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Water's Many Roles in Laser Photobiomodulation

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Abstract The roles of water and carbon dioxide in laser/light interactions in higher-order biological systems and their implications in cellular microenvironments and complex systemic processes for the restoration of homeostasis-homeokinesis, even when metabolic pathways have been compromised, are discussed. This lecture summarizes three decades of pre-clinical and clinical investigations and the basis for a potentially new therapeutic approach for the treatment of advanced cancer and other complex diseases using laser photobiomodulation. We propose that light-water interactions offer a potent, alternate and complementary pathway to activate and modulate tumor suppression and/or proto-oncogenic expression through energy transfer via water and CO_2 in multi-fractal regimes, leading to the coupling of spatiotemporal oscillators. Laser photobiomodulation may, thus, offer the possibility of targeting multiple hallmarks of cancer and other complex diseases using fit-for-purpose electromagnetic (light) energy to restore physiologically reparative and regenerative mechanisms that can help reestablish homeostasis-homeokinesis, constituting a new emerging paradigm in the treatment of cancer and other complex diseases.

Keywords: *photobiomodulation, water, exclusion zone (EZ), biobattery, cancer, complex diseases*

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1. Introduction

Cancer and other complex diseases, including age-related macular degeneration (AMD), diabetes, and Alzheimer's disease, stand amongst the greatest human and scientific challenges of our time. While the mortality of many cancers has been falling, many carcinomas and most sarcomas remain largely incurable [1,2,3,4,5]. This scenario is made worse by an increasing and aging global population. According to the World Health Organization (WHO), global cancer deaths will rise from 7.9 million in 2007 to 11.5 million by 2030 [5].

Here, we summarize three decades of investigations and the basis for a potentially new therapeutic approach for the treatment of advanced cancer and other complex diseases.

In cooperation with national and international research centers, our group completed pre-clinical and clinical research using a first, proof of concept, infrared pulsed laser device (IPLD) we developed and patented [6].

A phase I clinical trial in patients with late-stage solid tumors (TNM IV/UICC) found the IPLD to be clinically safe and to improve performance status and quality of life with more than 10 years of follow up [7]. Antitumor activity was over 88% [7]. Data showed activation and modulation of the immune system [8], selective activation of programmed cellular death (namely, apoptosis, necrosis, and anoikis) [9,10], and increased water content preceding tumor-volume reduction and therapeutic anticancer effects [11,12].

These results precede and are remarkably consistent with multiple independent studies in photobiomodulation [13-18] and with concurrent emerging developments in cancer research [1,2,4,19-24].

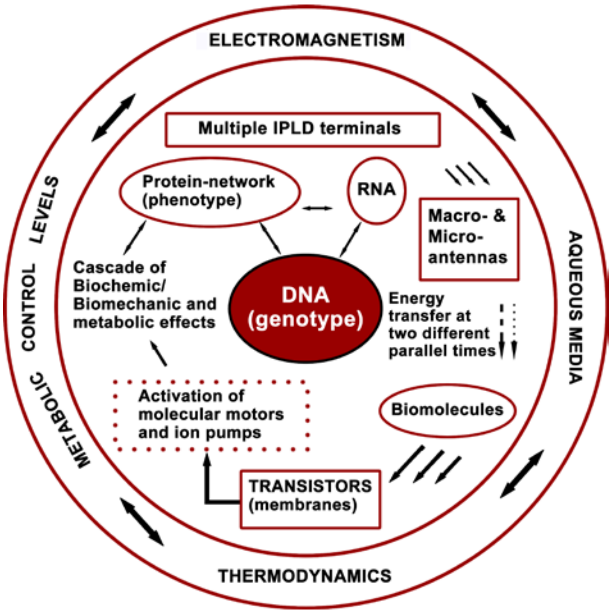

Figure 1. Photo-infrared pulsed photobiomodulation mechanism. ©Mary Ann Liebert, Inc. Publishers, 2005. (Ref. [25])

To explain these findings, we have documented their structural, kinetic, and thermodynamic implications and detailed mechanisms (Figure 1, Figure 2, Figure 3).

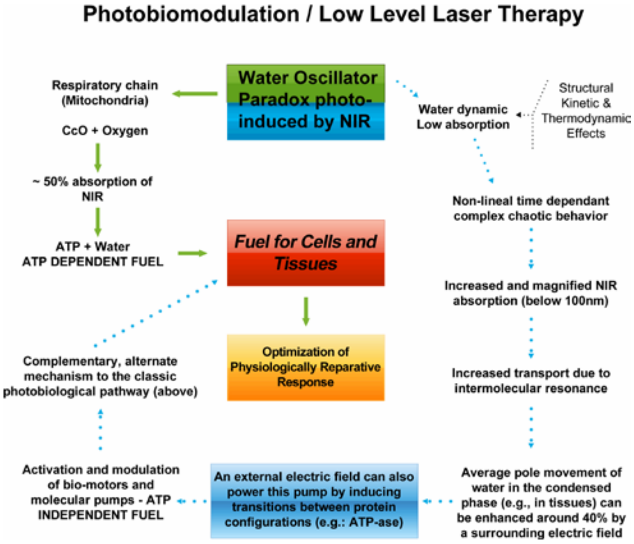

Figure 2. Water oscillator paradox mechanism. ©Mary Ann Liebert, Inc. Publishers, 2010. (Ref. [26])

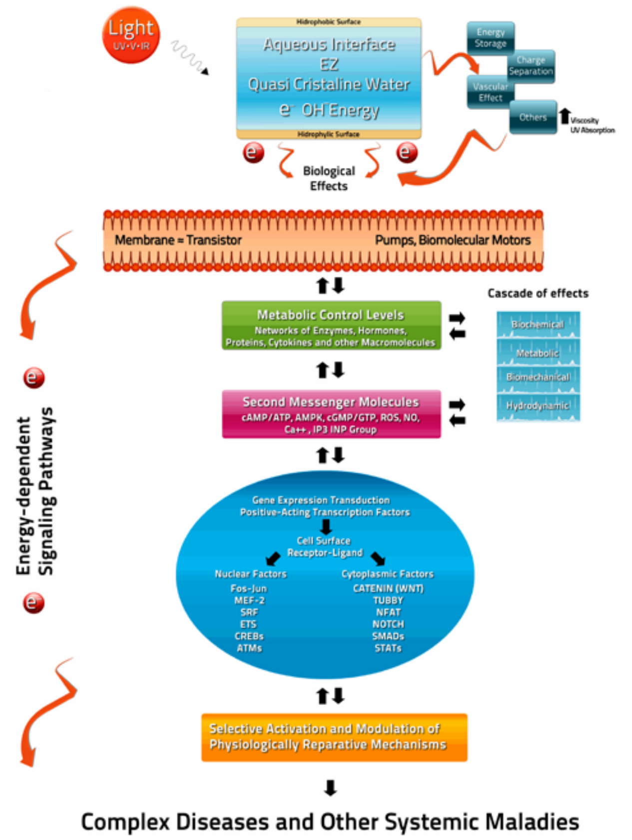

Figure 3. Use of exclusion zone (EZ) water as a selective, rechargeable, electrolytic biobattery. ©Mary Ann Liebert, Inc. Publishers, 2012. (Ref. [27])

Together, these mechanisms substantiate one basic premise: that external electromagnetic energy supplementation can enhance and even substitute for endogenous ATP to power and modulate physiologically reparative and regenerative mechanisms that can help reestablish homeostasis-homeokinesis, even when metabolic pathways have been compromised [10,25,26,27,28,30,31]

2. Basis for Selective, Non-invasive, Long-range, External Energy Supplementation and Absorption

Selective, non-invasive, long-range, external energy supplementation is based on the idea that physiologic processes (fluctuations and/or oscillations) can be activated and synchronized through the body's preeminent medium, water, CO_2 and membrane receptors. While a full elucidation of these ideas can be found elsewhere [29], it is worth reviewing some of its bases [25,32,33].

According to the Stark–Einstein law, only absorbed light can trigger photochemical change [32]. At less than 1100 nm, the absorption coefficient (AC) of water is low [34]. In materials with a low AC, light propagates with little attenuation. Hence, pulses as short as 60 fsec with a center wavelength of 800 nm can propagate through as much as 6 m of water [26,32,35,36]. Despite its low AC in the 600-1100 nm range, water is a major biologic photoacceptor for several reasons.

First, the adult human body is approximately 70% water by weight. In pure numbers, given its small molecular weight, 99% of our molecules are water. Hence, water is a major absorption target even for wavelengths with low AC's [26,32]. Second, high-AC values can establish harmonic or anharmonic resonance with water at lower or higher intervals (Figure 4).

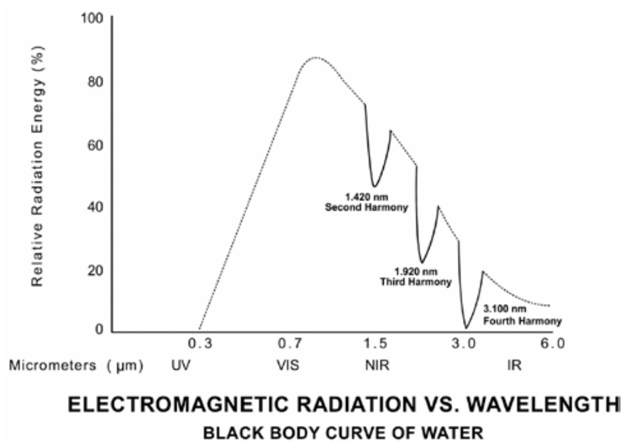

Figure 4. Black body curve of water ©Mary Ann Liebert, Inc. Publishers, 2005 (Ref. [26])

For instance, light's bandwidth to water's absorption bandwidth is similar at 800nm (0.36) and 1450nm (0.34), where there is strong resonance in water [35,36]. These values match a peak in biologic action spectra at 800 nm, where absorption by other chromophores, such as CcO, is relatively low [35,36]. In the 900-940 nm range, higher AC's coincides with another peak in action spectra [35,36] and with the black-body radiation of the human body. As wavelengths increase, AC is greater, but photon energy/penetration and ligand activity may decrease [26,32,34].

Third, photo-induced vibrations in water can be seen as Hamiltonian dynamic systems [37]. Hamiltonian dynamics normally conserve energy, though they can also exist in dissipative systems. When their degrees of freedom exceed 1, Hamiltonian dynamics are very complex [37]. Water and CO_2 molecules have 3 degrees of freedom in terms of movement, plus ½ degree attributable to time-dependence. Hence, water vibrations display extremely complex, nonlinear, time-dependent chaotic behavior [38,39].

Chaos is essential for everything from the stability of the solar system to cell homeostasis [26]. In chaotic systems, the interaction among nonlinear molecules with different degrees of freedom is strongly enhanced despite the smallness of coupling constants [26,37]. In addition, multi-fractal systems such as the human body can be in resonance while energy is transferred among different modes or trajectories [26,37], magnifying energy absorption and transport through extended biologic surfaces.

Resonant intermolecular energy transfer in aqueous solutions is faster than vibrational energy relaxation [40] and exhibits non-adiabatic relaxation. Such fast energy transfer is possible because protons act as moving targets, rapidly switching from one species to the next based on the number of water molecules with which they are associated [40].

Energy is selectively absorbed by target tissues in accord with the second law of thermodynamics and its extension for non-equilibrium thermodynamics: Onsager's theory of reciprocal relations as it applies to the thermodynamics of irreversible processes [42,43]. This occurs because redox potential differences between degrading and well-oxygenated tissues translate into injury potentials of up to 1.5 V in advanced cancer [44] (Figure 5).

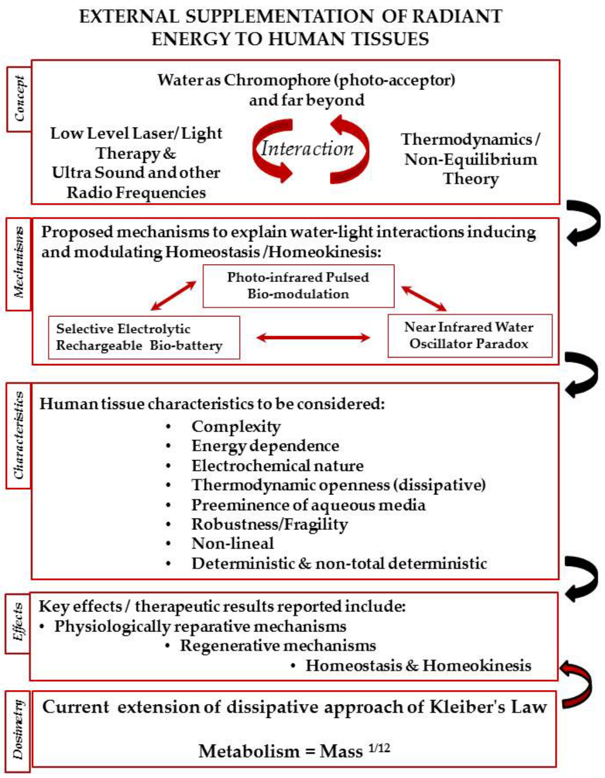

Figure 5. Diagram of proposed mechanisms. © Pan Stanford Publishing Pte (Ref. [32])

3. Downstream Effects

Our studies show that water provides potent pathways for light energy absorption, transport as well as charge storage, separation and subsequent release that can substitute and/or complement metabolic energy pathways through oxygen-dependent and independent effects with critical signaling pathways in primarily aqueous media [32,33,45]. In particular, the enhanced structuring of water favors the physiologic activity of energy-dependent network proteins and signaling nodes such as P53, PTEN, m-TOR, MYC, RB, NF-κB, and VHL, to mention a few of the transcription factors and genes which are often deregulated in cancer and other complex diseases [7,25,27,46-53].

Light can activate and regulate/modulate metabolic control levels [25,26,27] via two synergic pathways: 1- via molecular hydrophobic forces, including the folding and unfolding of proteins and the self-assembly of DNA/RNA [54,55]; and 2- via hydrophilic interfaces such as the exclusion zone (EZ) with its amazing potential for charge separation and storage, which can fuel the flow of protons [51] for cell signaling and the transfer of OH electrons as an energy reservoir for cellular work [27,33,34,35,36,56].

This is possible because the human body is a complex, dynamic (non-lineal), electrochemical system that is energy-dependent, thermodynamically open, primarily aqueous, deterministic and non-fully deterministic [10]. As such, the body displays a marked contrast between robustness, fragility and adaptability [10]. In it, 30% to 50% of proteins, RNA and DNA synthesized [26,57,58] are destroyed and re-synthesized. Remarkably, research suggests that oxidative proteome damage may be the most likely cause of aging and age-related diseases such as cancer and other complex diseases [58,59].

Such energy-intensive process, which requires no choreography [60,61] and involves millions of oscillations at all spatiotemporal scales, allows for adaptability that is as the heart of evolution. In contrast, cancer, and other complex diseases are marked by involution, or loss of differentiation and function, along with deregulation of apoptosis and other forms of programmed cellular death [45].

It has been argued that the study of self-organizing networks with system wide dynamics, such as metabolic and signaling pathways, may provide insights into the pathogenesis and treatment of complex diseases [24] (Figure 6).

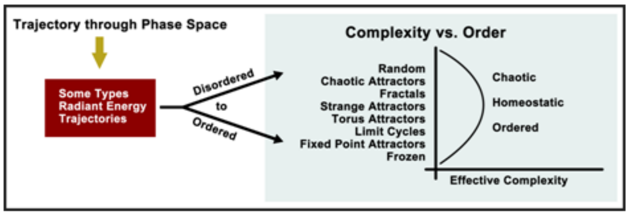

Figure 6. Complexity vs. Order (modified image from figure in http://www.necsi.edu/projects/mclemens/state_sp.gif.)

In addition, fresh publications report that: "pre-clinical and clinical research has provided evidence that cancer progression is driven not only by a tumor's underlying genetic alterations and paracrine interactions within the tumor microenvironment, but also by complex systemic processes" [24].

4. Conclusions

We propose that light-water interactions offer a potent, alternate and complementary pathway to activate and modulate tumor suppression and/or proto-oncogenic expression through energy transfer via water and CO_2 in multi-fractal regimes, leading to the coupling of spatio-temporal oscillators [10,19,45,62].

Laser photobiomodulation may, thus, offer the possibility of targeting multiple hallmarks of cancer

[62,63] (Figure 7) using fit-for-purpose electromagnetic (light) energy to restore physiologically reparative and regenerative mechanisms, that can help reestablish homeostasis-homeokinesis, [10,19,30,31,45,62]. While not a panacea, this approach offers unique potential. Challenges include developing and testing a new advanced treatment system and documenting its underlying mechanisms. Because light-based systems can be less expensive than many cancer drugs, we hope that this approach may lower treatment costs while raising anti-cancer effects, standard of care and quality of life/functional status, particularly, for the most vulnerable, such as the elderly, the poor and those suffering from currently-untreatable late stage disease [62].

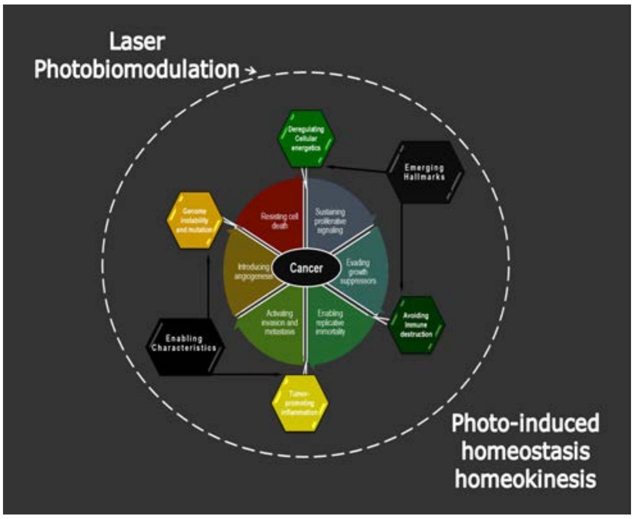

Figure 7. Photobiomodulation aimed at reestablishing homeostasis / homeokinesis by targeting multiple hallmarks of cancer. (Adapted from Figure 3 and Figure 6 in Ref. [63])

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Statement of Competing Interests

The authors have no competing interests.

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