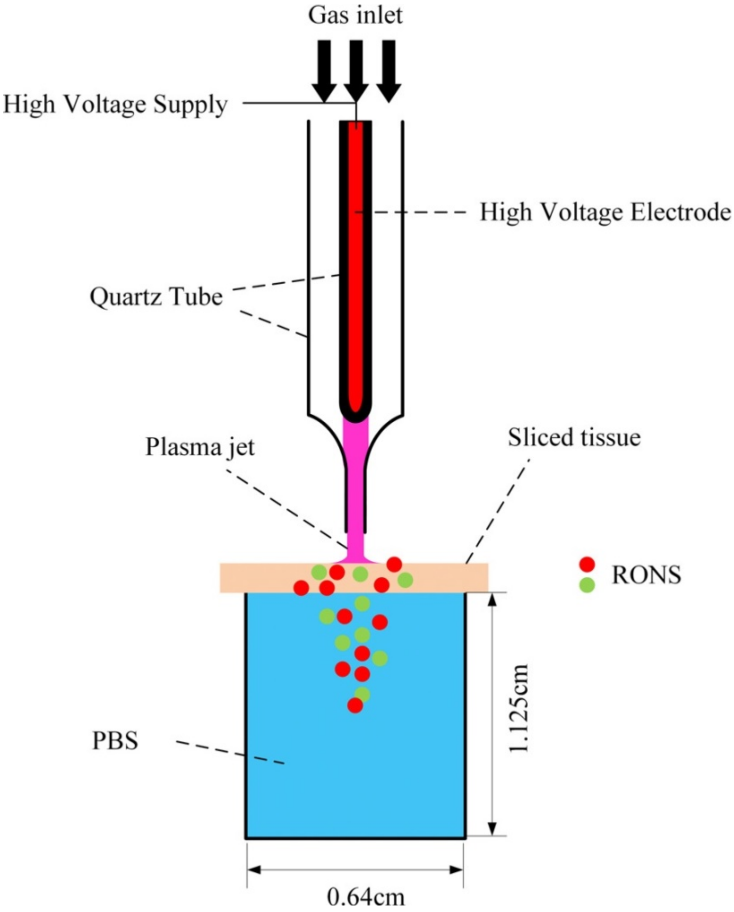

Figure 8. Experimental setup using pig muscle tissue [72]. Reproduced from Duan, J.; Lu, X.; and He, G. *Phys. Plasmas* **2017**, *24*, 073506, with the permission of AIP Publishing.

The concentrations of H_2O_2, OH, and that of the total of (NO_2^- + NO_3^-) were measured for different thicknesses of the tissue slice. A comparison of these concentrations when no tissue was used and when a tissue was placed on top of the solution showed that the concentrations of O_3, OH, and H_2O_2 were mostly consumed by the tissue and could not pass through 500-μm or greater tissue thickness. However, more than 80% of the (NO_2^- + NO_3^-) penetrated a 500-μm-thick tissue slice. Figure 9 shows the measured concentrations of (NO_2^- + NO_3^-) as a function of tissue thickness and for three plasma treatment times (5, 10, and 15 min).

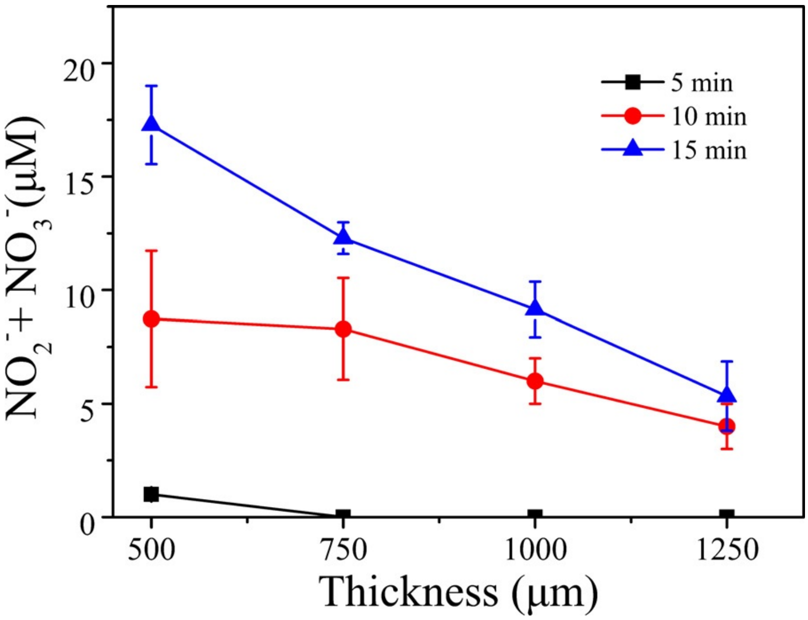

Figure 9. Total nitrite and nitrate concentration versus tissue thickness for three plasma exposure times [72]. Reproduced from Duan, J.; Lu, X.; and He, G. *Phys. Plasmas* **2017**, *24*, 073506, with the permission of AIP Publishing.

Figure 9 shows that the concentrations of the nitrogen reactive species, RNS, decrease with the tissue thickness, but increase with the plasma treatment time. The concentration of (NO_2^- + NO_3^-) for the 500-μm tissue thickness was comparable to the concentration when no tissue was placed on top of the PBS solution. This means that (RNS) were able to penetrate the tissue slice. This was not the case for ROS, which were absorbed by the tissue, unlike the case when a gelatin model (not real tissue) was used. For that model, ROS were able to penetrate the gelatin film.

The above examples illustrate that RONS do not simply react with the surface of tissues but can indeed penetrate relatively deeply. However, in more realistic conditions using actual tissue, it was shown that not all RONS can cross the same thickness. Some can be absorbed within a few tens of micrometers by the tissue, while others can penetrate up to 1.5 mm below the surface. Of course, the above results may not completely reflect what would happen under in vivo conditions. Such experiments need to be conducted and compared to results obtained for in vitro models and to those obtained under ex vivo conditions [95].

7. Conclusions

To conclude this brief introduction of the field of plasma medicine, it is safe to say that the biomedical applications of low temperature plasma have opened up an entirely new multidisciplinary field of research requiring close collaboration between physicists, engineers, biologists, biochemists, and medical experts. This multidisciplinary field started in mid-1990s with seminal experiments on the inactivation of bacteria by low temperature atmospheric pressure plasma generated by a dielectric barrier discharge and slowly expanded to include investigations on eukaryotic cells. Applications in dermatology, wound healing, dentistry, and cancer have led to various scientific advances and to the idea that LTP can be a technology upon which various innovative medical therapies can be developed to overcome present healthcare challenges. However, a lot remains to be done in order to fully understand the mechanisms of action of LTP against biological cells and tissues, both in vitro and in vivo. There is strong indication that LTP acts selectively on cancer cells and tumors and can penetrate deep below the surface, but much more work, including extensive clinical trials, is needed before LTP can be considered a safe technology ready for use in hospitals to treat chronic wounds, cancer lesions and tumors, and other ailments.

Conflicts of Interest: The author declares no conflicts of interest.

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