In vivo imaging of electropermeabilization effects

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Optical imaging is nowadays a powerful tool for laboratory animal studies in oncology. This emerging technology is in full development and is becoming a complementary tool in clinics for specific cancer diagnosis. For now, it allows detection with a high spatio-temporal resolution of specific signals like tumor markers in small animals. Different ways of in vivo imaging exist: luminescence, fluorescence macroscopy, intravital imaging to visualize molecular processes combined or not with multiphoton excitation to spatially detect deeper cellular phenomena.
Electropermeabilization/electroporation (EP) is one of the non-viral methods based on the native transmembrane electric potential modulation of the cell by applying electric pulses to cells. The selective permeability of the membrane disappears when threshold values of the transmembrane potential are reached. Permeabilization can be adjusted by the different electric parameters (intensity, number of pulses and duration) (1). This physical method thus enables the delivery of chemotherapeutic drugs into tumor cells in electrochemotherapy (ECT) (2) or nucleic acids for gene therapy purposes in electrogene therapy (EGT) (3) in healthy or cancerous tissues.
We have investigated by in vivo fluorescence macroscopy, the kinetic and the efficiency of electrically-mediated delivery of nucleic acids (DNA, Minicircle, shRNA and siRNA) into tumors (4). In vivo EP also has blood flow modifying effects; resulting in decreased blood flow and increased permeability of blood vessel walls. We have evaluated by intravital microscopy the effects of electric pulses used for ECT on blood vessels and on endothelial cells (5, unpublished data). Finally, we have used a transgenic mouse that expresses the luciferase reporter gene under a thermal stress inducible promoter to evaluate “thermal” like stress of EP parameters on the skin (unpublished data).
In the field of electroporation-based treatments, imaging techniques are powerful tools to observe the bio-distribution of molecules, to describe the mechanisms of their electro-delivery and to quantify their biological effects at the level of the organs or tissues as well as the level of the cell in living animal.

References

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