Characterisation of a cold atmospheric pressure plasma source for the treatment of cervical intraepithelial neoplasia

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Abstract: A promising new method for the treatment of cervical intraepithelial neoplasia is the treatment with atmospheric pressure plasma. In a previous pilot study, patients were treated with the well-known argon plasma coagulation (APC). The remission rate was significantly higher compared to spontaneous remission rates. In order to obtain a better understanding about the mechanisms behind the high remission rate of the treatment, the APC is characterised under the power conditions used in the pilot study and the concentrations of reactive species in a liquid sample are measured.

Keywords: plasma characterisation, line broadening, reactive species.

1. Introduction and medical background

Precancerous tissue transformations of the cervix uteri are defined as cervical intraepithelial neoplasia (CIN). CIN results from persistent human papillomavirus (HPV) infections within cervical cells. Invasion across the basement membrane leads to invasive cervical cancer, which is the fourth most common cancer for women worldwide leading to approximately 270,000 deaths / year [1]. Currently, different treatment modalities are recommended depending on the grade of CIN. These are often quite invasive and associated with a number of side effects, such as severe bleeding, reduced fertility rates and complications during pregnancy and delivery. [2]

In this context, the development of a novel method that avoids the excision of abnormal cells and affected tissue is desired. In support of these aims, a clinical proof-of-principle study was performed at the University Clinic Tübingen (UKT) using an electrosurgical instrument (argon plasma coagulation, APC) for the superficial treatment of the cervix uteri in order to reduce the grade of CIN. [5]In that previous proof-of-principle study with 20 patients, as well as the first evaluation of 48 patients in an ongoing confirmatory study, a significantly higher remission (up to 95 %) could be shown compared to spontaneous remission (approximately 25 %). [3] Although the treatment shows promising results, the main mechanisms that lead to remission are not known in detail.

To gain new insights and a fundamental basis for optimization, the APC plasma source with the minimal power setting used in the proof-of-principle study is characterized in this work. Since the APC is operated in an argon gas flow, the mixture of argon and air during the clinical procedure is not known. Therefore, the influence of different gas atmospheres is investigated using an air-tight vessel. The characterization involves the determination of plasma parameters, such as electron densities and gas temperatures. Furthermore, the production of reactive species, such as NO_2^-, NO_3^-, H_2O_2 and OH/O in liquids treated by the APC are measured using photometric techniques.

2. Experimental setup

The experimental setup is shown in figure 1 and consists of an air-tight vessel that is used to provide surrounding gas atmospheres with different mixtures of synthetic air and argon (2 slm, continuous flow). Furthermore, the relative humidity can be controlled using a gas bubbler system. An electrosurgical plasma generator (Erbe Elektrodmedizin, VIO 3, APC3) is used to power the plasma source, which provides a pulsed damped sine-wave voltage signal (8 kV peak-to-peak, 350 kHz, modulated at 20 kHz). 5 ml of ringer-lactate solution are treated in a petri dish. This solution has a similar ion concentration and conductivity as human tissue. The distance from the APC probe to the liquid was 6 mm, which is a typical distance during clinical use.

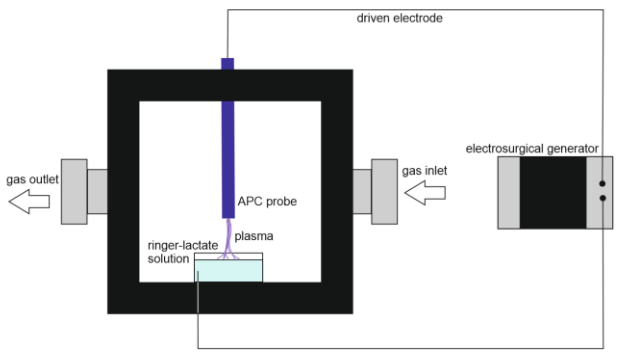

Fig. 1. Experimental setup

During the treatment, optical emission spectra are measured using an echelle spectrometer (ESA4000, LLA Instruments). The high spectral resolution of 15 – 60 pm allows for the analysis of spectral broadening mechanisms.

The ringer-lactate samples were treated for several treatment times under different gas atmospheres and mixed with specific reactants for the measurement of certain species after the treatment.

3. Analysis methods

The electron density in the APC was measured by analyzing the spectral line broadening of hydrogen lines using a Voigt-fit, as shown in figure 2. The method is described in detail in. [4] In order to compensate for the inhomogeneous discharge characteristics, two profiles are used to allow for a good fit of the measured emission line. This leads to two electron density values that may correspond to different spatial locations within the discharge. From the fit, the electron density can be inferred by analyzing the Stark broadening contribution to the width of the line profile.

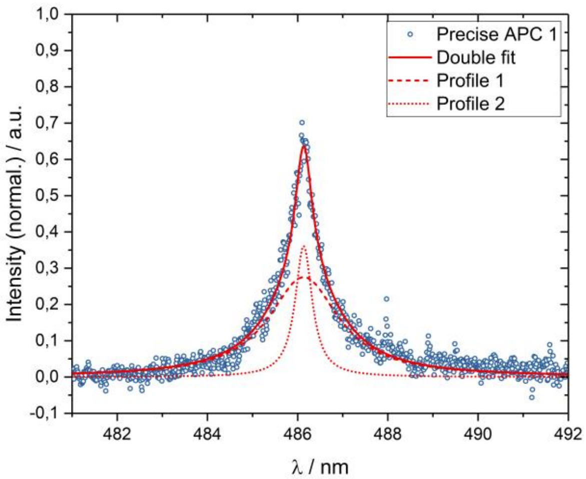

Fig. 2. Double Voigt fit of the H_β line

Gas temperatures were measured by analyzing the rotational distribution of N_2(C-B) emission band. Under atmospheric pressure conditions it can be assumed that $T_{rot} \approx T_g$ due to frequent collisions between the excited state investigated and the background gas. Comparing simulated spectra with the measured emission bands, gas temperatures can be derived from the best fit.

The concentrations of relevant species, such as NO_2^-, NO_3^- and H_2O_2 were measured using photometric techniques. The production of OH/O was analysed using terephtalic acid (TA). TA reacts with OH to 2-hydroxy terephthalic acid (HTA), which emits light at 425 nm when it is excited with UV light at 310 nm. [5] Recent work has also shown that HTA can form from TA during interactions with O [6]. Therefore, our measurements provide a convolution of the densities of both species.

4. Results and Conclusion

First measurements of the electron density and the gas temperature show comparable results to previous measurements with the APC, which used higher power settings. Electron densities in the order of 10^{16} cm^{-3} were found. The gas temperatures were in the range of 1500 K. It is found that these plasma parameters do not strongly depend on the surrounding gas atmospheres or relative humidity level. More significant changes were found in the concentration of reactive oxygen and nitrogen species. The concentrations of NO_2^-, NO_3^- and H_2O_2 as well as OH/O radicals show a linear behavior for different treatment times. For different gas atmospheres the H_2O_2-concentrations were almost unaffected from the gas atmosphere. However, the concentrations of NO_2^-, NO_3^- were significantly lower for higher argon fractions. The humidity did not show a significant influence.

5. Acknowledgements

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6. References

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