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High-Density Transcranial DC Stimulation (HD-tDCS): Targeting Software

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Transcranial Direct Current Stimulation (tDCS) is a non-invasive procedure where a weak electrical current (260 μA to 2 mA) is applied across the scalp to modulate brain function. tDCS has been applied for therapeutic purposes (e.g., addiction, depression, mood and sleep disorders) as well as cognitive performance enhancement (e.g., memory consolidation, motor learning, language recall). Despite safety and cost advantages, the developments of tDCS therapies have been restricted by spatial targeting concerns using existing two-channel systems. We have developed novel technology for High-Density tDCS (HD-tDCS) that improves spatial focality. To determine optimal stimulation electrode configurations, based on application specific constraints, we developed a HD-tDCS targeting software. High resolution (gyri/sulci precise) MRI derived finite element (FE) human head models are generated by segmenting grey matter, white matter, CSF, skull, muscle, fatty tissue, eyes, blood vessels, scalp, etc. The models comprised >10 million elements with >15 million degrees of freedom. The induced cortical electric field/current density values are calculated; activation of either radially and tangentially oriented neuronal structures are considered. Our HD-tDCS hardware (4×1-C1, 4×4-S1) currently supports the '4×1-Ring' and the '4×4-Strip' electrode configurations. The peak cortical electric field was matched to 'conventional' large rectangular-pad tDCS stimulation; however, the spatial focality was significantly enhanced by 4×1 configuration. Using patient specific head models, our software interface allows simple and rapid screening of stimulation electrode configurations. After selecting a target region, clinicians can customize the electrode configuration to balance: 1) cortical surface and brain depth stimulation focality; 2) total applied current/voltage; and 3) electrode/scalp current density. Our HD-tDCS system allows non-invasive, safe, and targeted modulation of selected cortical structures for electrotherapies that are individualized as well as optimized for a range of therapeutic applications.

Development of Photoinitiated Nitric Oxide Releasing Polymer Films for Controlled Drug Delivery

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Nitric Oxide (NO) is small, free radical gas that has been shown to have a wide variety of physiological functions, including the ability to hinder tumor angiogenesis at high, but non lethal, concentrations [1]. Previous work suggests that if NO could be effectively delivered in vivo to tumors of patients currently undergoing chemotherapy treatments at the appropriate levels, less damaging chemotherapy treatments could be used against cancer [2]. This could increase the overall survivability of cancer patients, especially in those prone to the harmful effects of chemotherapy: children, elderly, and those of weak immune systems. If NO is especially successful at preventing and eliminating tumor growth, angiogenesis, and carcinogenesis the need for stressful chemotherapy treatments could be eliminated altogether. This project is focused on developing novel photosensitive NO donors that can be incorporated into polymeric systems and used in a fiber optic drug delivery system. Development of these NO-releasing polymers will allow continued investigation of NO's role in tumor death by precisely controlling the surface flux of NO that cells are exposed to. Generating specific surface fluxes of NO from polymer films has been demonstrated by using polymer films that contain photoinitiated NO donors [3], prepared by synthesizing S-nitrosothiol (RSNO) derivitized polymer fillers that are blended into hydrophobic polymers and cast into a film. These films generate and sustain a surface flux of NO based on the wavelength and intensity of light used [3]. Polymers releasing NO are more promising as an NO donor than simply injecting NO into samples because they allow for spatial and temporal control of NO delivery. The specific concentration of NO needed to produce desirable effects on tumor cells (i.e., apoptosis) is not known. Data will be presented that show the synthesis and NO-release properties of novel RSNOs based on the nitrosation of benzyl mercaptan thiols. Specifically, UV-Vis spectrum of benzyl mercaptan in toluene and S-nitrosobenzyl mercaptan after the addition of t-butyl nitrite will be presented. We are currently investigating the effects of varying NO-surface fluxes generated from photolytic NO donating polymer films on aortic smooth muscle cell cultures obtained from mice. Once we have established that we can quantitatively determine the effects of different levels of NO on the proliferation of smooth muscle cell cultures, work will begin to apply this methodology and these novel NO-releasing polymeric systems to begin investigating what durations and surface fluxes of NO are necessary to have tumorcidal effects on specific cancer cells.

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