# Non-thermal plasmas in biomedical applications – beyond the long-lived species

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Non-thermal plasmas have reached evidence level 2 regarding acceleration of wound healing and in certain aspects of cancer treatment, with a growing community of physicians successfully using it (plasma medicine). Key players in such biomedical applications are reactive oxygen or nitrogen species (ROS/RNS), which are deposited in either tissue (in vivo) or liquid (in vitro) and subsequently influence cellular redox signaling. A huge variety of plasma sources for potential application has been developed and comparing these sources in respect of safety and efficacy remains challenging but desirable.

One aspect can be the identification and quantification of the sources ROS/RNS deposition in liquids. However, due to the short lifetime of many ROS/RNS and limited specificity of available probes their detection is demanding. To meet this challenge, we applied a variety of analytical techniques including high-resolution mass spectrometry of small molecules (cysteine, tyrosine), ion chromatography (RNS detection), electron paramagnetic resonance spectroscopy (O, $O_3$, $^1O_2$, $O_2^-$, OH), and colorimetric assays to infer on dominant active species. Two argon plasma jets (MHz jet kinpen, RF jet) and a helium based RF jet (COST jet) were investigated. In addition, cell biology experiments allowed a first estimation of the biological impact of plasma treated small molecules.

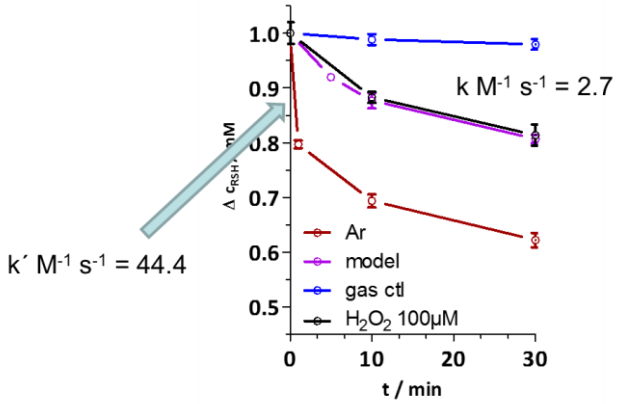


Fig. 1: Free thiol quantification of cysteine after Ar jet treatment (red), model (pink), $H_2O_2$ (black). Short lived species generated during treatment are most effective. Model (= remote plasma treatment) shows similar impact as $H_2O_2$.

A large number of covalent modifications have been detected and in part identified. The majority of changes to the chemical structure of cysteine was found in the vicinity of the thiol group, while in tyrosine the aromatic ring was targeted. The resulting products also occur in physiological situations in vivo, allowing to conclude that the covalent modification of small organic molecules is part of the mechanism of direct plasma-cell interaction. Predominantly short-lived oxygen species were found to be of relevance regarding the chemical and biological impact of plasma, challenging the popular concept of remote treatment (e.g. plasma treated buffers).