Thermochemical Ablation: A Novel Technique for Solid Tumor Therapy

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To overcome the limitations of existing ablation techniques, we propose a novel combinatorial approach that would utilize the thermal and chemical destructive effects of exothermic chemical reactions, such as an acid/base neutralization reaction, to treat solid tumors. Thermochemical ablation is a potential technique for percutaneous probe-based tumor therapy. It involves simultaneous intratumoral delivery of multiple reagents resulting in thermal energy released by an exothermic reaction to ablate tumor tissue with concurrent generation of a hyperosmolar byproduct that could accentuate tumor destruction. Besides the benefit of synergistic thermal and chemical effects for tumor tissue destruction, this technique is potentially highly cost-effective, easy to implement, and able to treat larger sized tumors. Our hypothesis is that thermochemical ablation can create an evenly distributed zone of coagulation in tumor tissue without systemic toxicity. A prototype device assembled using off-the-shelf components is being investigated in our lab for concurrent intraparenchymal delivery of an acid and a base. The distal portion of the multi-lumen device allows for passive mixing of the reagents before entering the tissue. The prototype device also satisfies other desirable design criteria such as rigidity to penetrate body tissue, reduced diameter, chemical stability to reagents, etc. However, the device can be improved upon by incorporating additional characteristics such as optimized imaging characteristic for real-time visualization and localization within tumor tissue, MRI compatibility, thermal insulation, improved mixing at the tip, etc. Our lab is currently working on improving the design of the infusion device as well as assessing the feasibility of the thermochemical ablation technique in vitro and in vivo. While currently being targeted conservatively for palliative therapy of unresectable or late-stage aggressive malignancies such as hepatocellular carcinoma, thermochemical ablation has potential use in the therapy of a majority of solid tumors such as breast cancer, lung cancer, prostate cancer, renal cancer, sarcomas, etc.

Design of an Endoreactor for the Cultivation of a Joint-Like-Structure

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To avoid revision surgeries in artificial joint replacements and to allow young people to have a joint replacement, using biological joint replacement created by tissue engineering is a promising alternative. Several research groups have tissue engineered bone [Warnke 2004] and cartilage [Chung 2007] separately. The tissue engineering of a joint, consisting of bone and cartilage is the next frontier. The present study focuses on the design of a novel device, named Endoreactor, that is employing the mechanosensitivity of cells to create a joint-like-structure (JLS) consisting of a bone and cartilage sandwich, similar to an amphiarthrosis, by applying a mechanical loading regime to a stem cell seeded scaffold construct during endocultivation. This way, the patients who will eventually need the new joint will serve as their own bioreactor, having the joint grow in their own body. In the JLS, the outside layers are designed to become bone, using a 6 mm thick scaffold with high stiffness. The center layer is a 4 mm thick scaffold which is compliant so as to experience more strain than the outside scaffolds to stimulate cartilage formation. Compression is realized by placing the JLSs between the long links of a kite-shaped four-bar linkage. This Endoreactor is powered by natural body motion through connection to the musculoskeletal system of the host, which in the experimental phase is a Gottingen minipig. The loading frequency and rest versus active time is dictated by the activity level of the minipig. This results in a natural loading pattern that is employed for the stimulation of cartilage formation in the JLS. A tensile force created during ambulation is converted into compressive action between the two long links of the mechanism. A mechanical stop limits the motion. This way controlled intermittent dynamic compression between 2.5% and 12.5% is realized in the cartilage layer of the JLS. All functions are integrated into a single piece compliant mechanism which is produced out of titanium using 3D rapid prototyping by selective laser melting technology. The mechanism can be fitted with cages that hold the scaffolds for bone and cartilage in place and protect them from external loads while being implanted. A safety spring was added to accommodate for large actuation excursions. A number of prototypes were produced and tested for fatigue, plastic deformation, failure load, and displacements of the long links at the JLS locations under different axial loads. These tests confirmed the proper mechanical functioning of the Endoreactor. Work with animal models making use of the device to culture an amphiarthosis-like joint is foreseen in the near future. This work was carried out at part of MYJOINT: Living Bioreactor—Growing a New Joint in a Human Back, EU FP6-2004-NEST-C-1, Proposal No. 028861.

