REVERSING ANTIBIOTIC RESISTANCE

A SCALABLE MEDICAL PLATFORM BASED ON

SIOOT OXYGEN–OZONE THERAPY

(MATERIALI E METODI)

SOCIETÀ SCIENTIFICA OSSIGENO OZONO TERAPIA

Maranno Franzini[1], Salvatore Chirumbolo[2], Giovanni Ricevuti[3], Luigi Valdenassi[1]

[1] Scientific Society of Oxygen-Ozone Therapy, Bergamo, Italy [2] Department of Engineering for Innovation Medicine, University of Verona, Italy [3] Department of Drug Science, University of Pavia, Italy

THE GLOBAL PROBLEM

- Antibiotic resistance is rapidly becoming the leading cause of death worldwide
- Current therapies are failing
- No new effective antibiotic classes are emerging
- Healthcare systems are facing collapse in infection control

THE TIME TO ACT IS NOW.

THE BREAKTHROUGH

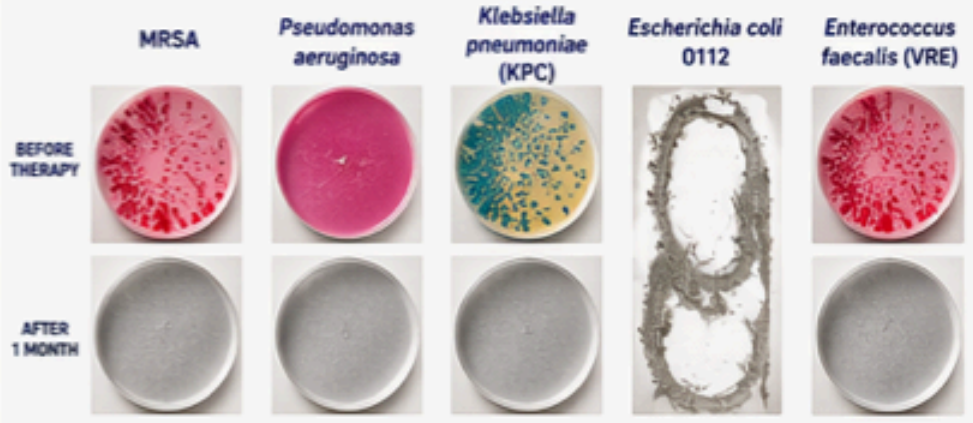
SIOOT OXYGEN–OZONE THERAPY (materiali e metodi)

A PARADIGM SHIFT IN MEDICINE

Does NOT replace antibiotics — SIOOT O_3 — Restores their effectiveness

Synergistic approach to defeat multidrug-resistant infections

MICROBIOLOGICAL ASSAYS BEFORE (LEFT) AND AFTER (RIGHT) 1 MONTH SIOOT OXYGEN–OZONE THERAPY

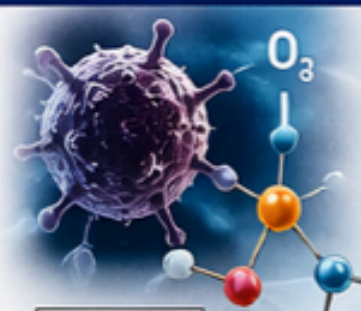


STRONG REDUCTION OF MDR BACTERIA

MECHANISM OF ACTION

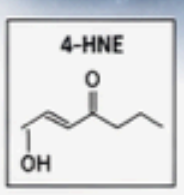
OZONE TRIGGERS IMMUNE ACTIVATION

- Stimulates immune cells (neutrophils, monocytes, macrophages)
- Induces oxidative burst and signaling pathways
- Promotes production of reactive oxygen species (ROS) and lipid aldehydes such as 4-HNE



EFFECT ON BACTERIA

- Oxidative damage to bacterial membranes, proteins and DNA
- Disruption of biofilms
- Reduction of virulence and antimicrobial resistance

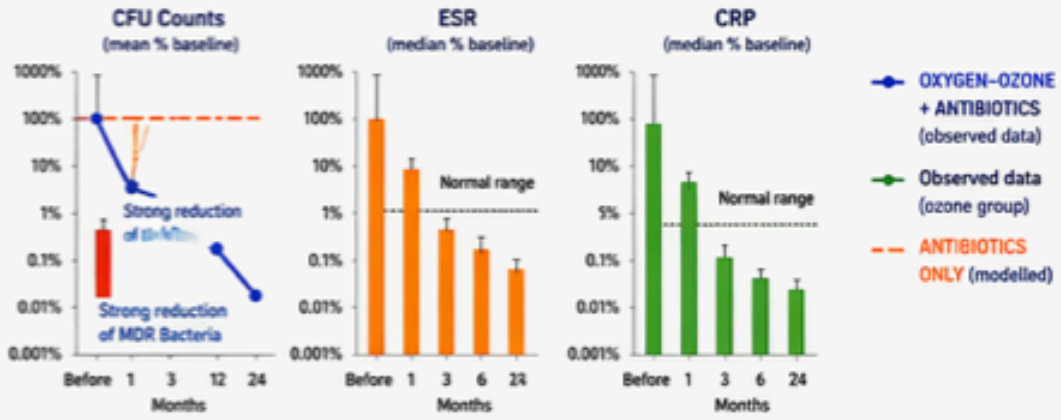


4-HNE KEY OXIDATIVE MEDIATOR



IMMUNITY + OZONE = RESTORED CONTROL OVER INFECTIONS

SUMMARY OF LONGITUDINAL PATIENT RESPONSE (MODELLED 24-MONTH BURDEN)



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.

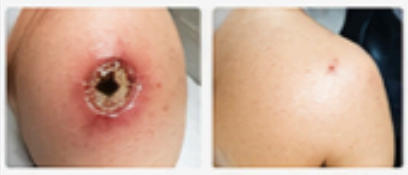
CLINICAL EVIDENCE

- Significant reduction of multidrug-resistant bacteria
- Sustained improvement up to 1 year
- Normalization of inflammatory markers: CRP and ESR
- Well tolerated and safe

In cohort studies and parallel single-patient analysis, SIOOT (materials and methods) combined with antibiotics showed significant microbiological and clinical improvement in MDR infections, with long-term benefits.

CLINICAL CASE – MRSA

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

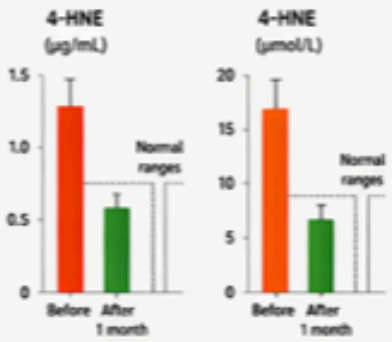


BEFORE THERAPY AFTER THERAPY

Full clinical case and follow-up data available on request

INFLAMMATORY MARKERS

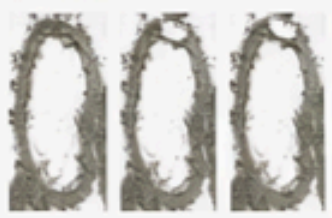
Activity of 4-HNE



Significant normalization of 4-HNE consistent with reduced oxidative stress and restored homeostasis.

E. coli 0112a:c

damage by antibody-mediated ozone production from immune cells (from Wentworth jr et al., Science, 2002)



SIOOT TECHNOLOGY

Multiossigen® instrumentation for oxygen–ozone therapy



BIBLIOGRAPHY – SIOOT (MATERIALI E METODI)

1. P. Wentworth, J. E. McDunn, A. D. Wentworth, C. Takeeuchi, J.Nieva, T. Jones, C. Bautista, J. M. Ruedi, A. Guitierrez, K. D. Janda, B. M. Babior, Al Eschenmoser, R. A. Lerner – Evidence for Antibody Catalized Ozone Formation in Bacterial Killing and Inflammation – SCIENCE Vol. 298 13.12.2002
2. Ranjbar R, Alam M. Antimicrobial Resistance Collaborators (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Evid Based Nurs. 2023 Jul 27:ebnurs-2022-103540.
3. Duckworth G. Clinical implications of antimicrobial resistance: how big is the problem? Int J Infect Dis. 2002 Mar;6 Suppl 1:S1-7.
4. Youssef Y, Hättich A, Klepka KL. Periprosthetic joint infections - a scoping review. Innov Surg Sci. 2024 Nov 20;9(4):191-197.
5. de Buys M, Moodley K, Cakic JN, Pietrzak JRT. Staphylococcus aureus colonization and periprosthetic joint infection in patients undergoing elective total joint arthroplasty: a narrative review. EFORT Open Rev. 2023 Sep 1;8(9):680-689.
6. Zimmerli W, Sendi P. Orthopaedic biofilm infections. APMIS. 2017 Apr;125(4):353-364.
7. Gbejuade HO, Lovering AM, Webb JC. The role of microbial biofilms in prosthetic joint infections. Acta Orthop. 2015 Apr;86(2):147-58.
8. Banerjee B, Thompson C, Nizet V, Bjånes E. Bactericidal efficacy of low dose gaseous ozone against clinically relevant multidrug-resistant bacteria. Front Microbiol. 2024 Dec 11;15:1480433.
9. Astuti SD, Pertiwi WI, Wahyuningsih SPA, Permatasari PAD, Nurdin DZI, Syahrom A. Effectiveness of ozone-laser photodynamic combination therapy for healing wounds infected with methicillin-resistant Staphylococcus aureus in mice. Vet World. 2023 May;16(5):1176-1184.
10. Rangel K, Cabral FO, Lechuga GC, Carvalho JPRS, Villas-Bôas MHS, Midlej V, De-Simone SG. Potent Activity of a High Concentration of Chemical Ozone against Antibiotic-Resistant Bacteria. Molecules. 2022 Jun 22;27(13):3998.
11. Silva V, Peirone C, Amaral JS, Capita R, Alonso-Calleja C, Marques-Magallanes JA, Martins Â, Carvalho Â, Maltez L, Pereira JE, Capelo JL, Igrejas G, Poeta P. High Efficacy of Ozonated Oils on the Removal of Biofilms Produced by Methicillin-Resistant Staphylococcus aureus (MRSA) from Infected Diabetic Foot Ulcers. Molecules. 2020 Aug 7;25(16):3601.
12. Chirumbolo S, Masiello G, Franzini M, Richelmi T, Tirelli U, Valdenassi L. The ability of ozone to counteract multidrug-resistant bacteria if used as an adjunct therapy: a bioinformatic modelling. J Med Microbiol. 2025 Jun;74(6):002035.
13. Chirumbolo S, Valdenassi L, Tirelli U, Pandolfi S, Franzini M. The use of the medical ozone in the immune challenge of multidrug resistant (MDR) bacteria and the role of mitochondria. Microbes Infect. 2024 Jan-Feb;26(1-2):105242.
14. Ioannidis M, Tjepkema J, Uitbeijerse MRP, van den Bogaart G. Immunomodulatory effects of 4-hydroxynonenal. Redox Biol. 2025 Sep;85:103719.
15. Chirumbolo S, Valdenassi L, Tirelli U, Ricevuti G, Pandolfi S, Vaiano F, Galoforo A, Loprete F, Simonetti V, Chierchia M, Bellardi D, Franzini M. The Oxygen-Ozone Adjunct Medical Treatment According to the Protocols from the Italian Scientific Society of Oxygen-Ozone Therapy: How Ozone Applications in the Blood Can Influence Clinical Therapy Success via the Modulation of Cell Biology and Immunity. Biology (Basel). 2023 Dec 11;12(12):1512.
16. Franzini M, Valdenassi L, Pandolfi S, Tirelli U, Ricevuti G, Chirumbolo S. The Role of Ozone as an Nrf2-Keap1-ARE Activator in the Anti-Microbial Activity and Immunity Modulation of Infected Wounds. Antioxidants (Basel). 2023 Nov 8;12(11):1985.
17. Cascini F., Franzini M, Andreoli A, Manzotti A., Cadeddu C., Quaranta G., Gentili A. Ricciardi W. Use of oxygen-ozone therapy to improve the effectiveness of antibiotic treatment on infected arthroplasty: protocol for a superiority, openlabel, multicentre, randomised, parallel trial, BMJ OPEN 2024. 14e076739 doi 10.1136 2023-076739
18. Cenci A, Macchia I, La Sorsa V, Sbarigia C, Di Donna V, Pietraforte D, Mechanisms of Action of Ozone Therapy in Emerging Viral Diseases: Immunomodulatory Effects and Therapeutic Advantages With Reference to SARS-CoV-2. Frontiers. 2022 Apr 21. 10.3389/fmicb.2022.871645
19. Cenci A, Carella C, Macchia I, La Sorsa V, Giancristofaro S, Pagnotta M, Pietraforte D, Sanchez M, Zini M, Cairo G, Fabiani M, Monaco M, Del Grosso M, Camilli R, Errico G, Pandolfi S, Valdenassi L, Franzini M, Bactericidal action and in vitro immunomodulatory effects of ozone on methicillin-resistant Staphylococcus aureus (MRSA).

WE ARE NOT DEVELOPING A NEW DRUG.

WE ARE RESTORING THE EFFECTIVENESS OF ALL EXISTING ANTIBIOTICS.

CONTACT
Mariano Franzini
info@ossigenoozono.it

SIOOT INTERNATIONAL
Bergamo, Italy
www.ossigenoozono.it