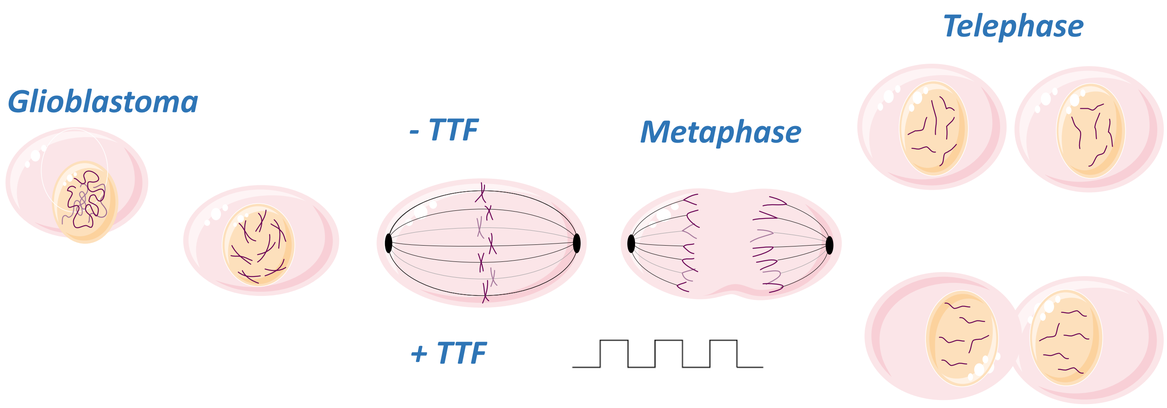
In vitro validation of electric fields using 2D and 3D systems to decrease cell proliferation in glioblastoma

A. Bouzas[a], A, Pendashteh[a], JJ. Vilatela[a], J. Llorca[a,b], R. Ramos[b], M. Jimenez Carrizosa[b], P. Sanchez Gomez[c], M. Echeverry-Rendón[a*]

[a]*IMDEA Materials, Madrid, 28906, Spain.* [b]*Universidad Politécnica de Madrid, Madrid, Spain.* [c]*Instituto de Salud Carlos III, 28220 Madrid, Spain.*
monica.echeverry@imdea.org.

Glioblastoma and Tumor Treating Fields

Glioblastoma (GBM) is highly aggressive and constitutes around 60-70% of malignant glial tumors. A therapy based on alternating electric fields of low intensity (1- 3 V/cm) and intermediate frequency (~ 100-500 kHz) called Tumor Treating Fields (TTF) has been used as a possible solution[1].



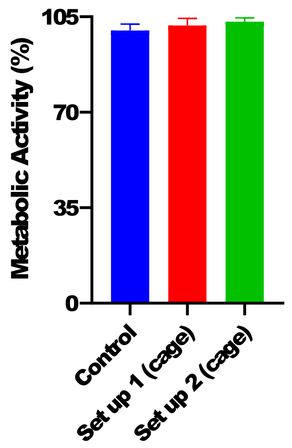
In the presence of TTF the chromosomes cannot align properly in the center of the dividing cell, preventing the even distribution of DNA. Consequently, one cell receives excess DNA while the other gets insufficient amounts. These tumor cells cannot survive and undergo apoptosis, a form of organized or programmed cell death[2].

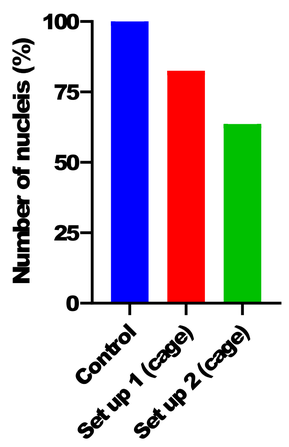
This study aimed to develop a screening to evaluate different variables related to TTF to obtain the best parameters to stop cell proliferation in a glioblastoma cell line at 2D and 3D system

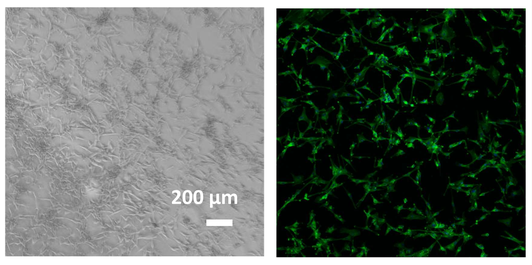
Experimental Design

Results

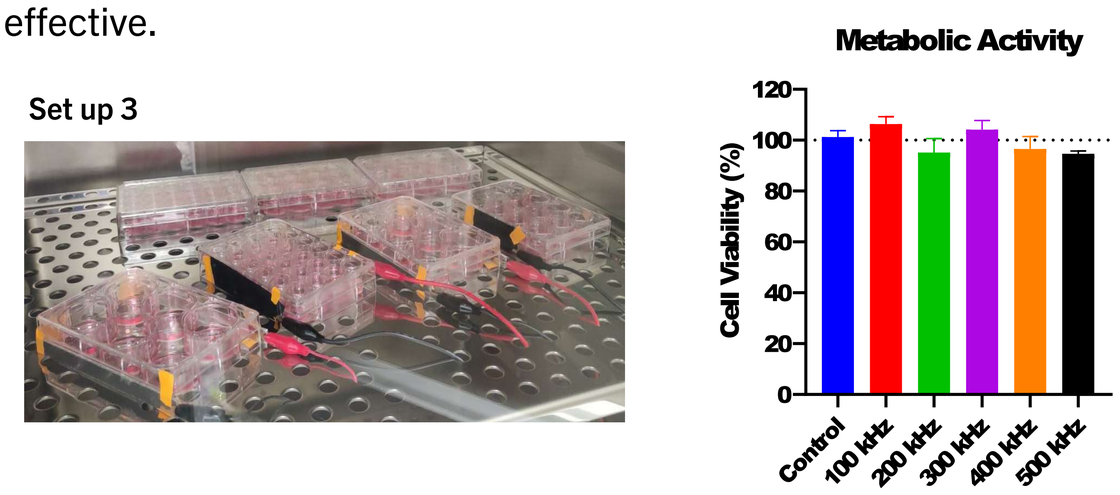
Different setups were designed to generate the TTF and study their effect on U-87 MG, a human glioblastoma cell line.

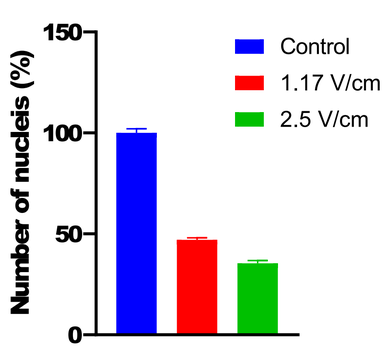


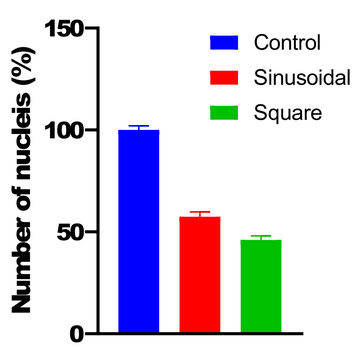


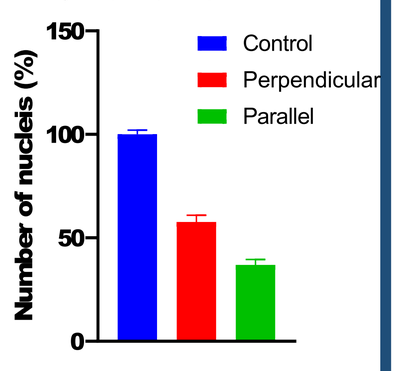


Cells were stimulated at 1.5 V-cm from 100 to 500 kHz. Metabolic activity and cell counting were performed to detect differences in a cell population. A frequency of 200 kHz was considered the most effective.

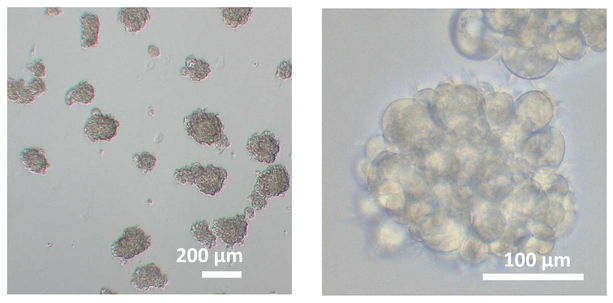








With a constant frequency of 200Hs, the best results for controlling cell proliferation were 2.5 V/cm, using square waves and with the electrodes located parallel to the cell culture.



These results were validated using 3D cell cultures with similar results to the 2D ones.

Conclusions

Electric fields can be used to stop the cell division of cancer cells. Controlling parameters such as electric field, frequency, signal shape, and field direction are critical to having a good response. This information generates a solid basis for designing biomedical devices to stop the progress of tumor cells. In the direction of personalized medicine, this type of screening could allow us to take biopsy cells from patients and see how to generate a therapy aimed at treating specific tumors, taking into account the individual variability of each patient.

References

1. *Rominiyi, O., et al . (2021). British Journal of Cancer, 124(4), 697-709, Moser, J. C., et al. (2022). Cancer Research, 82(20), 3650-3658.*

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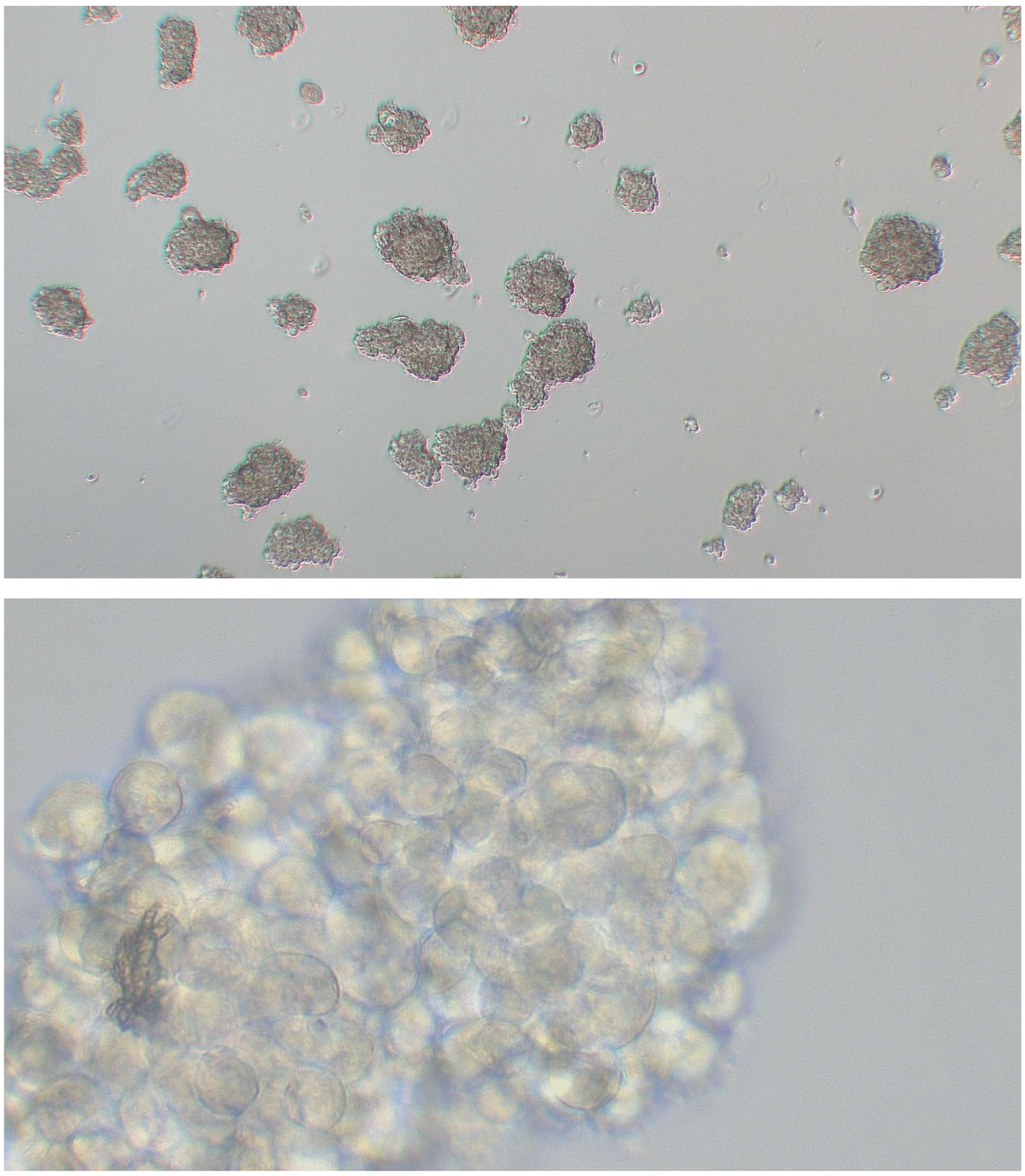
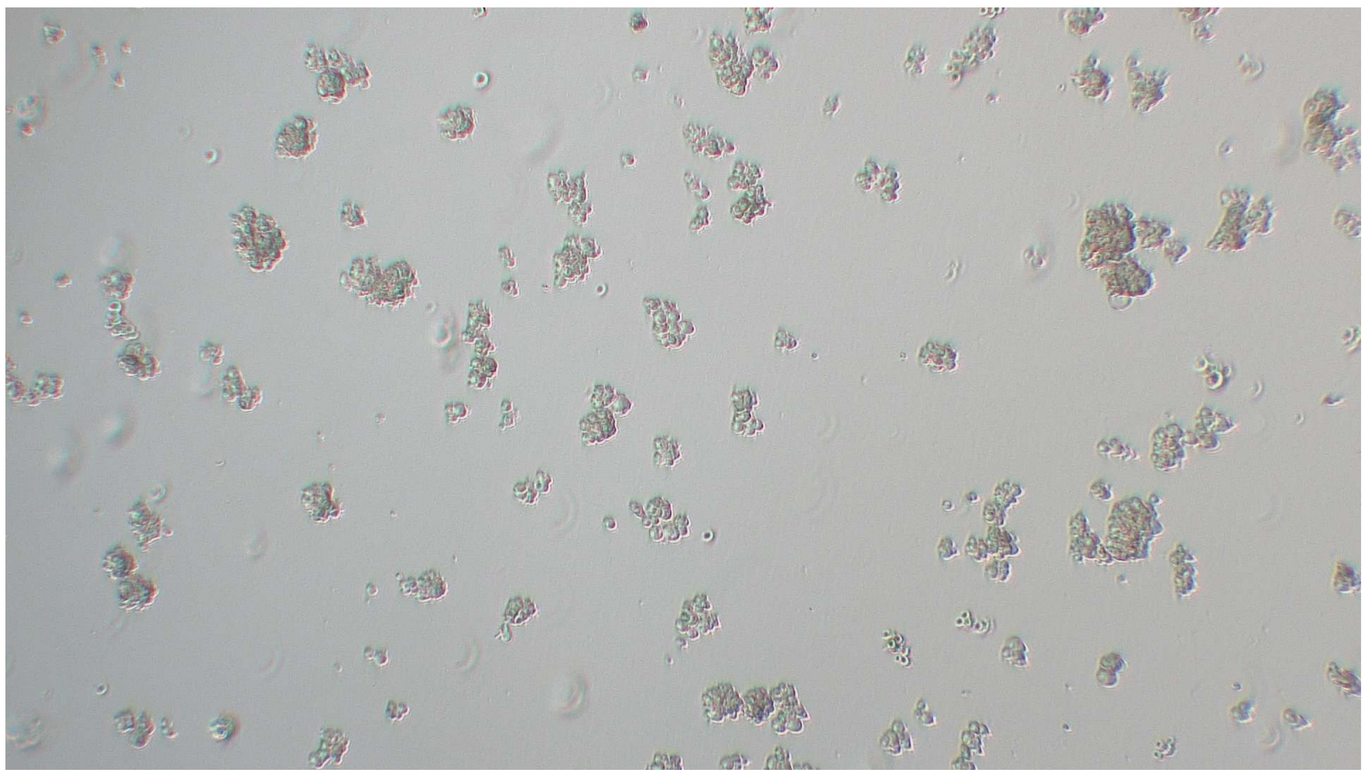
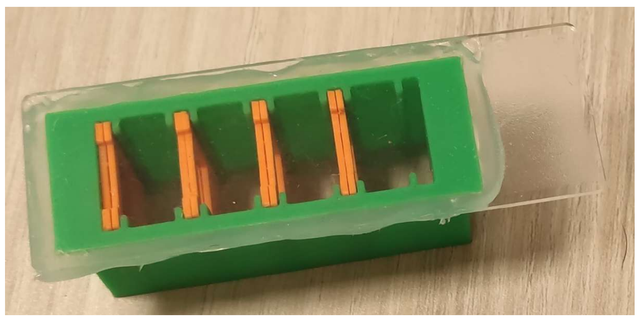
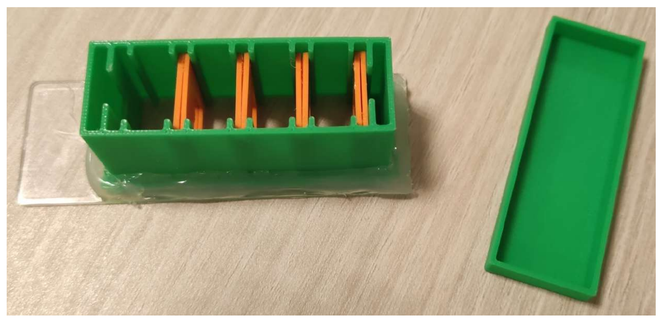


A las 72 h de sembrar
a 10.000 cells/cm^2

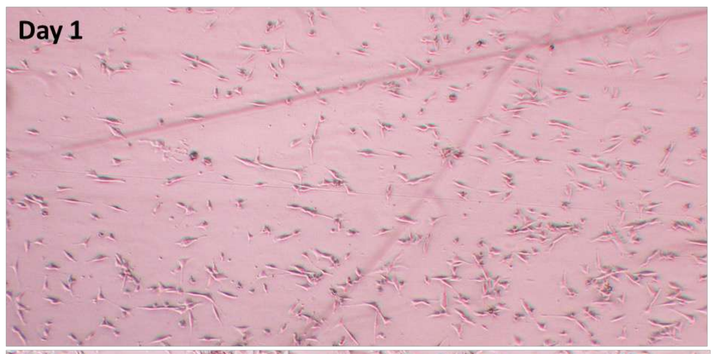


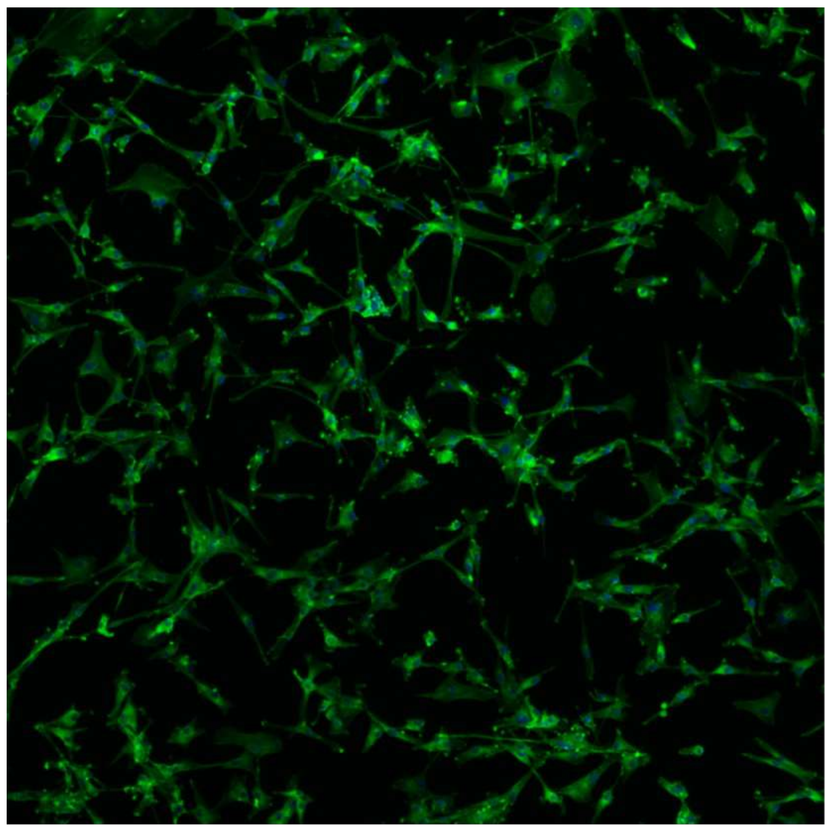
A las 72 h de una dilución 1/6
de la foto anterior

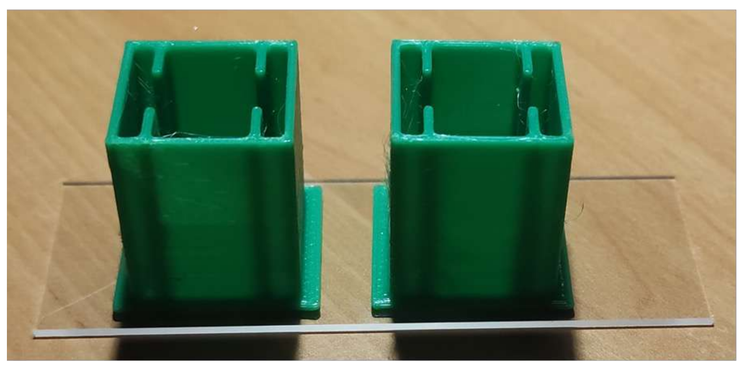


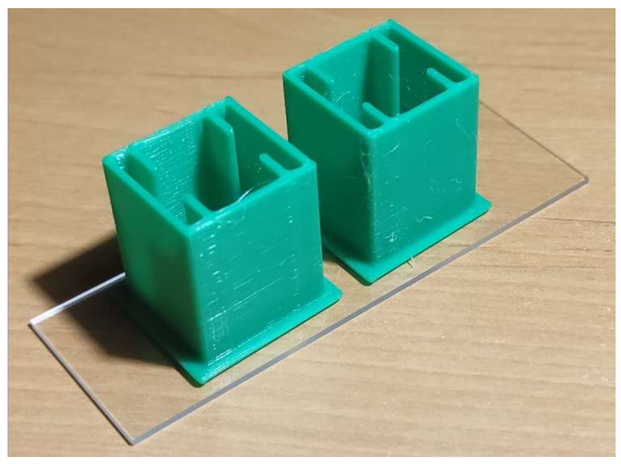


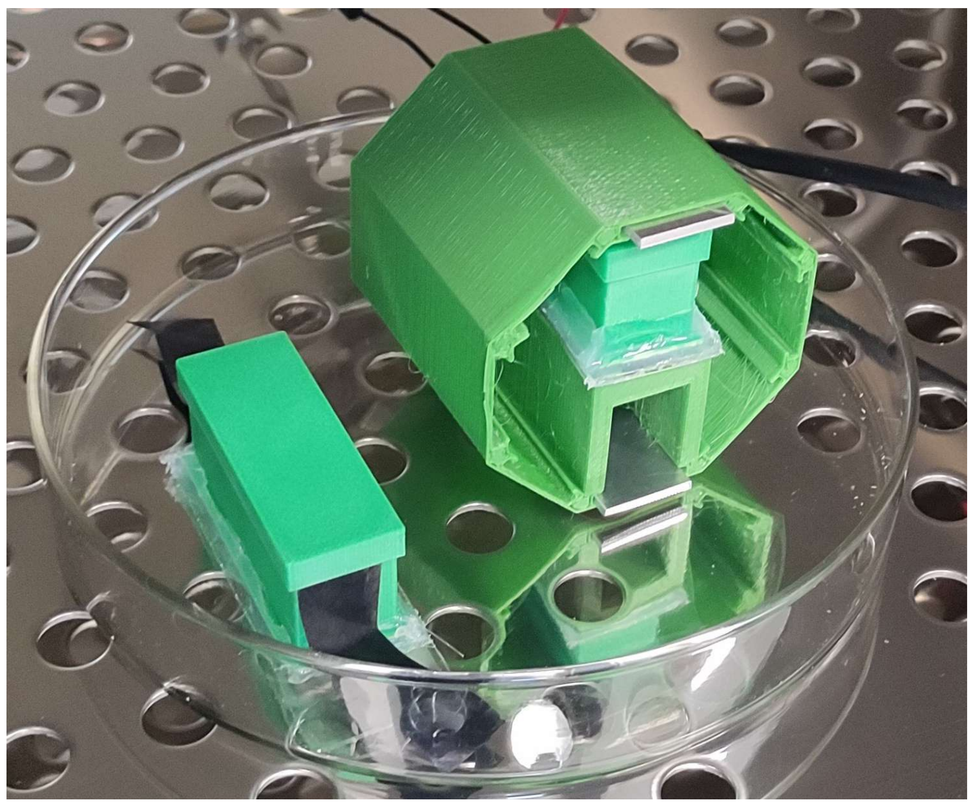
3D printed device



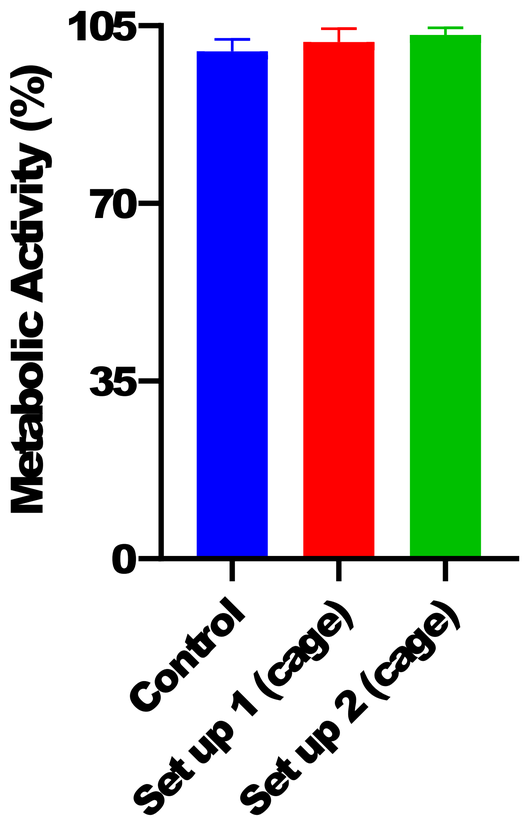




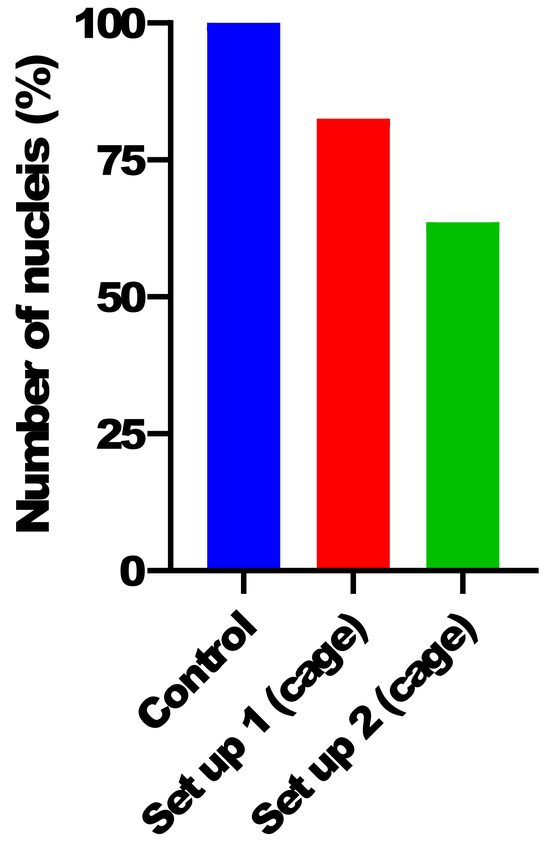


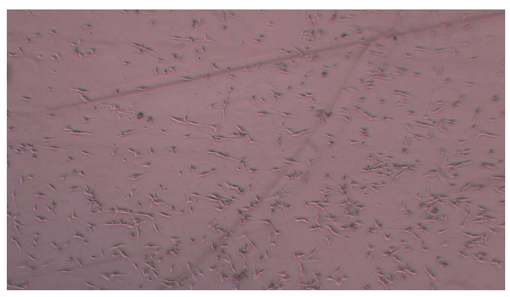


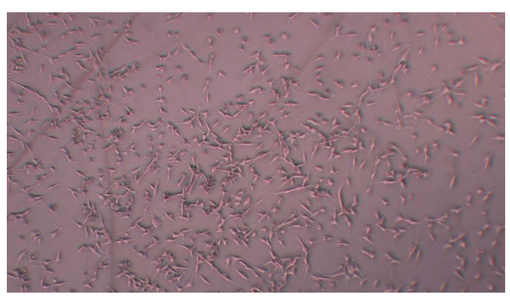
TTFields (abs); 1.5 V/cm 100 and 500 kHz



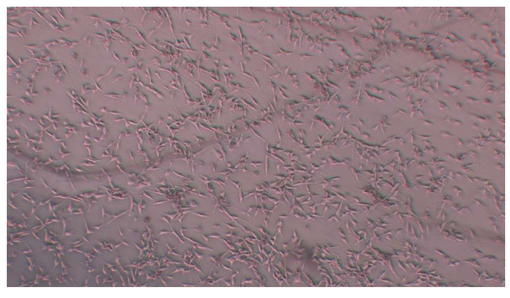
DAPI staining; 1.5 V/cm 100 and 500 kHz

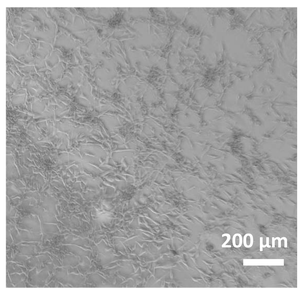


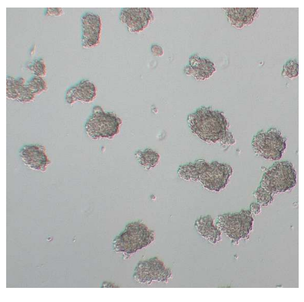


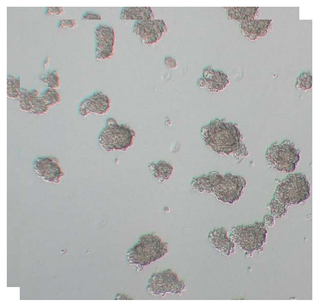


Day 1, 2, 3 and 6

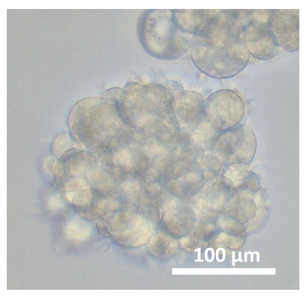








4x, vista general tras 72h despues de sembrar 10.000cells/cm2



20x, vista especifica tras 72h despues de sembrar 10.000cells/cm2

Gráficas en los formatos multiwell plate

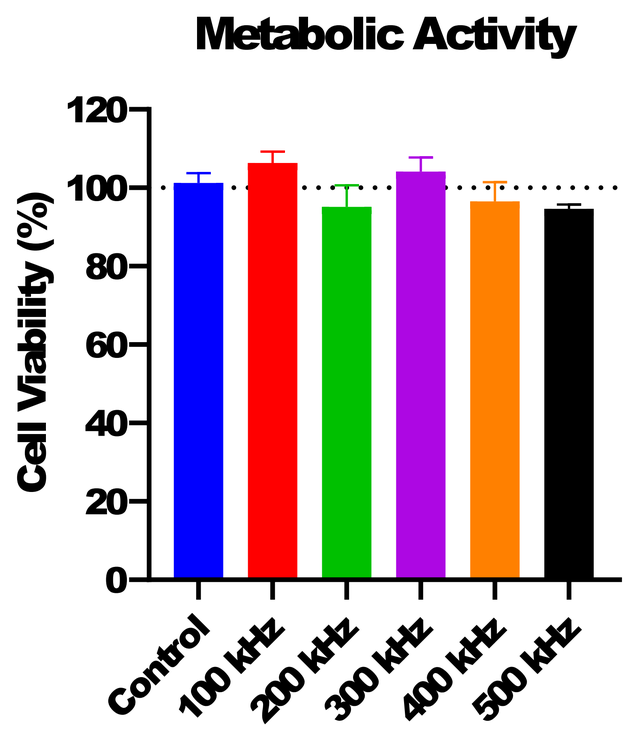
Metabolismo fallido (igual que antes)

Como afecta el multiwell

Como afecta la forma de la onda

Como afecta la dirección

Como afecta el voltaje



Metabolic activity is always comparable with controls. Resazurin neither MTT are not a good method to evaluate TTF´s effect.