International Scientific Committee of Ozone Therapy ISCO3

Guidelines and Recommendations for Medical Professionals Planning to Acquire a Medical Ozone Generator

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Background

In June 2012, during the International Ozone Therapy Congress of AEPROMO (Spanish Association of Medical Professionals in Ozone Therapy) in Madrid, the ISCO3 held a meeting, during which it decided to produce a document to be offered to any medical professional who is planning to acquire a medical ozone generating equipment.

This decision was the consequence of multiple questioning and requests of help by medical professionals who felt unable to decide which equipment to purchase if based only on technical criteria, but would feel uncomfortable to make a choice based only on the price of the machine.

The initial text for this document was written by Heinz Konrad, M.D., who has been working for 39 years with the medical application of ozone, in Sao Paulo, Brazil. To produce these guidelines, we asked a number manufacturers of medical ozone generators worldwide for help. Not all of them were willing to cooperate and to supply the information we asked for.

The present text by no means intends to bear the ultimate truth and a total and worldwide consensus about all the topics mentioned. It is rather meant to be a help and a commercially neutral guideline for all those who plan to buy their ozone therapy equipment.

Criteria

We divided the resources and technical details into three categories:

a) Which are the components, resources and technical details **absolutely necessary** in a medical ozone generator?
b) Which are the components, resources and technical details **desirable and recommendable** in a medical ozone generator?
c) Which are the components, resources and technical details **purely optional** in a medical ozone generator?

Furthermore, we mention other, not purely technical aspects, which should also be taken into account when choosing a medical ozone generator.

Absolutely necessary

We start with the resources and technical details we consider **absolutely necessary** in a medical ozone generator. Some of these will seem obvious to most of our readers, but they must be mentioned:

The machine must produce ozone exclusively from medicinal grade, at least 99,5% pure oxygen, coming from a medical quality certified container, e.g. a high pressure cylinder. Such pure oxygen contained in industrial purposes cylinders will not qualify for medical use because the requirements of hygiene and sterility inside these cylinders are different from the medical ones.

Machines using room air, including oxygen concentrators, do not qualify for ozone therapy. Medical grade oxygen should fit the quality standard of the local Pharmacopoeia. If local Pharmacopoeia is not available, the reference Pharmacopoeia should be:
European Pharmacopoeia,[(1)]
United States Pharmacopoeia [(2)]
or Japanese Pharmacopoeia.[(3)]

The quality criteria according those Pharmacopoeias are mentioned [(4)].

There is a tendency to substitute the "old" compressed oxygen cylinders by the oxygen concentrators based on the Pressure Swing Adsorption (PSA) technology. [(10)]

All external and internal tubing, hard or flexible, as well as all external or internal connections and fittings must be made of ozone-resistant material, such as glass, 316 stainless steel, silicone, Teflon and similar plastic material. Rubber, Latex or Polyurethane tubings / connections / fittings at any point are totally inappropriate. Unfortunately, these are details a potential customer cannot verify before buying the equipment, having to rely entirely upon the information given by the manufacturer.

How far such information is really trustworthy may vary widely all over the world. An international, respectable and commercially neutral seal of certification is, therefore, a welcome help to identify quality levels of different equipments (See also bellow "certification")

The machine must be able to generate the therapeutical, i.e. homogeneous oxygen-ozone mixture with a range of ozone concentration between 05 (five) and 80(eighty) micrograms / ml. No other substances besides O_2 and O_3 may be present in the produced gas mixture.

The user must be able to easily identify and adjust the desired ozone concentration, in micrograms / ml in the gaseous mixture, with an error margin not above 10 %.[(5, 6)] This may be accomplished either by clear and easily readable lists / tables on the face of the generator, which show the produced ozone concentration according to power input and oxygen flow rate, or by digital indicators showing the ozone concentration actually measured by sensors directly before the exit nozzle.

The measurement of actual ozone output can be made in several manners:

a) Direct method, by single or double beam photometric system, and
b) Indirect method, by wet chemistry or by mathematical algorithm calculation.[5,7]

Whichever the method used, accuracy should be ± 10 % or better.

The photometric direct system measures the concentration of a gas in contact with it and will require more or less frequent adjustments and calibrations. It is precise and trustworthy. Those which use a mercury lamp may be unstable, may need more frequent calibration, and may lose precision after a time. The photometric system using LED is preferable.

The wet chemistry method is practically not feasible in a clinical environment.

The algorithm method seems to be the simplest / sturdiest method. It determines the concentration by mathematical algorithm without contact with the gas. however, its exactness will depend to great extent on the good quality of the generator's components and the technically optimal design of the whole equipment.

There is also the ultrasound method, which is able to determine both the oxygen and the ozone concentration in the gas mixture.

The equipment must have a fully reliable internal cooling / ventilation system, switched in such manner as to interrupt the ozone generation when sufficient cooling is not warranted.

The material of which the electrodes are made must be of highest quality, so as to be able to withstand long term and frequent exposure to the high electric energy as well as the oxidation which may be caused by ozone. The most recommended material for these electrodes is quartz glass.

The exit nozzle must be protected against unwanted or accidental penetration of any solid or liquid contaminants when not in use.

A syringe port must be available, allowing easy attachment and detachment of a syringe to be filled, and which will not allow any ozone to escape from the generator into the ambient air. Such syringe port must be easily disinfected.

The O3 output flow must be between 20 and 50 L/h. The output flow will determine the time the generator needs to fill a syringe or a bag. The output flow is inversely proportional to the concentration. The more modern models of medical ozone generators do not adjust the ozone output through regulating the output flow. If an ozone generator does indicate the output flow, this should be indicated in a digital manner.

There is an enormous number of technical norms and regulations established by German and/or European authorities, which govern the necessary technical apparatus for medical ozone generation. [8] Although it is not mandatory by the authorities, the buyer in Europe might consider obtaining from the vendor a "Free Sales Certificate" (FSC), a document which certifies that the equipment complies with regulations.

Also, the American Academy of Ozone-therapy (AAOT) has established its own guidelines for the technical characteristics of medical ozone generating equipment. Until the date of this publication, the US Food and Drug Administration (FDA) has yet to approve any ozone generators for medical use. [9]

Desirable and recommendable

The following resources and technical details may be considered **desirable and recommendable**:

Catalytic ozone destructor built into or directly attached to the generator, to eliminate all ozone which may flow or be pumped into it. This destructor may not use carbon as active agent, due to the risk of overheating and maybe fire / explosion.

Vacuum pump built into or directly attached to the generator, and connected directly to an ozone destructor, allowing the aspiration and immediate internal destruction of ozone from any closed compartment (e.g. "bagging" of external wounds with ozone). Such pump should have a gauge showing the actual vacuum strength.

Possibility of manual or automatic adjustment for 110 V or 220 V power input. The possibility of adjustment for 50 Hz or 60 Hz alternate current input may be technically possible; however it would certainly increase significantly the cost of the equipment.

Purely optional

The following resources and technical details may be considered **purely optional**:

Attached or easily connectable system for the ozonization of water or oil.

Manometer attached to the vacuum pump mentioned under item 2.2 above, to measure the intensity of the vacuum produced.

Possibility to adjust the intensity of vacuum, so as to adequate the function of the system to different uses (e.g.: simple aspiration of ozone from a "bagging" system around an external wound, or aspiration of fistulae, deep abscesses or cavities).

Solenoid valves to open or close the admission of oxygen and / or the output of the $O_2 – O_3$ mixture.
A timer, to switch off ozone generation after a preset time, might be interesting for processes which require ozone generation for more than only a few minutes.

Other aspects

Easy maintenance
It is necessary that the manufacturer be able to provide technical assistance in a timely and geographically acceptable manner.

Calibration
Most professionals argue in favor, but many argue against the absolute necessity of regular, at least annual intervals for calibration of the ozone generators. Opinions are really very different or contradictory at times.

Many professionals argue that the simpler the generator's technical design and the less automatic and / or electronic circuitry devices it contains, the less maintenance and / or calibration it will require. There are already generators which include a direct LED photometric system *and* an indirect system in the same machine, thus offering highest quality level and reducing the frequency of necessary calibration.

Given the importance of doses in ozone therapy, it seems recommendable, however, to have the equipment checked periodically, according to the geographic and "administrative" possibility.

The use of a calibrated external spectrophotometer is a relatively simple method for calibration of the equipment *in loco*. Ideally, the manufacturer should supply the buyer a "Maintenance Book", containing instructions not only for the use but also for the adequate maintenance of the equipment, and in which any repair or calibration service made can be registered.

Certification
In most western countries, medical ozone generators must have a seal of approval or Certification of Medical Device, given by some public or equivalent institution. Naturally, the criteria for equipment inspection, testing and approval vary from country to country, or from one to another economic or geopolitical block.

Presently, it seems that the European Certificate is the most demanding and comprehensive one.

The Russian certification is also said to obey rather strict rules, however, as far as we know, the Russian rules for medical ozone generators are only recognized in Russia and its satellite nations.

As to the United States of America and Canada, we understand that there are several brands of ozone generators being produced and sold for medical use, but there seems to be much disagreement as to the actual quality of such generators, especially because many contain cheap components produced in far East countries.

In the United States quality and safety of the product can only be confirmed if the product carries a local Quality and Safety Approval, such as ETL, CSA, UL or QAI Approval. Products lacking a Quality and

Safety Approval should be avoided. As far as we know, the generators in use in the now 15 American states where some form of ozone therapy is permitted are mostly produced abroad, mainly in Canada and Europe.

Recently, a number of manufacturers have started medical ozone generator production in China, and more recently a Chinese ruling has been issued regarding the quality and safety standards for such equipment. In Latin America, we know of no country, besides Cuba, which has official approval and certification already established. Cuba, as far as we know, produces all medical ozone generators for its own use and does have a set of standards that must be locally followed.

A new European regulation RoHS (Restriction of Hazardous Substances) will mandatory apply from July 2014 to all electrical appliances therefore attention must be paid before purchasing a new medical ozone generator because non compliant devices will have a very short life due to foreseeable lack of spareparts. Purchaser must ask the vendor for a RoHS conformity certificate to protect his investment.

Concluding remarks

Understanding the machine
It is important that the buyer and future user of such equipment be well aware of the physical principles and technical details of the machine, as well as its natural limitations. Equally, the buyer needs to have very well established goals / uses / purposes for which he or she wishes to use the equipment.

Technical support
When deciding for equipment, the buyer must also consider the availability and distance from technical a support facility in his geographical area.

Stay in touch!
It can be taken for granted that questions of technical or medical nature will arise during the use of such newly acquired equipment. Therefore it is highly recommendable that the buyer pursuits a good relationship with the vendor, and, last not least, with ISCO3, this more experienced medical community, who has all the know-how, the capacity and the good will to guide, teach and support the colleagues all over the world.

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Mrs. Karin Herrmann. HERRMANN Apparatebau GmbH, O_3 generators, Kleinwallstadt, Germany.

Mr. Manuel Delgado. Ozone-Healthcare Division Manager. SEDECAL S.A., Spain.

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4) *European industrial gases association AISBL*. Comparison of European, US & Japanese pharmacopoeia monographs for medicinal gases. MGC Doc 152/11/E Revision of Doc 152/08. Avenue des Arts 3-5 B 1210 Brussels. www.eiga.eu [Revised 07/06/2013]

5) Kerwin Raknessl, Gilbert Gordonz, Bruno Langlaiss, *et al*. *Guideline for Measurement of Ozone Concentration in the Process Gas From an Ozone Generator*. Ozone Science and Engineering *1996;*18:209-229.

6) Gregorio Martínez Sánchez. Aspectos prácticos en ozonoterapia: Comprobación de la concentración de ozono generada / tiempo de vida media del gas en la jeringuilla. [Practical aspects of ozone therapy: Checking the generated ozone concentration / average lifetime of gas in the syringe]. *Revista Española de Ozonoterapia*, 2013, 3 (1): 67-73.

7) Delgado, M. *Ozone concentration measurements. State of the art*. Revista Española de Ozonoterapia 2011;1(1): 87-92.

8) DIN EN ISO 13485, DIN EN ISO 13971, DIN EN 60601-1-2, EN 62366, DIN EN 980, DIN EN ISO 11135-1, DIN EN ISO 11138-1, DIN EN ISO 11138-2, DIN EN ISO11737-1, DIN EN 556-1, DIN EN ISO 17665-1:2006, DIN EN ISO 11607-1, DIN EN ISO 11607-2, DIN EN 868-2, DIN EN 868-3, DIN EN 868-5, DIN EN 15986, DIN EN 1041, DIN 58369:1996, DIN EN ISO 10993-1, DIN EN ISO10993-7, DIN EN ISO 17665-1:2006, MEDDEV 2.7.1 Rev 3, USFDA LAL – Test Guideline, DIN EN ISO 19011, and especially MDD 93/42.

ISO - *International Standardization Organization*
DIN – *Deutsche Industrie Norm*
EN - *European Standard*

9) AAOT Guidelines for Ozone Generators Being Used in Medical, Dental, or Veterinary Applications. 3rd Edition: 2012-2013. www.aaot.us

10) *Remarks made by the Ukrainian colleague and also member of ISCO3, Dr. Veronika Vongai about the use of oxygen concentrators as source of medical oxygen for the purpose of medical ozone generation:*

"In theory, the PSA technology allows to reach a gas mixture of up to 96% oxygen at the best, so a balance of 4% or more of Nitrogen will remain. However, the oxygen concentrators used in practice, in many cases fall short not only of the theoretical limit for PSA technology, but also of parameters declared in the technical descriptions of these devices.

"For example: a test of four concentrators of different origins, showed that none of them was able to produce an oxygen concentration higher than 89%, at a gas flow rate of 1 L/min. At a gas flow rate of 3 L/min, the oxygen concentration at the machine's exit fell to 70-75%. Therefore the use of such concentrators is not recommendable, as the presence of Nitrogen oxide and Nitrogen dioxide may occur.

"Also, in many cases, the gas mix at the exit of these concentrators may contain gases

characteristic of closed rooms, e.g. Carbon dioxide, ammonia, Hydrogen sulfide, Carbon oxide, steam, as well as airborne aerosols, lythosols, dust, microorganisms, etc..

“Also, the percentage of oxygen at the exit of a concentrator will be reduced as time goes by. An oxygen concentrator providing 96% pure oxygen when brand new may come down to only 70% to 80% oxygen purity after 5000-10000 hours of work.

“The speed of decline of concentration efficiency depends on humidity of air, maintenance of carbonic acid gas and a number of other out-of-control parameters of the environment air. For all the above reasons, the uncontrolled use of oxygen sources using PSA technology should not be permitted.”