NEWS 1: Why OZONATED SALINE must be canceled as an ozonetherapy method.

We attach here the official document of the World Federation of Ozone Therapy:

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Some medical ozone associations are promoting the use of Ozonated Saline as method to be classified as Ozone Therapy.
This is documented also by the "Second edition of Madrid declaration on Ozone Therapy" edited by ISCO3 (International Scientific Committee on Ozone Therapy) that included this method in their training courses. This worry fact is also promoted by some medical ozone association like IMEOF.
The World Federation of Ozone Therapy – WFOT, through its scientific advisory committee, has made a deep study that concludes:

- Ozonated saline following the recommendation from the above related document, introduces in the body a very low amount of ozone dissolved in certain quantity of saline solution, compared with systemic indirect endovenous ozone therapy (SIEVOT), also known as major autohemotherapy. This small quantity doubtfully would induce any significant biological response, through the generation of ROS and LOPs. We must say that it is not an Ozone Therapy technique based on the ozone chemistry well documented by the German, Cuban and Italian schools, in which ozone is the only molecule that interacts with the body fluids.

- The ozonization of saline solution (0,9% NaCl) induces the generation of dangerous oxidized chlorine derivatives, not present in other techniques of medical ozone administration. Ozonated saline showed to induce mutagenicity and toxicity in clinical reports. Ozonized saline lacks of any kind of preclinical studies to support its security, as ozone has, which were developed in Cuba and following the recommendations of the World Health Organization – WHO.

For these reasons, WFOT cannot admit ozonated saline as part of ozone therapy meanwhile the biochemical reactions, biological effects and safety of this procedure have not been even minimally established.

Attached, you can find the details of the WFOT - Scientific Advisory Committee study.

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STUDY ON THE SCIENTIFIC BASIS OF OZONIZED SALINE SOLUTION
WFOT Scientific Advisory Committee[1]

Safety

The first reference[i] on ozonated saline solution comes from Korolev in 1977. A detailed review in Pubmed or Embase did not find any reference on safety preclinical studies in spite of 40 years of use.

The theoretical safety of this method was tried to argue by Razumovskii et al. publication[ii] that states that "the decomposition of ozone in the aqueous solution of NaCl is not accompanied by the formation of products different from the oxygen, and no noticeable amounts of hypochlorites and chlorates were observed in particular." Nevertheless, the promoters of this method warn not to use ozone concentrations higher than the very low limit that they recommend[i] (3 µg/mL). Therefore, this seems to indicate their recognition that something different from ozone, oxygen and NaCl is present in this method.

However, Levanov et al. tried to reproduce the experience[iii] and found methodological mistakes in Razumowsky work, because hypochlorite cannot be properly determined by direct spectophotometry, as he used, because there are sever interferences between O_3 and Cl^-. Moreover, the method used to determine chlorate, produced volatile HOCl, not measured in the experiment. Levanov states that other authors[iv] have used iodimetric method to asses HOCl in dilution process of ozone in aqueous NaCl solution and found a progressive amount of HOCl in time. Regarding chlorate, even at very low concentrations, as detected by Grguric, induce oxidative destruction of erytrocytes[v].

But a greater danger in ozonated saline does not only arise from NaCl but from bromide ions that are always present together with Na and Cl ions and are not regulated. Ozone can easily induce the formation of HOBr or bromates, that are potentially carcinogenic[iii.] We can find in the literature more works that support Levanov critics[vi].

Bocci[vii] clearly tested that the speed of ozone absorption into saline is greater and its dissapearance faster, due to the interaction with NaCl molecules. Fig.1.

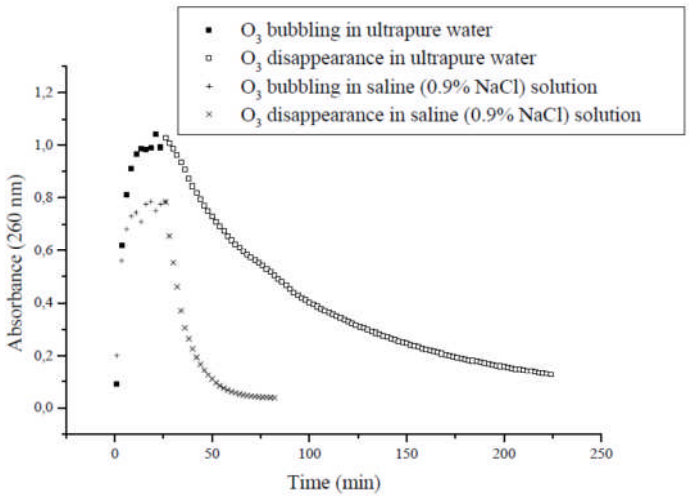

Figure 1

1 Lamberto Re, Manuel Gomez-Moraleda; others members pending evaluation at this moment.

In this document, Bocci states that even at ranges of 2-3 µg/mL of medical ozone, a proportional amount of ClO- is generated, inducing more oxidative stress and risk of DNA damage. In Bocci's experiments, he found that when using usual ozone concentrations (50 µg/mL) to ozonate saline solutions, their infusion produced intensive pain in the veins, lasting for about 24 hours. He thinks it is the reason why the promotors do not allow common concentrations used in standard SIEVOT (systemic indirect endovenous ozone therapy) procedure.

Regarding this fact, in 1999, Fokinski et al. detected an increase in oxidative damage markers in leucocytes of patients treated with ozonated saline for arteriopathy[viii]. This marker (8-oxodeoxyguanosine) is related with ageing and cancer[ix], so the theoretical risk pointed out by Bocci confirmed to be real. One of the most important dangers is that these authors refer to this method as "treatment with Ozone" when it is actually treatment with Ozone mixed with several byproducts that will also interact with the body fluids.

Other authors[x] have confirmed the "hyper coagulation syndrome" as a possible complication of ozonized saline when ozone concentration is over 3 µg/mL.

Efficacy

Using the methods referred in the Madrid Declaration[i] to generate ozonated saline and with the comments of the first chapter on top ozone concentration, the amount of ozone administered is 10 times lower than in a standard SIEVOT procedure.

According to this, they recommend:

Using 200mL to 400 mL of saline solution (NaCl 0,9%) in a 80 kg patient,

- For low dose:

80 X 20 = 1600µg (1,6µg/mL.) 1,6 X 0,25 = 0,4µg/mL. ozone concentration to use.
TOTAL DOSE = 0,4 X 200mL. = 80 µg. per session or 0,4 X 400mL. = 160 µg. per session.

- For medium dose:

80 X 40 = 3200µg (3,2µg/mL.) 3,2 X 0,25 = 0,8µg/mL. ozone concentration to use.
TOTAL DOSE = 0,8 X 200mL. = 160 µg. per session or 0,8 X 400mL. = 320 µg. per session.

- For high dose:

80 X 100 = 8000µg (8,0µg/mL.) 8,0 X 0,25 = 2µg/mL. ozone concentration to use.
TOTAL DOSE = 2,0 X 200mL. = 400 µg. per session or 2,0 X 400mL. = 800 µg. per session.

Advises on the usefulness of each dosage claim that Low dose (0,4 µg/mL.) is used to stimulate th immune system, cardiovascular diseases and obstetrics. Medium dose (0,8 µg/mL.) is recommended for endotoxemia and chronic inflammation diseases. High dose

(2 µg/mL.) is used for infections, skin injuries and burns. These advises are not supported by studies or publications in peer reviewed international journals.

In a recent (2014) presentation of Borrelli during EUROCOOP meeting[xi], she compared 1000 µg total dose per session versus initial 3750 µg dose and subsequent 5000 µg dose in EPOC and artheropathy, proving that lower dose had no biological neither therapeutically effect.

Bocci compares both method in the following table[vii] (table 1).

Table 1 Conceptual and practical differences between major oxygen-ozone therapy and ozonated physiological saline

	M-OOT (SIEVOT)	OS
Volume	150–200 ml[a]	~250–500 ml[b]
Reaction sites	*Ex vivo*, in the glass container	*In vivo*
Biochemical effects	Reactive oxygen species, *ex vivo* alkenals, *ex vivo* and *in vivo*	*In vivo*
Average ozone dose	4–16 mg	0.75–1.5 mg

M-OOT, major oxygen-ozone therapy; OS, ozonated physiological saline. [a]Usual ex-vivo blood volumes with Na-citrate or heparin in an ozone-resistant glass bottle. [b]The volume variability depends upon gender, flow rate and venous blood flow (the higher the flow, the lower the biochemical effect).

Reading both papers one can hardly expect any efficacy of ozonated saline. Maybe other biochemical mechanisms could be involved in the related benefits, but nothing to do with the well described ozone generation of ROS and LOPs and their biological effects referred in other WFOT documents[xii].

References

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