ISSN- 2350-0530(O), ISSN- 2394-3629(P)
DOI: 10.5281/zenodo.3249099

INTERNATIONAL JOURNAL OF RESEARCH – GRANTHAALAYAH
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Science

THE TRANSDUCTION OF CELLULAR MEMBRANE PROTEINS AND STRUCTURAL CELL MEMBRANE ALTERATIONS INDUCED BY EXOGENOUS ENERGY WAVES ENERGIZING LIPID DROPLETS AS THE PROPOSED UNDERLYING MECHANISM IN VERY INTENSIVE PRESSURE PULSES TREATMENTS CLAIMS TO A CANCER CURE

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Abstract

The purpose of this manuscript is to propose a mechanism for a cancer cure claim resulting from exogenous stimulation of cancer tumors by very intense pressure pulses (VIPPs) treatments from commercially available energy hardware (CellSonic). Could it be that exogenous continuous pulsating waves alter the cellular lipid bilayer; and this in turn also influence intracellular cell signaling? *In Vitro* experiments are presented supporting the above-stated thesis. The evidence will show via *in vitro* experiments how trapping energy from bursting oxygen bubbles induces static electricity discharges up to causing luminescence of intracellular lipid droplets. Figures and video recordings documenting the above-mentioned phenomena are presented. In summary, proposed is a mechanism explaining a cancer cure claim via VIPPs.

[1] AAE: Idealized, designed wrote manuscript and conducted in vitro experiments possibly demonstrating a mechanism for VIPPs cancer cure.

[2] SH: Added theoretical principles in the discussion supporting the proposed VIPPs mechanism to cancer cure.

Keywords: ROS Breakdown; Protein Transduction; Very Intense Pressure Pulses; Cell Respiration; Cell Signaling; Lipid Bilayer Membrane; Cancer Cure Treatment; Lipid Metabolism; Phonon Energy.

Cite This Article: Abraham A. Embi BS, and Steve Haltiwanger Md Ccn. (2019). "THE TRANSDUCTION OF CELLULAR MEMBRANE PROTEINS AND STRUCTURAL CELL MEMBRANE ALTERATIONS INDUCED BY EXOGENOUS ENERGY WAVES ENERGIZING LIPID DROPLETS AS THE PROPOSED UNDERLYING MECHANISM IN VERY INTENSIVE PRESSURE PULSES TREATMENTS CLAIMS TO A CANCER CURE."

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International Journal of Research - Granthaalayah, 7(5), 299-310. https://doi.org/10.5281/zenodo.3249099.

1. Introduction

Transduction is a change. The lipid protein interaction has been observed in biological membranes as quoted "**Lipid molecules bound to membrane proteins are resolved in some high-resolution structures of membrane proteins. An analysis of these structures provides a framework within which to analyze the nature of lipid-protein interactions within membranes.** Membrane proteins are surrounded by a shell or annulus of lipid molecules, equivalent to the solvent layer surrounding a water-soluble protein. **The lipid bilayer extends right up to the membrane protein, with a uniform thickness around the protein (1).**

The surface of a lipid bilayer membrane protein contains many shallow grooves and protrusions to which the fatty acyl chains (enzymes) of the surrounding lipids conform to provide tight packing into the membrane. A change in lipid metabolism and structure should have an effect on the adjacent membrane proteins metabolism (transduction), thus interrupting cell signaling up to and including apoptosis. That is the core of the thesis herein introduced of the role of intracellular lipids in cancer. As a corollary the absence of protein transduction is the norm.

2. Brief History

2.1. Molecular vs Biophysical Research and Cancer

The Cancer Etiology Branch of the National Cancer Institute has hosted workshops in an effort to delineate novel criteria in cancer causations. As stated in the summary of one of those meetings "participants were among the international leaders in the fields of epidemiology, chemistry, biochemistry, microbiology, virology, environmental and chemical carcinogenesis, immunology, pathology, molecular pathology, genetics, oncology, and surgical oncology"(2). The absence of Biophysical scientists is noted. This perhaps, due to the existing paradigm or norm by the Cancer Institute, and for that matter of most reputable publishers in selecting papers to find a "Cancer Genesis" (Origin) which could eventually lead to a "Cancer Cure" (Disease Eradication). For readers across the world, it behooves to explain that "PubMed Central® (PMC) is a free full-text archive of biomedical and life sciences journal literature at the U.S. National Institutes of Health's National Library of Medicine (3). In this part of the world is the "gold standard" of scientific publications. On the subject of sources of radiation and cancer causes, an updated version published by The National Cancer Institute Position is:

"High-energy radiation, such as x-rays, gamma rays, alpha particles, beta particles, and neutrons, can damage DNA and cause cancer. These forms of radiation can be released in accidents at nuclear power plants and when atomic weapons are made, tested, or used. Certain medical procedures, such as chest x-rays, computed tomography (CT) scans, positron emission tomography (PET) scans, and radiation therapy can also cause cell damage that leads to cancer. However, the risks of cancer from these medical procedures are very small, and the benefit from having them is almost always greater than the risks".

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Since 2003 (16 years later) there is still no mention of endogenous biophysical (read electromagnetism or biomagnetism) cause in cancer genesis.

2.2. Biophysics and Molecular Biology

Biophysics is defined as "The science of the application of the laws of physics to biological phenomena"; on the other hand "Molecular Biology" is defined as "the branch of biology that deals with the structure and function of the macromolecules (e.g. proteins and nucleic acids) essential to life". As stated by a British Professor: "In research, everything is significant even when we don't appreciate its importance at the time" (4).There have been numerous published seminal basic science works that at the time arose the skepticism of colleagues, such as the discovery of piezoelectricity by Jacques and Pierre Curie (5). Not until many years later is that the recognition and utility of the piezoelectric effect was accepted. Similar reactions are still expressed 135 years later by the scientific community. Research progress could be compared to climbing a stepladder; no skipping of steps allowed. For example, the introduction of a microscopy_tabletop method published in 2016; allows for research laboratories to image energy from plants and animal tissue (6,7). This novel technique facilitated the demonstration of biophysical phenomena, which are relevant to the present discussion. Examples are: The discovery that human hair follicles and shaft biomagnetical fields could penetrate glass barriers (8); and also a jointly published paper where biomagnetism was found to be a factor in bioluminescence (9).

2.3. A Cancer Cure Claim

In response to a publication by professor Dr. A. Hague's claims to a "Cancer Cure" (10), a Letter to the Editor was drafted, submitted and published. The title of the letter was "Proposed mechanism in cancer cure claim: The Lipid connection" (11). In 1956 intrinsic endogenous signals in the eukaryotic cells were hypothesized to be a factor in cancer origin (12). Every option should be explored and experimentally validated when seeking the elusive "cancer cure claim". This is the case here!!

As aforementioned, there is agreement with Dr. Hartman's observation; and an endogenous (internal) electrical mechanism in cancer origin was hypothesized and published in 2016 (13).
At the core of the hypothesis is the fact that since our cells act as individuals, they possess a mechanism to neutralize toxic substances. This event (detoxification) has been defined to be "cell respiration", thus implying the more we breathe the greater the number of individual toxic molecules decomposition, thus the more biomagnetical signals and the greater cancer incidence.

2.4. Cellular Respiration and Cancer Genesis

Image reproduction by Frank Sanchez Embí
7th Grade Project Belén Jesuit Preparatory School, Miami, USA

ISSN- 2350-0530(O), ISSN- 2394-3629(P)
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The consequences of an increase prevalence of a repetitive electromagnetic phenomenon could lead to unforeseen consequences such as DNA damage, cancer origin or cancer cell apoptosis. The above could be conceptualized by quoting the Spanish author Miguel de Cervantes Saavedra in his narrative in El Ingenioso Hidalgo Don Quijote de la Mancha "*tantas veces irá el cantarillo á la fuente, que alguna se quiebre";* meaning: *"So many times the clay pot will go to the source, that some break"* (14).

3. *In Vitro* Experiments Supporting the Cancer Cure Claim

3.1. The Lipid Connection

A stated, "It is known that shock waves arise in the presence of H_2O_2 decomposition (cellular respiration). In a paper recently published, a glass slide structure dubbed a sandwich (SDW) was designed to trap the energy from H_2O_2 decomposition. The top slide of the SDW could be either a 0.017 or 1 mm thin cover slide; sound waves (phonons) are known to cause minute oscillations of a not stiffly mounted thinner glass slides. This oscillation means that a small portion of the energy of the original H_2O_2 energy wave will be dissipated into heat through loses in the material and its mounting (15). But the vibrating glass will also, in turn, act as a transducer and generate a secondary sound wave traveling through saliva harvested precipitated DNA and intracellular lipids (16) and (Figures 1,2,3,4). The vibration of the secondary wave was documented to induce electrical discharges seen in evaporated saliva crystals (Fig. 6). Over time, the **repetitive** vibration energy from the trapped H_2O_2 decomposition was also documented triggering recurrent changes up to light emission of intracellular lipid droplets present in the samples. This is demonstrated in Figure 5 + video recording.

A careful examination of Figure 5 shows the diminishing recharging capacity of lipid droplets due to exposure to repetitive VIPPs.

3.2. Definition of Terms

Biophysics: The application of the laws of physics.
Cellular Membrane Lipid Bilayer: The **lipid bilayer** (or **phospholipid bilayer**) is a thin polar membrane made of two layers of **lipid** molecules. These membranes are flat sheets that form a continuous barrier around all cells.
Electroporation: Inducing of cell membrane perforation causing apoptosis.
Fatty Acyl Chains: Modulates the physical state of membrane lipids.
Piezoelectric Effect: Is the ability of certain materials to generate an electric charge in response to applied mechanical stress. The word **Piezoelectric** is derived from the Greek piezein, which means to squeeze or press, and **piezo**, which is Greek for "push".
Phonon: In condensed-matter physics, a unit of vibrational energy that arises from oscillating atoms within a crystal. ... A packet of these waves can travel throughout the crystal with a definite energy and momentum, so in quantum mechanical terms the waves can be treated as a **particle**, called a **phonon.**
Transduction: Transduction can refer to: Signal **transduction**, any process by which a biological cell converts one kind of signal or stimulus into another.
Exogenous
VIPPs: Very Intense Pressure Pulses

ISSN- 2350-0530(O), ISSN- 2394-3629(P)
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3.3. Figures

The purpose of this image is to show the path of the energy exiting the water surface. Video frame showing energy waves generated by underwater shockwaves seen moving under and above water level as shown in Figure 1.

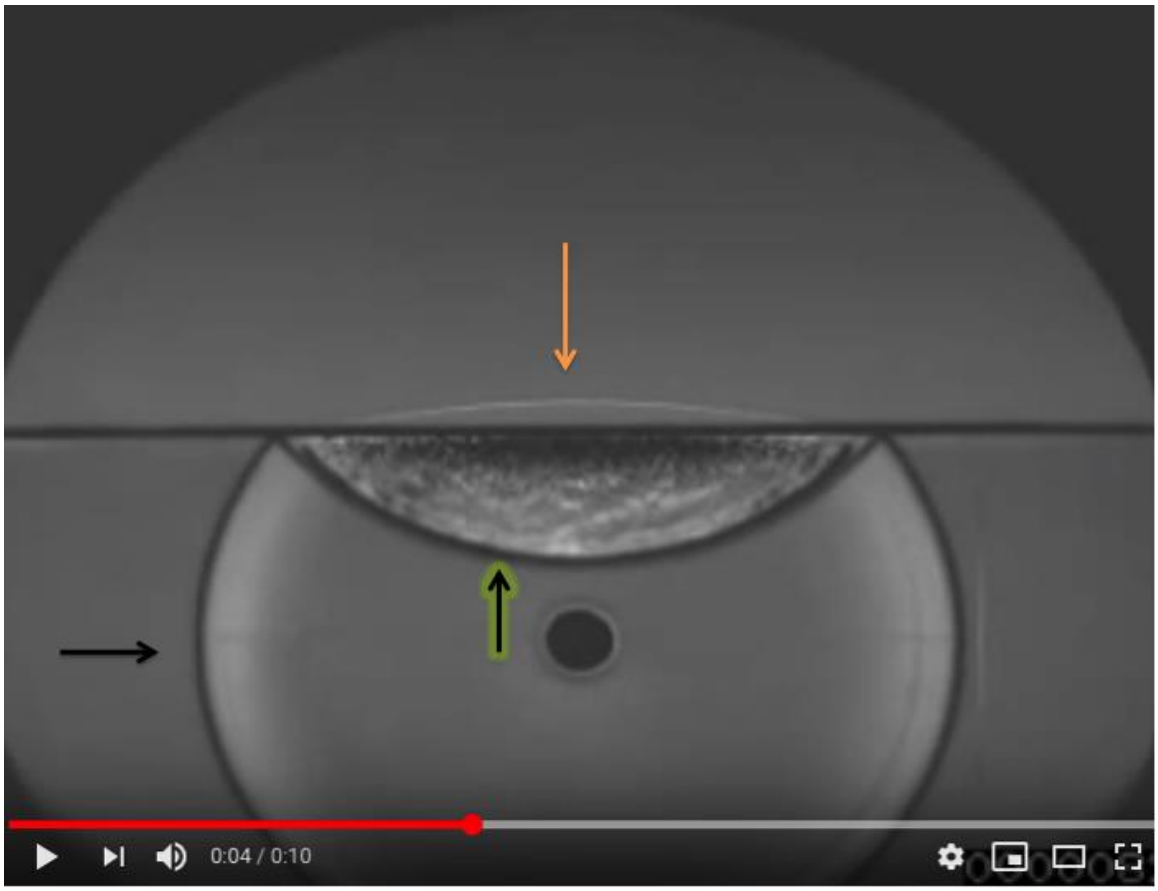

Figure 1: Underwater explosion showing: Black Arrow: Primary under water wave. Highlighted Black Arrow= Rebounding energy. Orange Arrow (top) Secondary wave dissipated above water.

Trapped H_2O_2 Decomposition Shockwaves

The trapped energy from the H_2O_2 decomposition simulates **repetitive** underwater explosions as seen in Figure 1 (above).

The slide below and video recording demonstrate the energy waves transmitted through glass by the trapped H_2O_2 decomposition. The gentle wave causing the cheek cell to flip.

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DOI: 10.5281/zenodo.3249099

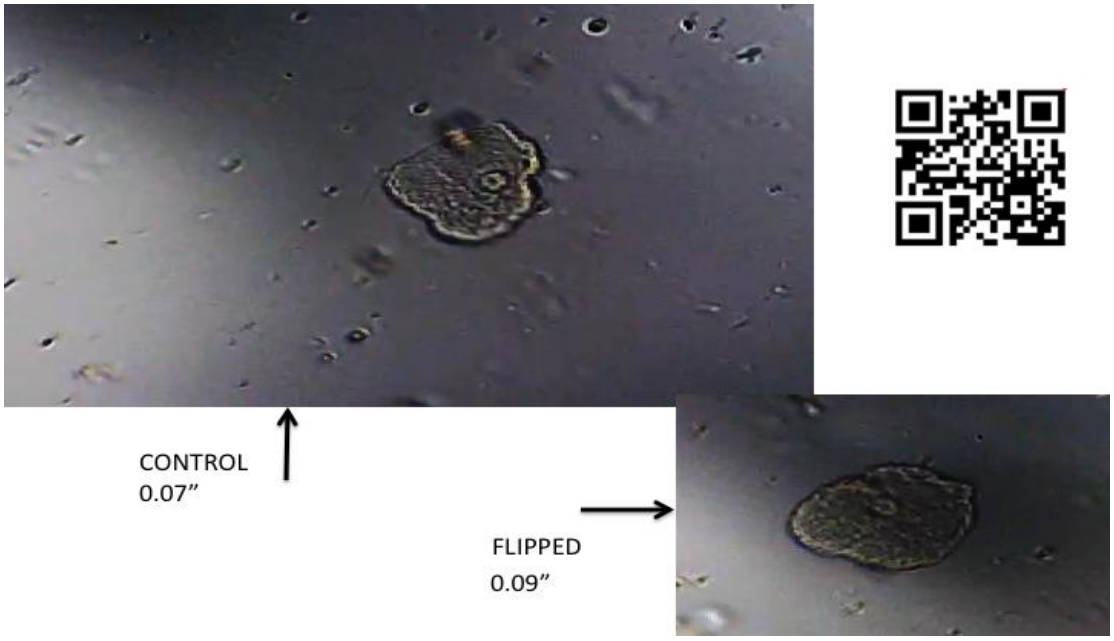

Figure 2: Video recording demonstrating H_2O_2 decomposition energy (seen as light change in background) through 1 mm glass barrier flipping cheek cell floating in liquid saliva also trapped in a SDW.

Please link to:
https://youtu.be/CgKgS4qaBAY or Scan QR Code (upper right corner of image).

Additional example of trapped energy from H_2O_2 decomposition penetrating a 1 mm in thickness glass slide This time breaking Potassium Ferrocyanide crystals.

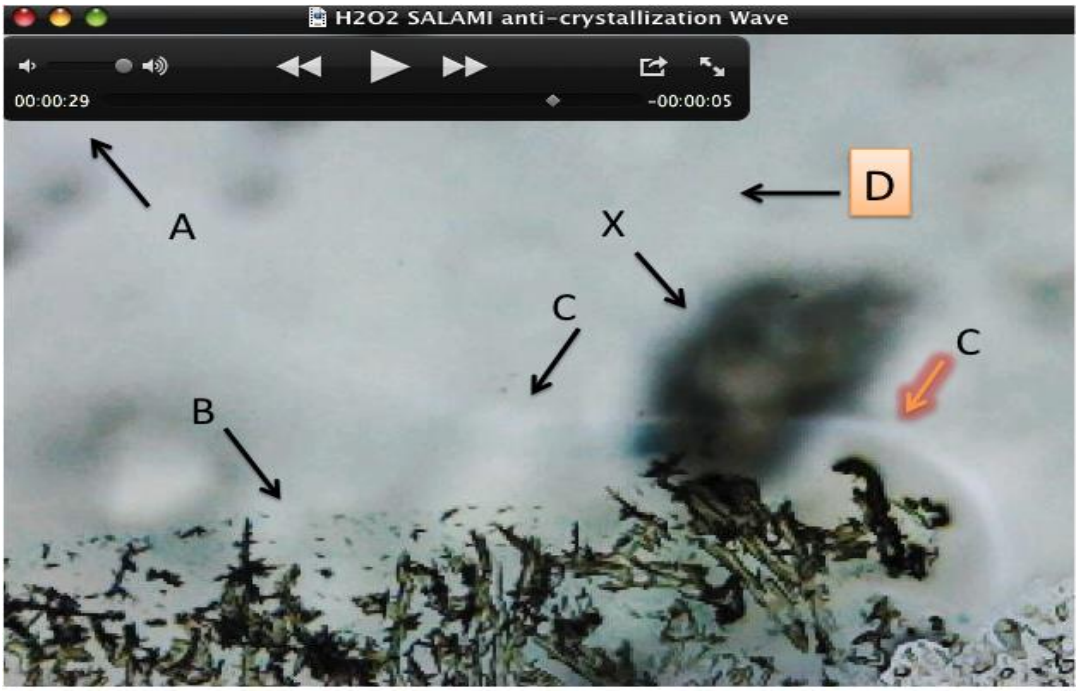

Figure 3: Showing advancing fluid wave from the trapped H2O2 breakdown energy breaking crystallized Potassium Ferrocyanide.

ISSN- 2350-0530(O), ISSN- 2394-3629(P)
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A= Recording time (29 seconds) B= Crystals disintegrating in evaporation line C= Highlighted orange arrow denotes advancing fluid wave from decomposition. D= Displaced fluid flow direction.
Image and video recoding duplicated from:
Abraham A. Embi. Cellular Respiration Oxidation Reduction Reactions Electromagnetic Fields Emissions as Possible Causative Agent in Diseases: A Chronic Bombardment Theory. Physics Journal, Vol. 2, No. 3, 2016, pp. 226-230
For additional details ling to: https://youtu.be/HMlBZdXbdqs

Or Scan QR Code below:

Demonstration of effect of energy waves inducing lipid droplet luminescence.

The relevance of Figure 4 + video (below) is the observation that when continuous energy is applied to the lipid droplets light emission is seen occurring during the video recording. Implied is that energy from H_2O_2 decomposition caused a change in lipid metabolism, this in turn could affect the structure of the cellular membrane lipid bilayer. Change in cellular membrane lipid metabolism causes transduction of proteins embedded in the membrane. Transduction then could cause a change in molecular signaling from the affected proteins, prior research supports this concept (17).

This figure shows the effect of energy waves transmitted through a glass barrier. The forces are from the decomposition of trapped H_2O_2 molecules.

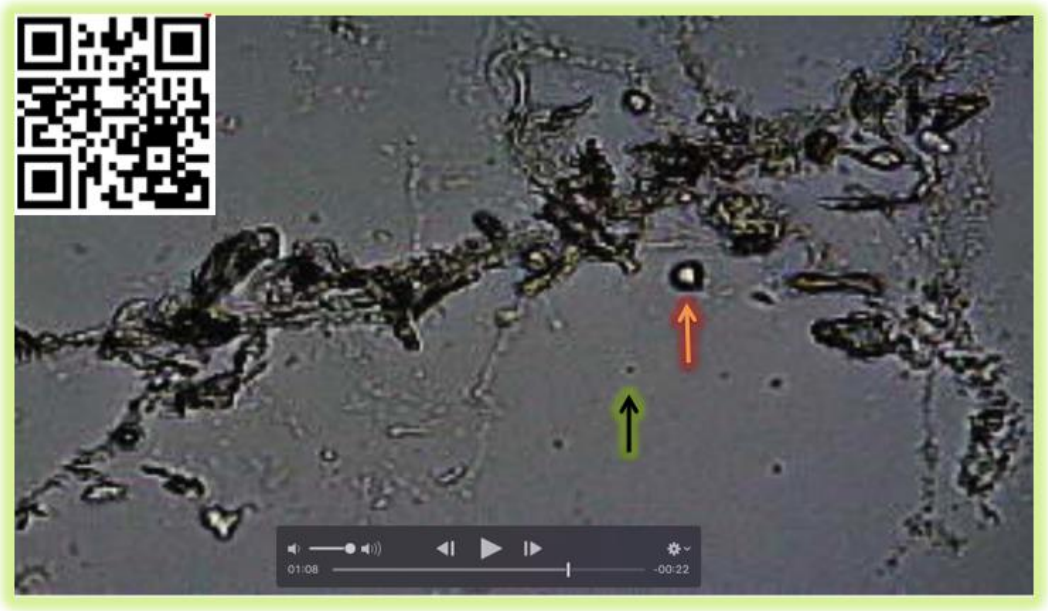

Figure 4: DNA precipitate (dark strands) and Orange arrow= Lipid droplet shockwave. Notice overall brightness including the lipid droplets. The shockwave effect documented by noticeable seesaw motion of small particle.

ISSN- 2350-0530(O), ISSN- 2394-3629(P)
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For additional details please link to: https://youtu.be/AiqextbQXME Or scan QR Code in upper left side of image. Suggested to use a smart phone.

Unpublished Image demonstrating repetitive shock waves decreasing the charging capacity of lipid droplets. Black arrows pointing at diminishing charging capacity. In panel D the lipid droplet failed to start a charging cycle.

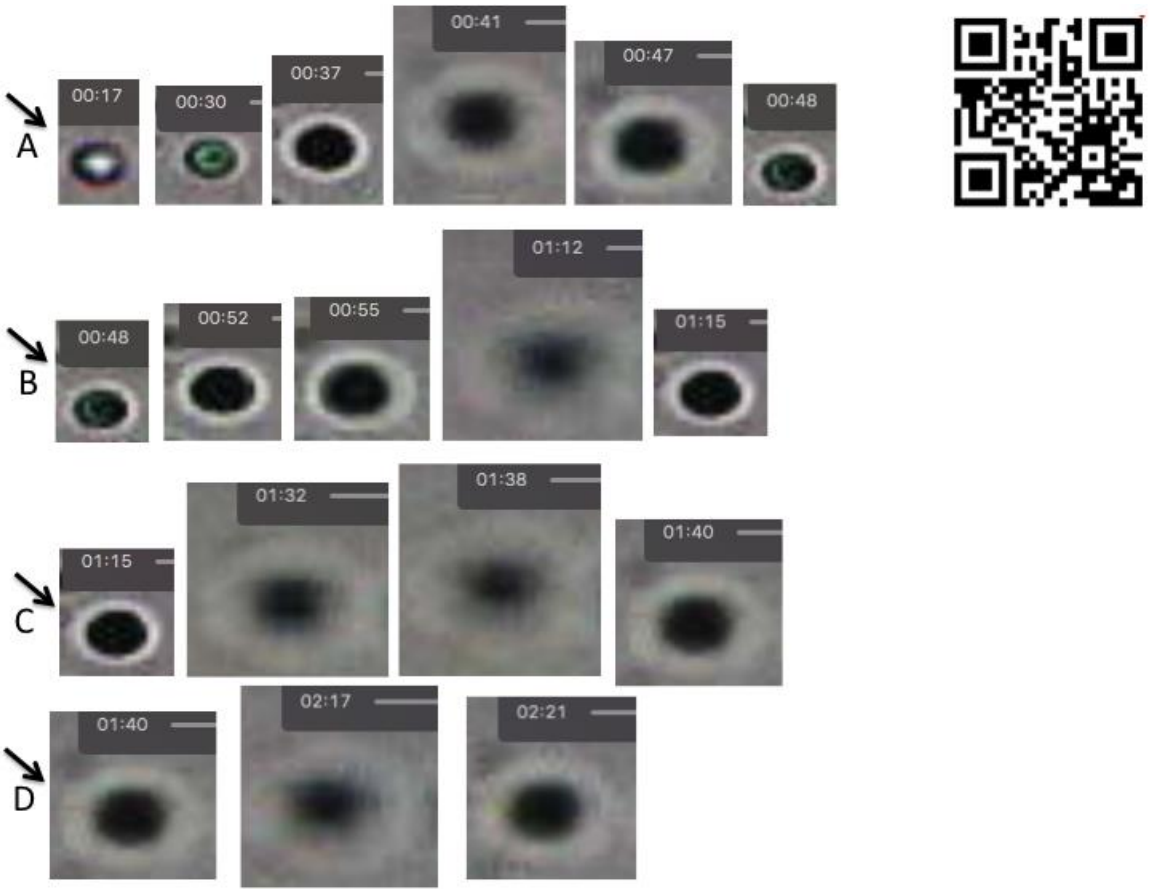

Figure 5: Unpublished image: Demonstration of irreversible damage to the lipid membrane by recurrent (Phonons) shockwaves transduction. Panels A, B, C, D black arrow indicating beginning of lipid droplet membrane changes. Black Arrows= Compare baseline images changes with each cycle, suggesting possible residual (cumulative) damage to the lipid droplet membrane from continuous shockwaves.
For additional details, please link to: https://youtu.be/hUFDnZXoCGc or scan QR Code in upper right of image

ISSN- 2350-0530(O), ISSN- 2394-3629(P)
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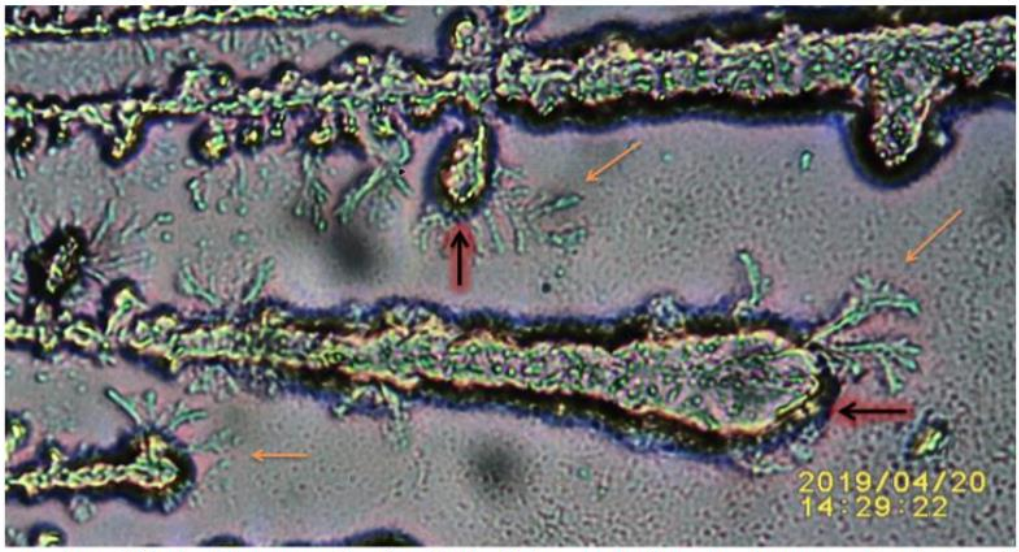

Figure 5: Amplified saliva crystals after O_2 bubbles cavitation shockwaves stimulation. Orange Arrows= Pointing at electrical discharges. Black Arrows= Pointing at distal ends of crystallized saliva.

Figure 6: Demonstration of energy from bursting oxygen bubbles causing saliva crystals (proteins) to express electrical discharges. Image duplicated from: Abraham A. Embi Bs. (2019). "INTRODUCING IN VITRO EXPERIMENTS OF OXYGEN BUBBLES SHOCKWAVES TRIGGERING INTRACELLULAR LIPIDS LUMINESCENCE: IMPLICATIONS IN CANCER ETIOLOGY." *IIGR* 7(4), 355-364. https://doi.org/10.5281/zenodo.2667714.

4. Discussion

The very first question in this manuscript stated: Could it be that exogenous continuous pulsating waves alter lipid molecules metabolism and structure present in lipid bilayer cell membranes? The *in vitro* experiments shown above are in support of an electrical phenomenon altering lipid molecules metabolism, thus in theory causing cancer cells apoptosis.

5. Additional Theoretical Comments in Support

Another aspect of the mechanism of action may involve the combination of the sudden shock wave along with an electromagnetic effect. A combined sonic and electromagnetic effect could produce irreversible electroporation. Irreversible electroporation is a non-thermal ablative modality that has been in clinical use since 2008 in the treatment of locally advanced soft tissue tumors. It has been reported to be utilized intraoperatively, laparoscopically or percutaneously. Irreversible electroporation in the clinical setting has recently been established to induce permanent cell death through cell membrane perforation which induces electrolyte instability and causes protracted cell death by apoptosis (18). In clinical practice, short electrical pulses are sent between needles placed around the tumor. This causes cell death without generating heat.

ISSN- 2350-0530(O), ISSN- 2394-3629(P)
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6. Proposed Mechanism for Very Intensive Pressure Pulses

VIPPs and Cancer Cells Apoptosis

The CellSonic head produces both a very large pressure wave as well as a significant electromagnetic field (EMF). The shock wave or the combination of the shock wave with the electromagnetic properties of the probe could create a dynamic phase transition. This could be producing a type combination effect with the ultrasound-producing multi-bubble sonoluminescence. The bubbles could be produced by the process of cavitation. The breaking bubbles mimicking the energy emitted during H_2O_2 decomposition. When examining sonoluminescence we find that the bubbles have a thermal aspect with temperatures measured over 10,000 degrees.

We do know from studies of the use of ultrasound in fat lipolysis that it has been shown that adipose cell cavitation can induce focal alterations of the cell membrane and ion and lipid leakage. So, it is reasonable to hypothesize that cancer cells may be uniquely sensitive to thermal, electrical and or mechanical disruptions. The piezoelectric currents could possibly produce electro conformational coupling in the surrounding proteins/enzymes thus changing their physical properties.

This presupposes that cancer cells have different membrane structures than healthy organ cells and or inability to survive electrical shocks. The ability to handle sudden changes in electrical currents must be a property retained in normal cells but lost in cancer cells or at least certain types of cancer cells.

The bioelectric currents present in all living organisms are involved in cellular metabolism. However, cancer cells are isolated from the normal flows of bio currents in tissues. This may have significance in allowing cancer to proceed with different cellular metabolism than the surrounding tissues.

In addition, alterations in surface charges on cancer cells may occur after CellSonic treatment. It may be that there is an extensive change in surface charges and current density that occurs through the cell membrane when CellSonic treatment is delivered. A big question is why normal cells are not destroyed by CellSonic while cancer cells are killed. The inability of cancer cells to handle the biophysical properties of changes in cell surface charges, resting membrane potential, alterations of voltage-dependent gating of ion channels, membrane disruption and increased inward electric current density is part of the answer. It could be thought of as cellular electrocution.

Electric currents are produced by ion flow of sodium, potassium and calcium ion channels. So, further investigation of how ion channels are different in cancer cells is warranted. It is now recognized that the most energy-dependent processes inside of cells are stimulated by increasing the inward flow of calcium. It may be part of the mechanism in cancer death in that CellSonic therapy might be producing significantly increases intracellular calcium flow and produces energy failure in cancer cells. This is another potential mechanism that requires additional research.

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As an additional note, a very recent press release from the Mayo Clinic in Science Daily (19), researchers have confirmed that in tumor cells the intracellular protein PD-L1 function is to "make the cells resistance to change". The Cell Sonic therapy could block the PD-L1 function, thus making cancer cells vulnerable to the very intense pressure pulses (VIPPs); while concomitantly a dual effect of VIPPs is to induce luminescence (as documented) in lipids (read metabolism) intertwined with proteins in the bilayer cellular membrane.

7. Summary and Conclusions

A claim to a "cancer cure" by repetitive treatments of cancerous tumors via a very intensive pressure pulses (VIPP) method has been previously published. Claims of a cure rate with this technology are an eye opener; and there are many types of cancers, which contribute to the challenge in finding a common mechanism for a universal cure for this disease. For example, how do you apply VIPP treatment to cancers cells present in blood and other fluids?
The thesis hereby stated is limited (applies) to localized solid tumors that are anatomical accessible to VIPPs.

Cancer Cure Claim and "The Cellular Membrane Lipid Connection"

At the core of a proposed mechanism is a deviation from the pure molecular signaling paradigm to a combined biophysical-molecular one. In other words, by exposing proteins present in the cellular lipid bilayer membrane to **repetitive energy waves** (biophysics) lipid metabolism could be altered (molecular)

As previously stated, the big question is why normal cells are not destroyed by CellSonic VIPPs while cancer cells are killed. The inability of cancer cells to handle the biophysical properties of changes in cell surface charges, resting membrane potential, alterations of voltage-dependent gating of ion channels, membrane disruption and increased inward electric current density is part of the answer. It could be thought of as cellular electrocution. Additionally, a change in cellular membranes PD-L1 proteins functions also contribute to making the cancerous cells vulnerable to exogenous stimuli. Overall, VIPPs treatments for destroying existing cancerous tumors deserve unbiased independent institutional research.

Conflict of Interests

* Main Author: None to declare.
** Co-Author: None to declare. Declares familiarity with Cell Sonics VIPPs Equipment.

Funding Sources

None- Self funded.

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ISSN- 2350-0530(O), ISSN- 2394-3629(P)
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