"Water-light interaction: A novel pathway for multi hallmark therapy in cancer"

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It has been suggested that new anticancer therapies should no longer aim solely at killing tumor cells, but at reestablishing homeostasis/homeokinesis—a micro-environment effect which may be induced by water light interactions in human tissues. Laser photobiomodulation (L-PBM) has been proposed as a multi-target (multi-hallmark) therapy for cancer and other complex diseases (CDs) based on an approach that aims to substitute and/or complement metabolic energy pathways through oxygen-dependent (e.g., cytochrome c oxidase (CcO)) and/or oxygen-independent (e.g., light-water interactions (F0-F1 motors)) mechanisms with critical signaling pathways in primarily aqueous media. Long considered an innocuous medium, water has increasingly been found to be a key player in numerous physiologic mechanisms, including first-contact events in which cells decide between survival and apoptosis. Consequently, externally applied electromagnetic energy (light) may selectively target the organization of water to steer biological function. Whereas signal and receptor characteristics determine biological outcome, which is optimal for only one set of conditions, properly tailored LPBM can trigger a cascade of biochemical, metabolic, biomechanical and hydrodynamic mechanisms that control cellular fuel (i.e., ATP, GTP and other high-energy molecules) and receptors purine (P) and adenine(A). These power and modulate, in a specific and selective manner, work at the cell and tissue level, and are required in extensive signaling networks that span the energy-dependent path from the genotype to the phenotype. Previously, cellular and molecular bases had been presented for water-mediated, long-range, energy supplementation aimed at inducing and modulating physiologically reparative processes, including apoptosis, through a mechanism termed Photo Infrared Pulsed Biomodulation (PIPBM). Subsequently, the role of water as an oscillator in near infrared (NIR) LPBM was documented, adding to a more coherent description of the central effects of NIR light over redox centers and key transmembrane enzymes, such as CcO. Water, thus, provides a pathway for NIR absorption and transportation, complementing and facilitating CcO energy transfer for increased efficiency in the production of ATP—a vital molecule required not only for energy but also as part of the signaling pathways connected with family-specific receptors P2 and P1 of growing importance in cancer and other CDs. Recently, these ideas were complemented and expanded by integrating the role of the quasi-crystalline exclusion zone (EZ) described by Pollack as the fourth phase of water. A retrospective analysis of published experimental and clinical data using an infrared pulsed laser device (IPLD) showed photo-induced effects over the water dynamics of burned rat tissue monitored by ^{1}H-NMR transverse relaxation times (1/T2), indicating significantly greater structuring of water. Also a microdensitometry study of T2 weighted tumor heterogeneities from a phase I clinical trial of the IPLD in patients with advanced neoplasias and an algorithm for tumor characterization showed significantly increased structuring of water, possibly proving a photobiomodulation effect over the EZ associated with histologically-confirmed selective photo-induced tumor cell death.
To the best of our knowledge, this is the first clinical demonstration of light-induced effects over the EZ. It supports our novel premise that LPBM can increase potential energy in the EZ, which can then act as a rechargeable electrolytic bio-battery for the external selective supplementation of the energy demand required for cellular work, signaling pathways and gene expression in the presence of injury-induced redox potentials. It further suggests that EZ structuring may be used as a predicator of anticancer response before measurable tumor volume reduction.