	6.36
12	4.13	7.02
14	4.59	7.79
16	5.81	9.87
18	6.27	10.7
20	7.28	12.4

The beam width was determined through equation (4). From the beam width determined from the FWHM of the Red Laser Experiment, seen in Table 1, the divergence half-angle was calculated to be 0.32 rad. Inputting θ_0 into equation (2) results in a spot size of 1.8 µm. Inputting the values found for θ_0 and ω_0 results in a focal length of 73.2 µm.

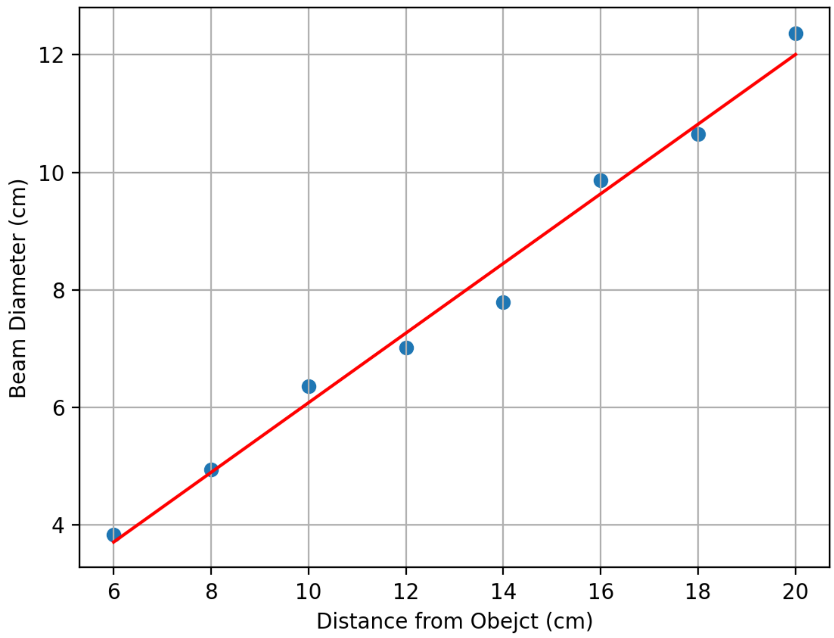

Figure 9: The beam diameter as a function of distance from paper

In Figure 9, the beam diameter is plotted as a function of distance of the laser from the paper and has an r^2 value of 0.986. In the far-field, the divergence of the beam likens that of a geometrical function.

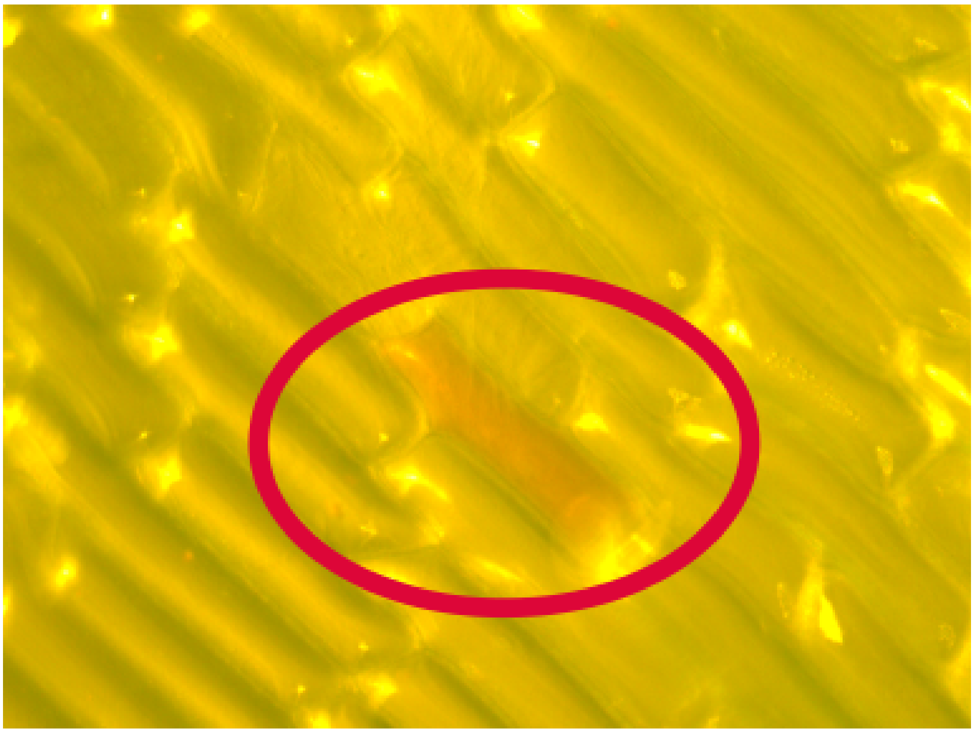

Figure 10: Epithelial Onion Cell Killed by Laser

In Figure 10, a darker colored onion cell can be observed inside of the red circle. It was shot by the 980 nm laser for 10 seconds with 240 mW of power and is therefore presumably not viable.

5 Discussion

The development of a fiber optic probe used to target cancer cells is dependent on several factors. The properties of the fiber and laser have an effect on the energy outputted to the cell. Due to the microscopic size of these cells, precision is crucial, however this experimental setup was not precise enough for that. Targeting an onion cell, which is ten times larger than a cancer cell was challenging as the focal length of the fiber was difficult to observe and adjust using the 3D-stage, making the targeting random. In vivo, this procedure must be precise within 1 µm as the purpose is to target cancer cells and spare healthy cells. By determining the focal length of the lens it is possible to investigate the energy density at the focal spot and conduct studies on the amount of energy needed to kill a specific cell.

5.1 Limitations of Study

Small deviations could be observed from the Gaussian curve yet the data corresponds well to the distribution. Instrument wise, the measured distance from the fiber to the paper has a precision of $\pm 1\,\mathrm{mm}$ due to the ruler. It is difficult to determine the focal length of the laser or measure it experimentally through the microscope during the experiment with our current setup making it challenging to target the cells at the right distance resulting in a significantly less power delivered to the cells.

5.2 Further Research

This study was conducted on onion epithelial cells. As such, we cannot be certain of how cancer cells nor other body cells will react to this laser therapy. This method needs to be tested on cancer cells in vitro to start. The wavelength of the laser we used for termination was 980 nm, however there may be wavelengths that are better suited for this specific task. Additionally, other radii of curvature for the lens of the fiber with a shorter focal length and a spot size closer to the desired range of 15 µm and 25 µm need to be investigated.

5.3 Conclusion

It is possible to target and terminate cells using an optical fiber probe with a lens. The focal length of the fiber must first be calculated so as to target the cell using the highest possible concentration of power. By using a 3D-stage, movements toward desired cells can be controlled automatically. This study found that However,the precision of this method needs to be improved before moving on to the next step.

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