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### **Cold Atmosphere Plasma in Cancer Therapy**

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Plasma is an ionized gas that is typically generated in high-temperature laboratory conditions. Recent progress in atmospheric plasmas led to the creation of cold plasmas with ion temperature close to room temperature. Areas of potential application of cold atmospheric plasmas (CAP) include dentistry, drug delivery, dermatology, cosmetics, wound healing, cellular modifications, and cancer treatment. Various diagnostic tools have been developed for characterization of CAP including intensified charge-coupled device cameras, optical emission spectroscopy and electrical measurements of the discharge properties. Recently a new method for temporally resolved measurements of absolute values of plasma density in the plasma column of small-size atmospheric plasma jet utilizing Rayleigh microwave scattering was proposed [1,2]. In this talk we overview state of the art of CAP diagnostics and understanding of the mechanism of plasma action on biological objects. The efficacy of cold plasma in a pre-clinical model of various cancer types (lung, bladder, and skin) was recently demonstrated [3]. Both in-vitro and in-vivo studies revealed that cold plasmas selectively kill cancer cells. We showed that: (a) cold plasma application selectively eradicates cancer cells in vitro without damaging normal cells. For instance a strong selective effect was observed; the resulting 60–70% of lung cancer cells were detached from the plate in the zone treated with plasma, whereas no detachment was observed in the treated zone for the normal lung cells under the same treatment conditions. (b) Significantly reduced tumor size in vivo. Cold plasma treatment led to tumor ablation with neighbouring tumors unaffected. These experiments were performed on more than 10 mice with the same outcome. We found that tumors of about 5mm in diameter were ablated after 2 min of single time plasma treatment. The two best known cold plasma effects, plasma-induced apoptosis and the decrease of cell migration velocity can have important implications in cancer treatment by localizing the affected area of the tissue and by decreasing metastatic development. In addition, cold plasma treatment has affected the cell cycle of cancer cells. In particular, cold plasma induces a 2-fold increase in cells at the G2/M-checkpoint in both papilloma and carcinoma cells at about 24 hours after treatment, while normal epithelial cells (WTK) did not show significant differences. It was shown that reactive oxygen species metabolism and oxidative stress responsive genes are deregulated. We investigated the production of reactive oxygen species (ROS) with cold plasma treatment as a potential mechanism for the tumor ablation observed.

[1] Shashurin A., Shneider M.N., Dogariu A., Miles R.B. and Keidar M. *Appl. Phys. Lett.* (2010) **96**, 171502.

[2] Shashurin A., Shneider M.N., Keidar M. *Plasma Sources Sci. Technol.* 21 (2012) 034006.

[3]. M. Keidar, R. Walk, A. Shashurin, P. Srinivasan, A. Sandler, S. Dasgupta, R. Ravi, R. Guerrero-Preston, B. Trink, *British Journal of Cancer*, 105, 1295-1301, 2011