SIOOT oxygen-ozone therapy against multidrug-resistant bacteria. Perspectives and future remarks

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Abstract

Antibiotic resistance is one of the most pressing global health threats, diminishing the effectiveness of standard antimicrobial therapies and contributing to increased morbidity, mortality, and healthcare costs.
In response to this challenge, ozone therapy has emerged as a potential adjunctive treatment against multidrug-resistant (MDR) bacterial infections.
Notably, protocols endorsed by the Italian Scientific Society of Oxygen-Ozone Therapy (SIOOT) and clinical insights from Prof. Marianno Franzini, have advanced understanding of ozone dual mechanisms of action in counteracting MDR bacterial infection.

Rationale. Chronic multidrug-resistant infections remain difficult to eradicate because prolonged antibiotic exposure often fails to clear microbial persistence and inflammation. Although ozone shows antimicrobial and immunomodulatory effects experimentally, its clinical role in established chronic MDR infection is unclear. The study therefore examined whether oxygen–ozone autohemotherapy could reduce bacterial burden and inflammation.

Results: Sixteen patients contributed complete 1-year longitudinal microbiological follow-up, including 9 MRSA, 4 KPC-producing Klebsiella pneumoniae, 2 Pseudomonas aeruginosa, and 1 Escherichia coli infection. Baseline bacterial burden averaged 7.048 $\log_{10}$(CFU+1), corresponding to approximately 1.12×10^7 CFU/mL. This declined significantly at every follow-up visit, reaching 5.999 at 1 week, 3.532 at 1 month, 2.713 at 2 months, 2.206 at 3 months, 0.396 at 6 months, and 0.000 at 1 year. By 6 months, 11 of 16 patients had undetectable bacterial counts, and by 1 year all patients had cleared detectable bacteria. The mixed-effects model confirmed a strong overall time effect on bacterial burden.

Inflammatory markers improved in parallel. All 16 patients showed a reduction in erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) within 1 week. Median ESR fell from 88.5 to 25.5 mm/h, with a mean paired decrease of 53.19 units. Median CRP decreased from 6.10 to 4.05 mg/L, with a mean paired reduction of 2.15 units. By 1 month, all ESR values were below 10 mm/h and all CRP values below 3 mg/L, remaining normalized thereafter. At 1 week, the mean bacterial reduction was 1.05 $\log_{10}$ units, equivalent to an approximately 11.2-fold decrease, indicating a rapid early microbiological response accompanied by synchronized inflammatory improvement.

Before ozone, paired antibiogram analysis showed worsening antimicrobial resistance over time. Ozone did not reversed genetics but largely contributed in the complete clearance of MDR bacteria of the ESKAPE group in few times. Across 130 paired isolate–antibiotic observations, resistance increased from 32.3% at 1 year to 40.8% at 2 years, an absolute rise of 8.5 percentage points. There were 11 transitions from non-resistant to resistant and no reversions, yielding a significant exact McNemar test. Species-specific analyses suggested the largest resistance increase in P. aeruginosa, while K. pneumoniae had the highest overall resistance burden. Thus, microbiological clearance and inflammatory normalization occurred despite persistence or progression of resistance phenotypes.

Table 1. Overall statistical results

Analysis set	n pairs	Resistant at 1 year	95% CI at 1 year	Resistant at 2 years	95% CI at 2 years	Absolute change	95% CI of change	New R	Lost R	Exact McNemar p
Overall paired isolate-antibiotic tests	130	42/130 (32.3%)	24.4–41.1%	53/130 (40.8%)	32.2–49.7%	8.5%	3.8–13.8%	11	0	<0.001

Table 1. Antimicrobial resistance before ozone therapy

Across 130 paired isolate-antibiotic tests, resistance increased from 42/130 (32.3%) at 1 year to 53/130 (40.8%) at 2 years, an absolute rise of 8.5 percentage points. There were 11 new resistant results and no reversions, with McNemar p<0.001, showing a statistically significant worsening of antimicrobial resistance over time in patients.

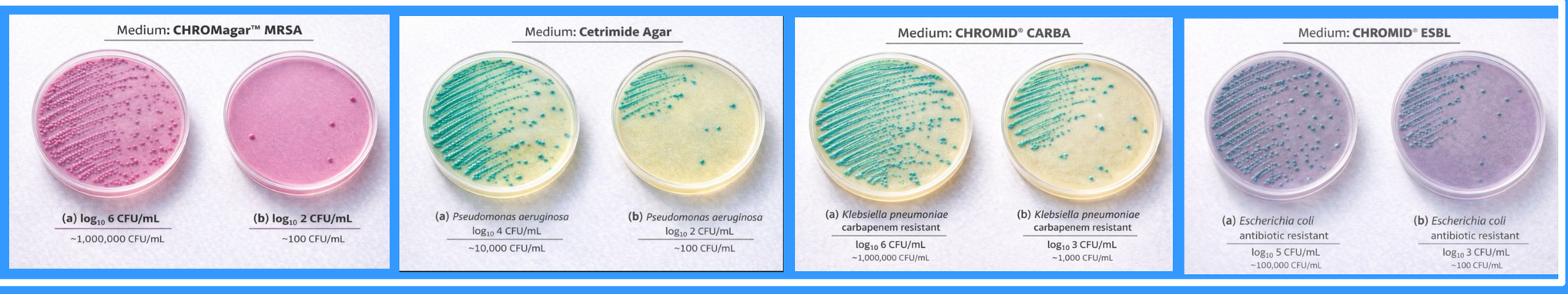
Table 2. Linear mixed-effects model for log10 (CFU +1)

Parameter	Estimate	SE	95% CI	z	p
Intercept (baseline mean)	7.048	0.150	6.754 to 7.342	47.01	<0.001
1 week vs baseline	-1.050	0.164	-1.372 to -0.728	-6.39	1.68×10^{-10}
1 month vs baseline	-3.516	0.164	-3.838 to -3.194	-21.40	1.28×10^{-101}
2 months vs baseline	-4.335	0.164	-4.657 to -4.013	-26.39	1.93×10^{-153}
3 months vs baseline	-4.842	0.164	-5.164 to -4.520	-29.47	6.94×10^{-191}
6 months vs baseline	-6.652	0.164	-6.974 to -6.330	-40.49	<0.001
1 year vs baseline	-7.048	0.164	-7.370 to -6.726	-42.90	<0.001

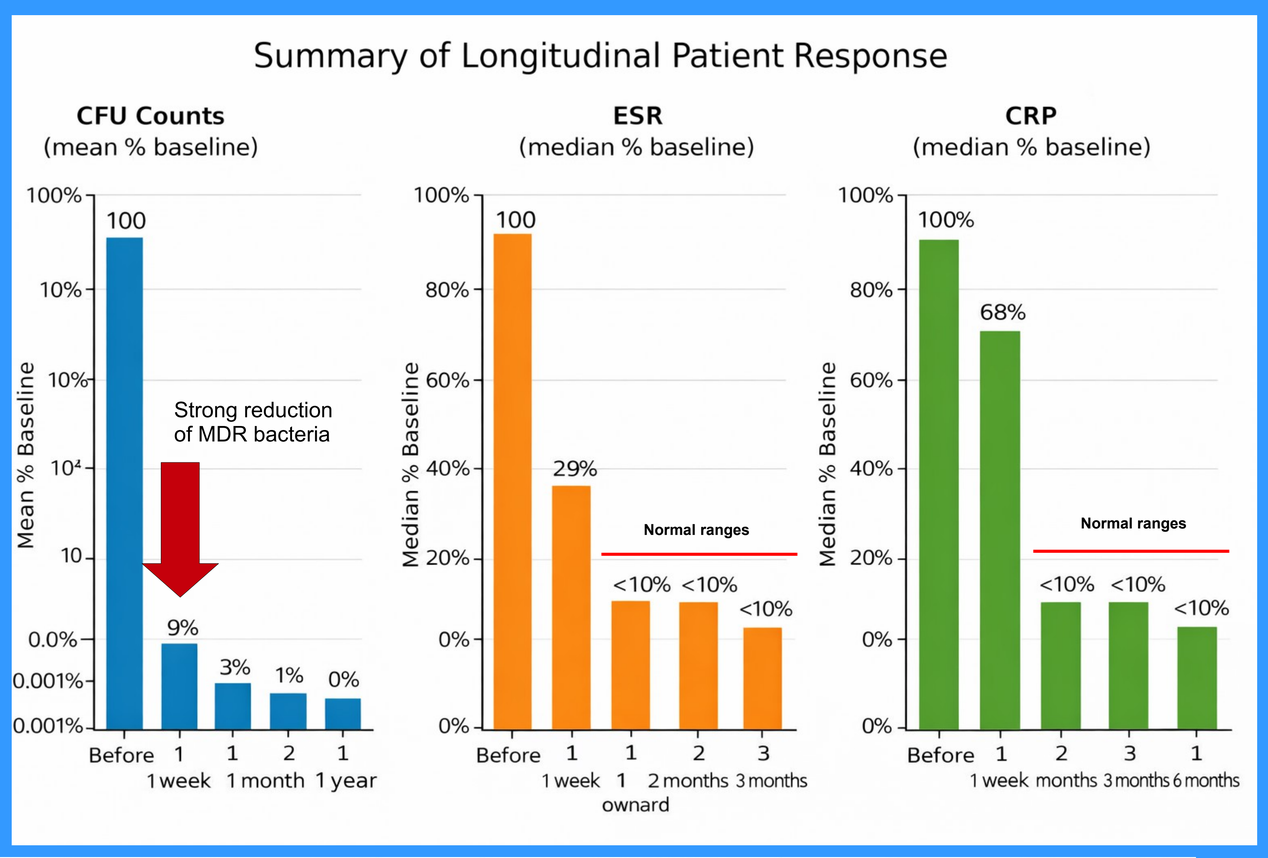
Abbreviations: SE, standard error; CI, confidence interval. Model-level statistics: likelihood-ratio test for time effect, χ_6^2=351.24, p=8.38×10^{-73}; random-intercept variance τ^{A2} = 0.144; residual variance σ^{A2}=0.216; ICC =0.400=0.400=0.400.

Table 2. Antimicrobial resistance after ozone therapy

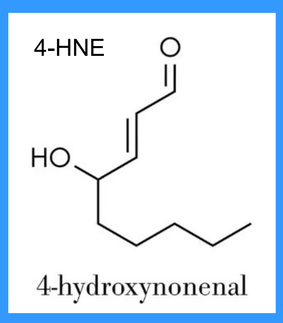
The model shows a strong, progressive decline in bacterial burden after treatment. Mean baseline log10(CFU+1) was 7.048, falling significantly at every follow-up: 1 week, 1, 2, 3, and 6 months, reaching complete suppression by 1 year. Extremely small p values indicate these reductions were highly statistically significant and consistent.

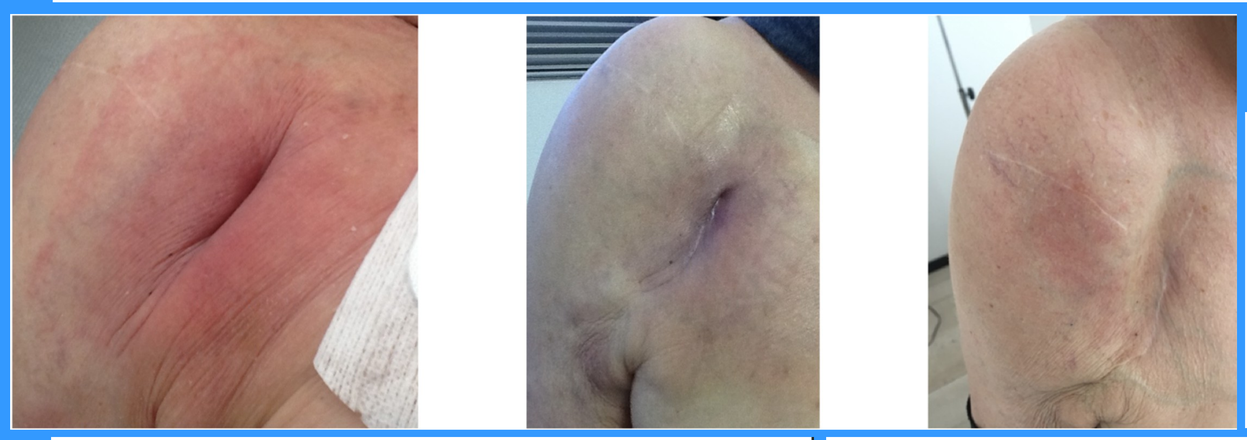


Microbiological assays before (left) and after (right) 1 month SIOOT oxygen-ozone therapy

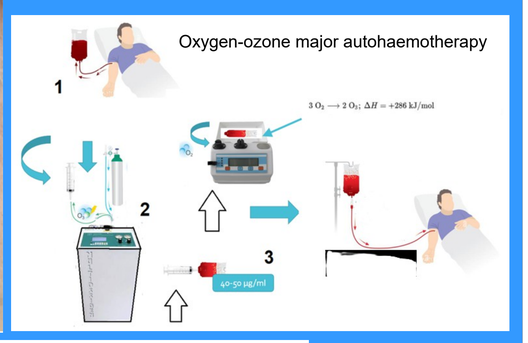


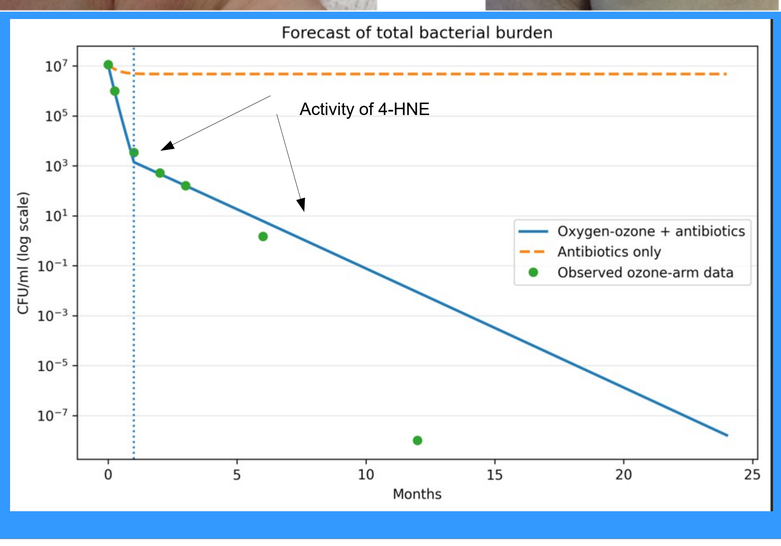
Multiossigen® instrumentation for oxygen-ozone therapy





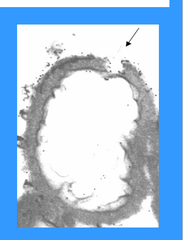
MRSA infection of a woman's shoulder, resolved after a complete cycle of oxygen-ozone major autohaemotherapy (40 µg/ml O_3)





This graph compares a modeled 24-month bacterial burden under two scenarios. The blue line (oxygen–ozone plus antibiotics) shows a steep, sustained fall in CFU/ml on a logarithmic scale, reaching near-eradication by two years max, thanks to immunity aided by ozone. The orange dashed line (antibiotics only) remains high, suggesting persistent infection and clearance, for two years.Green dots are observed data from the ozone-treated group and closely follow the blue curve, supporting the model's fit. The vertical dotted line at 1 month marks the end of active ozone treatment. Overall, the figure illustrates the study's hypothesis that adjunct oxygen–ozone therapy may accelerate bacterial reduction and improve control beyond antibiotics alone.

Conclusions. In conclusion, adjunct oxygen–ozone major autohaemotherapy was associated with rapid, sustained reductions in bacterial burden and systemic inflammation in adults with long-standing chronic multidrug-resistant infections, particularly in association with antimicrobial treatment, enhancing this latter. CFU declined markedly within 1 week, continued to fall throughout follow-up, and became undetectable in all monitored patients by 1 year, while ESR and CRP normalized by 1 month. Ozone treatment did not revert genetic resistance but improved MDR bacteria clearance and recovered complete patients' health. Because this was a small, retrospective, heterogeneous study without a concurrent control group, the findings are preliminary and require prospective controlled validation in larger cohorts.



E.coli O112 a,c damaged by antibody-mediated ozone production from immune cells (from Wenthworth jr et al., Science, 2002)

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