Nanosecond pulsed electric field ablation (nanoelectroablation) of melanoma and hepatocellular carcinoma

Anti-neoplastic effects of a pulse power ablation (PPA) with nanosecond pulsed electric fields (nsPEFs) are investigated as a non-thermal, non-ionizing, non-drug, local treatment for ablation of melanoma and hepatocellular carcinoma (HCC). The pulses are high in power, but low in energy, so they differ from thermal ablation methods such as radiofrequency ablation. NsPEFs (60-600 ns, ≤ 60kV/cm) induce PCD, including apoptosis in vitro, by mitochondria- and caspase-dependent and –independent mechanisms. Mitochondria are primary targets of nsPEFs. Mitochondria membrane potential decreased, intracellular calcium increases, cytochrome c-is released in most cancer models, phosphatidylserine externalized, Bid is cleaved by calpains and caspases and DNA is damaged by caspase-dependent mechanisms. In ectopic mouse B16f10 melanoma and Hepa1-6 HCC and orthotopic rat N1S1 HCC tumors, nsPEFs eliminated 75-100% of tumors without recurrence. NsPEFs target anti-apoptotic mechanisms as indicated by chromosomal condensation, nuclear pyknosis, H2AX phosphorylation, TUNEL and caspase activation. Furthermore, nsPEFs targeted angiogenesis, decreasing tumor blood supply with decreased levels of VEGF, PD-ECGF and microvascular density markers (CD-31, -35 and -105). The activation of caspase-associated apoptosis, anti-vascular effects, tumor infarction and inhibition of revascularization demonstrate that nsPEFs recruit at least two dominant cancer therapeutic targets with a single treatment modality and explain, at least in part, the success of nsPEF application for tumor treatment in vivo. With development of catheter electrodes nsPEFs could be useful to treat internal organs with laparoscopic surgery. NsPEF ablation of melanoma, HCC and other tumors could provide an effective therapeutic modality alone or in combination with other therapies.

Biography

Stephen J. Beebe received his PhD (1982) in Medical Sciences from the Medical College of Ohio, (now University of Toledo- College of Medicine). He was a post-doctoral fellow at the Howard Hughes Medical Institute and Department of Molecular Physiology and Biophysics at Vanderbilt University, Nashville. He was Fulbright and Marshall Scholar at the University of Oslo, Department of Medical Biochemistry and National Hospital before becoming an Assistant and Associate Professor in Department of Physiological Sciences and Pediatrics at Eastern Virginia Medical School in Norfolk, Virginia. He is now a Professor at Old Dominion University in the Frank Reidy Research Center for Bioelectronics in Norfolk.