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作品名稱　Using Focused Ultrasound and Pulsed Ultrasound as a Solution to Viral Infection

得獎獎項　三等獎

就讀學校　Peterhouse Girls
指導教師　Ngwenya Gugulethu Rose
作者姓名　Mufaro Nazare
Naledi Taundi

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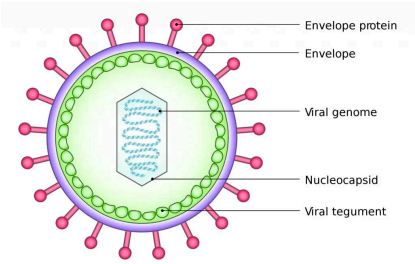
ZIMBABWE
NAZARE Mufaro and TAUNDI Naledi

Problem Statement And Aim:

Using focused ultrasound and pulsed ultrasound as a solution to viral infection

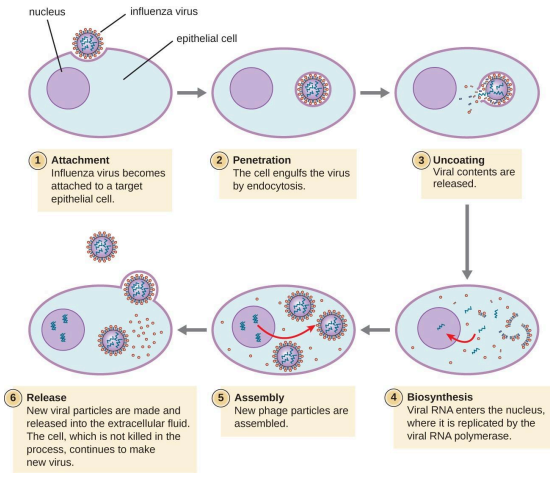
Using ultrasound in an attempt to reduce the effectiveness of a viral infection.

Background Research:



Viruses

Both enveloped and non-enveloped viruses conceal their membrane-penetrating peptide, usually within a glycoprotein of the virion membrane, inside the coat, or within the virion lumen. Cellular signals expose membrane-penetrating peptides that influence the virus during its entry. Instances of cellular signals regulating virus entry include receptors, enzymes, and substances like proteases, metal ions, and reducing agents. Recently, motor proteins or virus maturation have been seen to regulate virus entry through mechanical processes.



Viral Life Cycle

Image from https://biologynotesonline.com/viral-replication-cycle-definition-steps-mechanisms/

Attachment: The virus attaches to a target cell > Penetration: The virus enters the target cell > Uncoating: The viral coating is removed > Replication: The viral genome is replicated >Assembly: The viral genome is packaged into infectious progeny > Release: The progeny leave the cell

Antiviral resistance:

Potentially Affected Viruses

- Influenza, or the flu, Respiratory syncytial virus (RSV), Human metapneumovirus (hMPV), Parainfluenza, Herpes, Chickenpox, Mumps, Human papillomavirus (HPV)

Disadvantages of Antiviral Medication:

- Expensive
- Viruses don't have a lot of their proteins and enzymes to target.

- You can only use one type of antiviral to treat a virus and it is unlikely it will work for any other viruses.
- Takes too long to make them: It usually takes years to develop and approve new antiviral drugs because the discovery pipeline involves a painstaking process of identifying chemical compounds that target the virus and then testing their efficacy and safety.
- Viruses are quick to replicate and change
- The strong outer virus shell: The shell is extraordinarily robust, resisting the negative effects of the environment on the way to its host. Only then does it decompose or eject its content, which contains its genetic information.

HIFU Ultrasound

High-intensity focused ultrasound (HIFU) is a minimally invasive medical procedure that uses ultrasound waves to treat certain conditions, such as tumours, uterine fibroids and tremors. The very high-intensity and highly focused sound waves interact with targeted tissues in your body to modify or destroy them. 500 kHz to approximately 3 MHz The very high-intensity and highly focused sound waves interact with targeted tissues in your body to modify or destroy them. The ultrasound transducer used for HIFU is similar to those used for diagnostic imaging but it emits sound waves of much higher intensity. Much as a magnifying glass can focus sunbeams to burn a hole in a piece of paper, the HIFU transducer focuses sound waves onto a tiny area of abnormal tissue, generating enough heat to destroy the cells.

Thermal effects

- Energy in an ultrasound beam is attenuated and absorbed elsewhere in the tissue. This causes heat to be produced as there is molecular vibration in the tissue caused by the sound wave which results in heat generation causing a thermal effect in the tissue.
- So by furthering this, we can also propose that the ultrasound can be used to further denature the virus when found in tissue in the body. By using controlled HIFU (graph in the data section) and possibly LIPU

LIPUS (Low-Intensity Pulsed Ultrasound) vs HIFU

LIPUS frequency intensity at 0.03 W/cm^2, pulse ratio 1:4 at 1,000 Hz, and frequency at 1.5 MHzXin Z, Lin G, Lei H, Lue TF, Guo Y. Clinical applications of low-intensity pulsed ultrasound and its potential role in urology. Transl Androl Urol. 2016 Apr;5(2):255-66. doi: 10.21037/tau.2016.02.04. PMID: 27141455; PMCID: PMC4837316.

HIFU frequency 500 kHz to approximately 3 MHz Serup J, Bove T, Zawada T, Jessen A, Poli M. High-frequency (20 MHz) high-intensity focused ultrasound: New Treatment of actinic keratosis, basal cell carcinoma, and Kaposi sarcoma. An open-label exploratory study. Skin Res Technol. 2020 Nov;26(6):824-831. doi: 10.1111/srt.12883. Epub 2020 Jun 17. PMID: 32557832; PMCID: PMC7754281.

Table 1. Classifications and applications of ultrasound waves.

Ultrasound waves	Classifications	Applications
Ultrasound intensity	Low-intensity ultrasound (<3 W/cm^2)	Therapeutic medicine, imaging medicine, medical diagnosis, and drug delivery
	High-intensity ultrasound (≥3 W/cm^2)	Surgery, cancer ablation, and palliative treatment
Ultrasound frequency	Low frequency ultrasound (20–200 kHz)	Drug delivery, surgery, cancer ablation, and palliative treatment
	Medium frequency ultrasound (0.7–3.0 MHz)	Therapeutic medicine, such as bone-fracture healing, soft-tissue lesions healing, inhibiting inflammatory responses, and erectile dysfunction treatment
	High frequency ultrasound (1–20 MHz)	Imaging medicine and medical diagnosis

Lopez W, Nguyen N, Cao J, et al. Ultrasound Therapy, Chemotherapy and Their Combination for Prostate Cancer. Technology in Cancer Research & Treatment. 2021;20. doi:10.1177/15330338211011965

Research Question And Goal:

HIFU ultrasound could potentially be used to destabilise the outermost membrane of a virus to increase the effectiveness of the immune system in fighting viruses

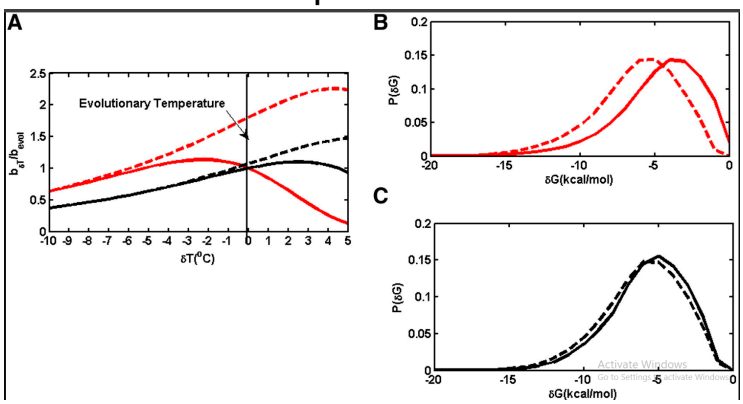
Method:

By using High-Intensity Focused Ultrasound (HIFU) and Low-Intensity Pulsed Ultrasound (LIPUS) to weaken the protein coat of the virus cells. This would make the digestion of the viruses by the immune system to be much easier.

- This would be obtained using the same mechanism as antiviral infection: a virus sample would be used to measure the resonance emitted by the virus's protein coat. The study would then be targeted towards the places where viruses tend to gather in immunopriveledged sites.

- Immunopriveledged sites; Brain, Spinal cord, pregnant uterus, testes, eyes.
- These are extremely sensitive sites so therefore the best place to do this would be the spinal cord in case of viruses affecting the body and in illnesses such as pneumonia which affects mainly the lungs this can be carried out in the chest cavity with LIPUS to avoid necrosis.
- By using the resonance frequency of the bonding in the capsid we can damage the membrane and therefore decrease the effectiveness of the virus within the cell.
- If we target the HIFU at this immunodeficient site at the frequency that damages the protein envelope the envelope decreases the efficiency of a virus to penetrate a cell and increases the ability of the immune system to attack and digest the virus.
- This can decrease the killing of the cells and infection.
- Glycoprotein is the protein layer around the cell. HIFU can be used to denature the protein envelope and the protein membrane and even puncture it allowing the immune system more time to deal with infection.
- This treatment would then be carried out by the spine. This would mean that when this mutated virus moves throughout the body then when specialised white blood cells (leukocytes) have an easier time digesting the virus before the multiplies (RNA) or takes the white blood cells' nucleus.
- When using LIPUS, a controlled temperature increase can be made. This would be done to induce a moderate fever temperature in the target area. Moderate fever is at 38.1 to 39 degrees Celsius.

Results/Stats/Graphs



Graph from https://www.cell.com/biophysj/fulltext/S0006-3495(09)06098-6

"Figure 1 Thermal response of fitness and protein stability distributions for a model bacterium species (*black lines*) and a model RNA virus species (*red lines* (*grey* in print)) (see text for details). Solid lines correspond to wild-type species equilibrated at an evolutionary temperature, of 37°C, and dashed lines correspond to strains evolved at 42°C. (*A*) Fitness response to temperature variation. (*B* and *C*) Protein stability distributions for the wild-type RNA virus (*B*) and bacterium (*C*) and the corresponding strains cultured at 42°C."

However, maintaining the temperature of the viral site is not conducive as shown in this paper that when viruses evolve at this temperature then they retain a level of resistance. So, ultrasound is to weaken and denature the virus using the resonance of HIFU and temperature in sites where.

Determine the frequency using Mass Spectrometry Moon JH, Oh JY, Kim MS. A systematic and efficient method to estimate the vibrational frequencies of linear peptide and protein ions with any amino acid sequence for the calculation of Rice-Ramsperger-Kassel-Marcus rate constant. J Am Soc Mass Spectrom. 2006 Dec;17(12):1749-57. doi: 10.1016/j.jasms.2006.08.001. Epub 2006 Sep 13. PMID: 16978873.

Limitations and Errors: This may not work with viruses that directly attack the immune system (autoimmune system)

- This may have an issue with the sensitive body parts that the viruses location parts. This also could be reflected (like ultrasound does).
- This has not been medically tested.
- The data given has been derived from studies done by other researchers. By using a program a program such as MATLAB a more accurate result can be deducted to show feasibility.

- If the HIFU is not calculated to frequency then the natural proteins in the body would denature and become useless and mutated.
- HIFU causes a thermal increase in the area which may damage some enzymes in the spinal fluid. Perhaps to combat this LIPUS was used instead.

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【評語】070010

The proposed use of High-Intensity Focused Ultrasound (HIFU) and Low-Intensity Pulsed Ultrasound (LIPUS) to weaken the viral protein coat and enhance immune clearance is innovative, offering the potential for antiviral therapy. The concept demonstrates a clear understanding of resonance frequency and targeted treatment in immune-privileged sites, emphasizing the importance of safety in sensitive areas such as the brain, spinal cord, and testes. However, the approach is purely hypothetical and lacks experimental validation, significantly undermining its credibility and practical relevance. Furthermore, presenting data published by others as results of this study raises concerns about academic integrity.

The methodology also lacks sufficient details, particularly regarding how resonance frequencies will be measured and how ultrasound parameters will be optimized to ensure both efficacy and safety. The absence of a structured scientific format further detracts from the study's professionalism and readability.

To strengthen the proposal, the study should include preliminary experiments, such as in vitro testing of viral particles exposed to HIFU or LIPUS, to evaluate the effects on capsid integrity and immune response enhancement. The methodology must be explicitly outlined, explaining how resonance frequencies will be determined and

ultrasound parameters calibrated. Adopting a structured format such as introduction, methods, results, and discussion will enhance clarity and academic rigor. A thorough risk assessment should address potential side effects and minimize off-target impacts.

While the idea holds promise, significant refinement, methodological clarity, and experimental evidence are critical to establish its credibility and feasibility for practical application.