The use of ozone in dentistry and maxillofacial surgery: A review

Stefan Stübinger, Dr med dent¹/Robert Sader, Dr med, Dr med dent¹/ Andreas Filippi, Dr med dent³

Ozone has been successfully used in medicine because of its microbiologic properties for more than 100 years. Its bactericide, virucide, and fungicide effects are based on its strong oxidation effect with the formation of free radicals as well as its direct destruction of almost all microorganisms. In addition, ozone has a therapeutic effect that facilitates wound healing and improves the supply of blood. For medical purposes, ozone may be applied as a gas or dissolved in water. Despite the advantages that the therapeutic use of ozone offers, reservations remain in terms of its application in the oral and maxillofacial area. Particularly, the gaseous application of ozone is critically evaluated because of its possible side effects on the respiratory system. The objective of this article is to provide an overview of the current applications of ozone in dentistry and oral surgery. Research was based on peer-reviewed sources found through a Medline/PubMed search and other textbooks, reviews, and journals. (*Quintessence Int 2006;37:353–359*)

Key words: caries, dentistry, disinfection, germs, microbiologic effect, oxidation, ozone, soft tissue, surgery

Ozone (O_3 , molecular weight of 47.98 g/mol) is a triatomic, endothermic, and thermody-

'Assistant/Dentist, University Clinic for Reconstructive Surgery, Department of Cranio- and Maxillofacial Surgery, University Hospital Basel, Basel, Switzerland.

Professor/Oral and maxillofacial surgeon, Department of Oral Surgery, Oral Radiology, and Oral Medicine, University of Basel, Basel, Switzerland.

"Professor/oral surgeon, Department of Oral Surgery, Oral Radiology, and Oral Medicine, University of Basel, Basel, Switzerland

Reprint requests: Dr Stefan Stübinger, University Clinic for Reconstructive Surgery, Department of Cranio- and Maxillofacial Surgery, University Hospital Basel, Spitalstrasse 21, CH-4031 Basel, Switzerland, Fax; 41 61 265 7458. E-mail: sstuebinger@uhbs.ch namically highly instable oxygen compound that, dependent on system conditions like temperature and pressure, decomposes to pure oxygen with a short half-life. The decomposition produces, apart from molecular oxygen, atomic oxygen,¹ which is highly reactive; oxidizes all nonnoble metals immediately; and attacks numerous organic compounds as a radical.² This makes ozone, apart from fluorine, one of the strongest oxidants.³ Its oxidation effect ranges clearly above that of molecular oxygen. Therefore, materials used in ozone production or processing must be ozone-resistant.

Dissolved in water, ozone is relatively instable. Its decomposition rate, which may

range from seconds to hours,^{4,5} is essentially dependent on the quality of water (purity of water) and system conditions (temperature, mechanical movement of the water, vessel material).⁶ During the decomposition in water, hydroxyl (OH) is formed as a second oxidant accelerating the decomposition process of ozone,⁷

At room temperature, ozone is a blue gas with a characteristic smell that can still be noticed in air at a concentration of 2 ppm. Gaseous pure ozone passes the mucous membrane of the upper respiratory tracts essentially without absorption and can therefore reach the unprotected bronchioli and alveoli directly.8 Ozone oxidizes parts from sulfhydryl groups of enzymes, peptides, and proteins of certain lipoproteins on cell membranes, which causes an accumulation of toxic intermediate products like free radicals and peroxides. These can lead to vascularinflammatory damage of the bronchioli and alveoli walls, forming fibrinous coats and destroying the surfactant.9 Particularly, the oxidative reactions of ozone with unsaturated fatty acids and phospholipids on membrane surfaces and erythrocytes have been described several times.10,11 Long-time exposure to high ozone concentrations can cause an acute collapse of the alveoli and bronchioli and potentially irreversible damage of the alveoli function.12,13

However, pure ozone is not used for medical purposes; a mixture of ozone and oxygen or a solution of ozone in distilled and demineralized water is used. The ozone-oxygen mixture is very tissue-friendly, revealing a positive effect on the flow properties of blood. It is based on a structural modification of the erythrocyte membrane that causes an inhibition of the surface Na*-K* adenosinetriphosphatase (ATPase).¹⁴ The effect of ozone on the erythrocytes changes the proteins of the cytoskeleton and increases the elastic molding properties of the membrane in dependence on the concentration.¹⁵ This prevents adhesions between erythrocytes; their improved elasticity facilitates their passage through fine capillaries.

Apart from stimulating the blood flow, ozone also has strong bactericide, virucide, and fungicide effects,^{16,17} making it a possible

therapeutic agent in inflammatory and infectious diseases.18,19 Intraorally it can be used for the treatment of chronic periodontitis, caries, infections after tooth extractions, chronic wound-healing impairments after radiotherapy, aphthae, mycoses, or root canal disinfection.20-22 The current use of ozone for oral soft and hard tissue application is summarized in this article. For gathering the vitally important information for this article a Medline/Pubmed search was performed, setting the emphasis on peerreviewed dental and medical journals containing the terms ozone, surgery, caries, dentin, microbiological effect, and oral. Additionally, common textbooks, reviews, and open source journals were scrutinized.

CLINICAL APPLICATION

Molecular level effects of ozone

Ozone was first investigated in 1933 by the Zürich dentist Fisch for the treatment of infected wound cavities and chronic periodontal infections.23 Ozone has a broad antimicrobiologic spectrum24 and a strong disinfecting effect²⁵ superior to that of chlorinated water.26 Ozone dissolves better in water than does oxygen, even if the solubility quotient is stated differently.27 However, ozone does not have the same strength on all germs, and there is a difference in action between applications involving individual bacteria and complete bacterial strains.28 For example, enteroviruses and rotaviruses,29 hepatitis A,30 and human immunodeficiency viruses31,32 are more ozone-sensitive than poliomyelitis and coxackieviruses.33 The main antiviral actions of ozone are the change of the capsid and the irreversible destruction of viral DNA.34 In bacterial cultures, Escherichia coli and Candida albicans are by far more ozone-sensitive than staphylococci.35 Apart from an inhibition of their metabolic activity, the cell walls of bacteria are primarily damaged.36 Current results have shown that bacteria can be completely destroyed by ozone-produced antibodies.37 A study on human pathogenic germs showed the effectiveness of local ozone gas



application in bone surgery.³⁸ By the formation of peroxides on the surface of the mucous membrane, ozone is stimulating gluthation peroxidase, catalase, and superoxide dismutase.³⁹ This leads to enhanced phagocytosis.⁴⁰

These antimicrobial properties make ozone an effective therapeutic agent for gingivitis or periodonitis.⁴¹ The application of ozonated water in the peridontal ligament has revealed good results.⁴² But, despite the promising results, no further clinical or experimental studies concerning ozone and periodontitis are currently known in the English literature.

Effects of ozone on bone and soft tissues

In oral surgery ozonated water is suitable for prophylactic applications against infections after osteotomies. In a prospective study involving 250 patients, the application of ozonated water during surgery as a cooling and rinsing medium in the osteotomy of third molars reduced the occurrence of infectious complications after the operation.43,44 In another prospective study, the positive effect of ozone water in oral soft tissue healing could be demonstrated clinically and histologically.45 Apart from the microbiologic effect, a therapeutic one must also be assumed. Several experimental studies on blood treated with ozone showed that the contact with ozone led to an increased release of interferons (IFN- α , - β , - γ), interleukins (IL-1β, IL-2, IL-6, IL-8), tumor necrosis factor (TNF- α), as well as transforming growth factor (TGF-B1).46-50 In addition, ozone improves the rheologic properties of erythrocytes and facilitates oxygen release in tissue,51 which can be attributed to the stimulation of 2.3-diphosphoglycerate and adenosine triphosphate (ATP) production in the erythrocyte metabolism.62,53 In addition, it was possible to show in reinfused ozonated serum that an increased nitosyl reduction results in human endothelial cells, leading to a vasodilatation of vessels with an improved supply of blood to ischemic zones or to a reduction of a hypoxia.54

Particularly after radiotherapy in the maxilla or mandible, oxygen supply may be con-

siderably reduced in the affected area: Apart from numerous intraoral side effects like xerostomia, mucositis, or loss of the sense of taste,55 the obliteration of intraosseous vessels is caused, resulting in a deficient vascular supply of the spongy medullary spaces. The consequences are fibrosing and aseptic osteonecrosis. Such compromised bone as that after surgical interventions like tooth extractions⁵⁶ or implant dentistry⁵⁷ heals later than does healthy bone with a good blood supply. Also, surface wounds, eg, caused by denture pressure, frequently heal much later. Such cases always carry the risk of a persisting osteoradionecrosis.58,59 Ozone might possibly be successfully used to treat such wound-healing impairments after radiotherapy. A clinical survey involving 11 radiotherapy patients demonstrated the local effectiveness of ozone in intraoral infected wounds after high-dose radiotherapy.60 The wound areas of about 1 to 3 cm² were covered by necrotic tissue and superinfected. For 4 days, an ozone-oxygen mixture (3%) with an ozone concentration of 59 µg/mL was applied daily for 15 minutes under vacuum (1.5 bar) via a custom-made suction cup with respective feed and discharge tubes. Subsequently, the mixture was reduced to 30 µg/mL (1.5%) until the wound had completely healed. Prior to the therapy the wounds were curetted and cleaned. The result was significant hyperemia in the wound area as well as complete healing in nine patients.

The literature also contains varving results in relation to ozone application for the treatment of wound-healing impairments or severe skin reactions after radiotherapy outside of the oral cavity. While some authors report good results after ozone application,61,62 a study group basing its findings on the evaluation of statements of the nursing staff and the treated patients could not recognize any properties of ozone promoting wound healing.63 The patients of the same study reported, however, a pain-alleviating effect of ozone, which had been described earlier.54 It should be mentioned, however, that simultaneously with the ozone therapy a drug therapy was performed so that it was not possible to evaluate the single action of ozone.



Stübinger et al

Apart from osteoradionecrosis, chronic and refractory osteomyelitis in the head-neck area can also be difficult to treat.65,66 Also in this case, diffusion hypoxia results with reduced vascular blood supply and subsequent destruction of bone tissue. Several gram-positive and gram-negative germs are involved in an acute or chronic osteomyelitis67 in which staphylococcus aureus is considered problematic and methicillin-resistant.68 It could be shown that ozone has a good microbiological effect on methicillin-resistant strains of Staphylococcus aureus.69 This potentially could make ozone an alternative to hyperbaric oxygen therapy after the removal of the bone sequestra.⁷⁰ Its action is based, on the one hand, on the enormous oxidation strength and, on the other hand, on the fact that bacteria can be more easily recognized and destroyed by granulocytes and the complement system after contact with ozone,71,72 as well as on an increased phagocytosis performance of polymorphonuclear cells.73

Application of ozone in endodontics, treatment of dental caries, and prosthodontics

The oral application of ozone, however, is not limited to surgery. It is also applied in endodontics and prosthodontics.74,75 Apart from the well-examined water disinfection of dental units,76,77 gaseous ozone is particularly suited for caries therapy.78,79 An in vitro survey showed the bactericide effect of ozone on Streptococcus mutans and Streptococcus sobrinus.80 In comparison to a control group, a blood agar demonstrated a significant reduction of the 2 germs responsible for caries after 10 seconds of ozone gas application. Furthermore, it was shown that the microorganisms were reduced to less than 1% in 40 freshly extracted teeth with a slight incidence of root caries after 10 or 20 seconds of ozone water application as compared with a control group. These results correspond to the positive findings of other study groups⁸¹: In a study involving 89 patients with primary root caries, ozone application led to a complete arrest or hardening of caries in the sense of remineralization after ozone application of 18 months. A control group showed a deterioration of the original caries lesions. These results raise the hope for a new approach to caries therapy, facilitating, particularly in pediatric dentistry, a treatment free of anxiety and stress.⁸² Controlled long-term studies in caries therapy with ozone are, however, still not available.

Another area of ozone use in dentistry would be the decontamination of root surfaces of teeth avulsed in accidents prior to replantation. A study on 23 extracted third molars showed immunohistochemically that the proliferation rate of cementoblasts and periodontal fibroblasts were not affected by the rinsing of the root surface with ozonated water for 1 minute as compared with sterile isotonic natrium solution.83 Moreover, a slight increase in the proliferation rate was noted under ozone influence. This could have been observed on the epithelium, too, as confirmed by the results of other study groups⁸⁴: Nonisotonic ozone water does not have any negative effect on the cells of the root surface at an exposure time of less than 2 minutes. These results raise the hope of future application of ozone in tooth transplantation or replantation and regenerative periodontal therapy.

In implant dentistry, the use of ozone is currently being investigated for the decontamination of the implant surface in periimplant therapy (not as the sole therapy, but only for the removal of microorganisms).⁸⁵

Furthermore, the disinfecting action of ozone is used to clean dentures.⁸⁶ The action of ozone on the typical oral germs of S mutans (strain IID 973), Sta aureus (strain 209-P), and C albicans (strain LAM 14322), which are also found on dentures, have been investigated.87 Apparently gaseous ozone revealed a more effective antimicrobial action than ozonated water and thus is more recommendable for denture cleaning. Similar results have been reported about denturecleaning solutions enriched with ozone (concentration 10 ppm) against methicillin-resistant Sta aureus and E coli T1 phage strains.88 All available studies show the effective bactericide, virucide, and fungicide action of ozone.

356

CONCLUDING REMARKS

- Despite the positive properties of ozone gas or ozonated water—not only in waste water and pool water treatment but also in many fields of medicine—the use of ozone in oral and maxillofacial surgery is considered rather limited to date. This might be due, on the one hand, to the described possible side effects of ozone gas on the upper respiratory system during intraoral applications and, on the other hand, to the few long-term studies in the English literature.
- The intraoral use of ozone must be performed by preventing ozone from getting into the respiratory air of the patient. This may be achieved by suction cups or vacuum caps.
- 3. The information related to proper ozone therapeutic dosage is controversial.
- Initial data indicates promising potential of ozone usage for the treatment of certain carious lesions.
- Additional clinical trials are needed to validate the feasibility and safety of routine usage of ozone in dentistry and oral and maxillofacial surgery.

REFERENCES

- Stockburger D. Ozon-Therapie-Grundlagen und Technik der Ozonbehandlung. München: Foitzick, 2002.
- Fan Z, Lioy P, Weschler C, Fiedler N, Kipen H, Zhang J. Ozone-initiated reactions with mixtures of volatile organic compounds under simulated indoor conditions. Environ Sci Technol 2003;37:1811–1821.
- Eliakim R, Karmeli F, Rachmilewitz D, Cohen P, Zimran A. Ozone enema: A model of microscopic colitis in rats. Dig Dis Sci 2001;46:2515–2520.
- Hoigne J. Chemistry of aqueous ozone, and transformation of pollutants by ozonation and advanced oxidation processes. In: Hubrec J (ed). The Handbook of Environmental Chemistry Quality and Treatment of Drinking Water. Berlin: Springer, 1998.
- Stettler R, Courbat R, von Gunten U, et al. Utilisation de l'ozone pour le traitement des eaux potables en Suisse. Gas Wasser Abwasser 1998;78:76–89.
- Sehested K, Corfitzen H, Holcman J, Fischer CH, Hart EJ. The primary reaction in the decomposition of ozone in acidic aqueous solutions. Environ Sci Technol 1991;25:1589–1596.

- Staehelin J, Hoigne J. Decomposition of ozone in water: Rate of initiation by hydroxide ions and hydrogen peroxide. Environ Sci Technol 1982;16: 676–681.
- Mehlman MA, Borek C. Toxicity and biochemical mechanisms of ozone. Environ Res 1987;42:36–53.
- Uhlson C, Harrison K, Allen CB, Ahmad S, White CW, Murphy RC. Oxidized phospholipids derived from ozone-treated lung surfactant extract reduce macrophage and epithelial cell viability. Chem Res Toxicol 2002;15:896–906.
- Santrock J, Gorski RA, O'Gara JF. Products and mechanism of the reaction of ozone with phospholipids in unilamellar phospholipid vesicles. Chem Res Toxicol 1992;5:134–141.
- Pryor WA, Das B, Church DF. The ozonation of unsaturated fatty acids: Aldehydes and hydrogen peroxide as products and possible mediators of ozone toxicity. Chem Res Toxicol 1991;4:341–348.
- Werkmeister H. The efficacy of O2/O3 low-pressure application in badly healing wounds. [Proceedings of the Tenth World Ozone Conference, 1991, Monaco]. Monaco: Int Ozone Assoc, 1991.
- Goldstein BD. The pulmonary and extrapulmonary effects of ozone. Ciba Found Symp 1978;6:295–319.
- Tukel SS, Bilgin R, Gul S. Effects of ozone on the activity of erythrocyte membrane Na(+)-K+ ATPase. Biochem Mol Biol Int 1994;33:1033–1040.
- Gornicki A, Gutsze A. In vitro effects of ozone on human erythrocyte membranes: An EPR study. Acta Biochim Pol 2000;47:963–971.
- Emerson M, Sprone OJ, Buck CE. Ozone inactivation of cell-associated viruses. Appl Environ Microbiol 1982;43:603–608.
- Dyas A, Boughton BJ, Das BC. Ozone killing action against bacterial and fungal species: Microbiological testing of a domestic ozone generator. J Clin Pathol 1983;36:1102–1104.
- Margalit M, Attias E, Attias D, Elstein D, Zimran A, Matzner Y. Effect of ozone on neutrophil function in vitro. Clin Lab Haematol 2001;23:243–247.
- Di Paolo N, Bocci V, Cappelletti F, Petrini G, Gaggiotti E. Necrotizing fasciitis successfully treated with extracorporeal blood oxygenation and ozonization (EBOO). Int J Artif Organs 2002;25:1194–1198.
- Schmidlin PR, Zimmermann J, Bindl A. Effect of ozone on enamel and dentin bond strength. J Adhes Dent 2005;7:29–32.
- 21. Baysan A, Lynch E. The use of ozone in dentistry and medicine. Prim Dent Care 2005;12:47–52.
- Nagayoshi M, Kitamura C, Fukuizumi T, Nishihara T, Terashita M. Antimicrobial effect of ozonated water on bacteria invading dentinal tubules. J Endod 2004;30:778–781.
- Fisch EA. Die ozontherapie in der Zahn-, Mund-, Kleferheilkunde [thesis]. Bonn, Germany: Rheinische Friedrich Wilhelms Universität, 1934.
- 24. Wallhäußer KH. Praxis der Sterilisation-Desinfektion-Konservierung. Stuttgart: Thieme, 1995.

Stübinger et al

- Bocci V.Ozone as a bioregulator. Pharmacology and toxicology of ozonetherapy today. J Biol Regul Homeost Agents 1996;10:31–53.
- Fischer P, Thofen E, Botzenhart K. Vergleichende Untersuchungen zur Wirksamkeit von Chlor und Ozon auf Bakterien und Sporen. Zentralbl Bakteriol Orig B 1978;166:399–407.
- Langlais B, Reckhow D, Brink D. Ozone in Water Treatment. Chelsea, Michigan: Lewis, 1991.
- Kowalski WJ, Bahnfleth WP, Whittam TS. Bacterial effects of high airborne ozone concentrations on Escherichia coli and Staphylococcus aureus. Ozone Sci Eng 1998;20:205–221.
- Vaughn JM, Chen YS, Lindberg K, Morales D. Inactivation of human and simian rotaviruses by ozone. Appl Environ Microbiol 1987;53:2218–2221.
- Vaughn JM, Chen YS, Novotny JF, Strout D. Effects of ozone treatment on the infectivity of hepatitis A virus. Can J Microbiol 1990;36:557–560.
- Carpendale MT, Freeberg JK. Ozone inactivates HIV at noncytotoxic concentrations. Antiviral Res 1991; 16:281–292.
- Wells KH, Latino J, Gavalchin J, Poiesz BJ. Inactivation of human immunodeficiency virus type I by ozone in vitro. Blood 1991;78:1882–1890.
- Thraenhart C, Kuwert E. Vergleichende Untersuchungen über die Wirkung von Clor und Ozon auf Polioviren bei der Trinkwasseraufbereitung der Stadt Essen. Zentralbl Bakteriol Orig B 1975;160: 305–341.
- Roy D, Wong PK, Engelbrecht RS, Chian ES. Mechanism of enteroviral inactivation by ozone. Appl Environ Microbiol 1981;41:718–723.
- Häufele A, von Sprockhoff H. Ozon als Desinfektionsmittel gegen vegetative Bakterien, Bazillensporen, Pilze und Viren in Wasser. Zentralbl Bakteriol Orig B 1973;157:53–70.
- Bünning G, Hempel D. Vital-fluorochromization of microorganisms using 3',6'-diacetylfluorescein to determine damages of cell membranes and loss of metabolic activity by ozonation. Ozone Sci Eng 1996;18:173–181.
- Wentworth P Jr, McDunn JE, Wentworth AD, et al. Evidence for antibody-catalysed ozone formation in bacterial killing and inflammation. Science 298 2002;5601:2195–2199.[Au: What is "298"?]
- Gehring W, Glutsch J, Schönian U, Gehse M, Gloor M. Vergleichende Untersuchung über die Wirkung verschiedener Antiseptika und der Ozonbegasung auf Ulcus-cruris-übliche Keime. Z Hautkrankh 1990;65: 746–750.
- Larini A, Bianchi L, Bocci V. The ozone tolerance: I) Enhancement of antioxidant enzymes is ozone dose-dependent in Jurkat cells. Free Radic Res 2003;37:1163–1168.
- Rilling S, Viebahn R. Praxis der Ozon-Sauerstoff-Therapie. Heidelberg, Germany: E. Fischer, 1990.
- Brauner AW. Periodontology: New methods. Ozone Sci Eng 1992;14:165–176.

- Brauner A. Klinische Untersuchung über den therapeutischen Erfolg von ozoniertem Wasser bei Gingivitis und Parodontitis. Zahnärzt Praxis 1991; 42:48–50.
- Filippi A. Lokalbehandlung von Ostitis circumscripta mit ozoniertem Olivenöl. Quintessenz 1993;44: 1531–1537.
- Filippi A. Klinisch-experimentelle Untersuchungen zur Wundheilung von Oralgeweben unter Einfluss von Ozonwasser. Giessen, Germany: Habil, 1999.
- Filippi A. Der Einfluss von ozoniertem Wasser auf die epitheliale Wundheilung. Dtsch Zahnärztl Z 2001; 56:104–108.
- Bocci V, Paulescu L. Studies on the biological effects of ozone: 1. Induction of interferon γ on human leukocytes. Haematologica 1990;75:510–515.
- Bocci V, Luzzi E, Corradeschi F, Silvestri S. Studies on the biological effects of ozone: 6. Production of transforming growth factor 1 by human blood after ozone treatment. J Biol Regul Homeost Agents 1994;8:108–112.
- Bocci V, Luzzi E, Corradeschi F, et al. Studies on the biological effects of ozone: 4. Cytokine production and glutathione levels in human erythrocytes. J Biol Regul Homeost Agents 1993;7:133–138.
- Bocci V, Valacchi G, Corradeschi F, Fanetti G. Studies on the biological effects of ozone: 8. Effects on the total antioxidant status and on interleukin-8 production. Mediators Inflamm 1998;7:313–317.
- Bocci V, Luzzi E, Corradeschi F, Paulesu L, Di Stefano A. Studies on the biological effects of ozone: 3. An attempt to define conditions for optimal induction of cytokines. Lymphokine Cytokine Res 1993;12: 121–126.
- Verrazzo G, Coppola L, Luongo C, et al. Hyperbaric oxygen, oxygen-ozone therapy, and rheologic parameters of blood in patients with peripheral occlusive arterial disease. Undersea Hyperb Med 1995;22:17–22.
- Bocci V. Ozone as a bioregulator. Pharmacology and toxicology of ozone therapy today. J Biol Regul Homeost Agents 1996;10:31–53.
- Viebahn-Hänsler R. Allgemeine Eigenschaften des Ozons. In: Beck EG, Viebahn-Hänsler R (eds). Ozon-Handbuch: Grundlagen-Prävention-Therapie. Landsberg: EcoMed, 1995.
- Valacchi G, Bocci V. Studies on the biological effects of ozone: 11. Release of factors from human endothelial cells. Mediators Inflamm 2000;9:271–276.
- Vissink A, Jansma J, Spijkervet FK, Burlage FR, Coppes RP. Oral sequelae of head and neck radiotherapy. Crit Rev Oral Biol Med 2003;14:199–212.
- Sulaiman F, Huryn JM, Zlotolow IM. Dental extractions in the irradiated head and neck patient: A retrospective analysis of Memorial Sloan-Kettering Cancer Center protocols, criteria, and end results. J Oral Maxillofac Surg 2003;61:1123–1131.

- Harrison JS, Stratemann S, Redding SW. Dental implants for patients who have had radiation treatment for head and neck cancer. Spec Care Dentist 2003;23:223–229.
- Reuther T, Schuster T, Mende U, Kubler A. Osteoradionecrosis of the jaws as a side effect of radiotherapy of head and neck tumour patients—A report of a thirty year retrospective review. Int J Oral Maxillofac Surg 2003;32:289–295.
- Jereczek-Fossa BA, Orecchia R. Radiotherapyinduced mandibular bone complications. Cancer Treat Rev 2002;28:65–74.
- Sader R, Zeilhofer HF, Deppe H. Ozontherapie chronischer Wundheilungsstörungen im bestrahlten Kiefer. Dtsch Z Mund Kiefer Gesichts Chir 1996; 20:60–64.
- Church L. Ionozone therapy for skin lesions in elderly patients. Physiotherapy 1980;66:50–51.
- Dolphin S, Walker M. Healing accelerated by Ionozone therapy. Physiotherapy 1979;65:81–82.
- Jordan L, Beaver K, Foy S. Ozone treatment for radiotherapy skin reactions: Is there an evidence base for practice? Eur J Oncol Nurs 2002;6:220–227.
- Schellander F. Ozone therapy. J Altern Complement Med 1992;10:15–16.
- Hudson JW. Osteomyelitis of the Jaws: A 50-year perspective. J Oral Maxillofac Surg 1993;51:1294–1301.
- van Merkesteyn JP, Groot RH, van den Akker HP, Bakker DJ, Borgmeijer-Hoelen AM. Treatment of chronic suppurative osteomyelitis of the mandible. Int J Oral Maxillofac Surg 1997;26:450–454.
- Cunha BA. Osteomyelitis in elderly patients. Clin Infect Dis 2002;35:287–293.
- Canawati HN, Sapico FL, Montgomerie JZ, Zucchero J. Temperature effect on cephalothin sensitivity of methicillin-resistant Staphylococcus aureus. Am J Clin Pathol 1981;75:391–394.
- Yamayoshi T, Tatsumi N. Microbicidal effects of ozone solution on methicillin-resistant Staphylococcus aureus. Drugs Exp Clin Res 1993;19:59–64.
- Steinhart H, Schulz S, Mutters R. Evaluation of ozonated oxygen in an experimental animal model of osteomyelitis as a further treatment option for skull-base osteomyelitis. Eur Arch Otorhinolaryngol 1999;256:153–157.
- Jankowski S, Doroszkiewicz W. Preliminary studies of the effect of ozone on the bactericidal properties of complement. Complement Inflamm 1990;7:57–62.
- Doroszkiewicz W, Sikorska I, Jankowski S. Ozone as sensitizer of bacteria to the bactericidal action of complement. Acta Microbiol Pol 1993;42:315–319.
- Bocci V. Autohemotherapy after treatment of blood with ozone. A reappraisal. J Int Med Res 1994;22: 131–144.

- Nagayoshi M, Kitamura C, Fukuizumi T, Nishihara T, Terashita M. Antimicrobial effect of ozonated water on bacteria invading dentinal tubules. J Endod 2004;30:778–781.
- Türk A. Ozone in dental medicine. Ozonnachrichten 1985;4:61–65.
- Filippi A. Disinfection of dental units using ozonemicrobiological results after 11 years and technical problems. Ozone Sci Eng 2002;24:479–483.
- Filippi A. Water contamination in conventional and in ozone disinfected dental treatment units after a prolonged period of time between treatment. Ozone Sci Eng 2001;23:255–258.
- Noack MJ, Wicht MJ, Haak R. Lesion orientated caries treatment—A classification of carious dentin treatment procedures. Oral Health Prev Dent 2004;2 (suppl 1):301–306.
- Rickard GD, Richardson R, Johnson T, McColl D, Hooper L. Ozone therapy for the treatment of dental caries. Cochrane Database Syst Rev 2 2004;(3):CD004153.
- Baysan A, Whiley RA, Lynch E. Antimicrobial effect of a novel ozone-generating device on micro-organisms associated with primary root carious lesions in vitro. Caries Res 2000;34:498–501.
- Holmes J. Clinical reversal of root caries using ozone, double-blind, randomised, controlled 18month trial. Gerodontology 2003;20:106–114.
- Dähnhardt JE, Lussi A. Rund ums Ozon—in der Zahnmedizin. Zm 2004;7:40–44.
- Ebensberger U, Pohl Y, Filippi A. PCNA-expression of cementoblasts and fibroblasts on the root surface after extraoral rinsing for decontamination. Dent Traumatol 2002;18:262–266.
- Weinstein F, Worsaae N, Andreasen JO. The effect on periodontal and pulpal tissues of various cleansing procedures prior to replantation of extracted teeth. Acta Odontol Scand 1981;39:251–255.
- Krozer A, Hall J, Ericsson I. Chemical treatment of machined titanium surfaces. An in vitro study. Clin Oral Implants Res 1999;10:204–211.
- Murakami H, Sakuma S, Nakamura K, et al. Disinfection of removable dentures using ozone. Dent Mater J 1996;15:220–225.
- Oizumi M, Suzuki T, Uchida M, Furuya J, Okamoto Y. In vitro testing of a denture cleaning method using ozone. J Med Dent Sci 1998;45:135–139.
- Murakami H, Mizuguchi M, Hattori M, Ito Y, Kawai T, Hasegawa J. Effect of denture cleaner using ozone against methicillin-resistant Staphylococcus aureus and E. coli T1 phage. Dent Mater J 2002;21:53–60.