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RIVISTA ITALIANA DI
# OSSIGENO-OZONOTERAPIA
ORGANO UFFICIALE DELLA FIO - FEDERAZIONE ITALIANA DI OSSIGENO-OZONOTERAPIA

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*Cover:* Lizard endemic to the rain forest of Puerto Rico
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# *Editorial*

*The annual symposium of the ASSR - American Society of Spine Radiology was recently held in St Juan de Puerto Rico from 24th to 27th February 2005 and attended by around 300 participants and speakers with separate sessions devoted to spine neuroradiological diagnosis and treatment.*
*This year "*The intradiscal and intraforaminal treatment of herniated discs using oxygen-ozone*" was once again chosen for a lecture by the President of the meeting (Gordon Sze of the University of Connecticut) and inserted in the meeting's official programme. This is the fourth year running that a lecture on this topic has been requested by the scientific committee with Dr. C. Andreula as speaker for the first two years followed in the last two editions by myself.*
*Without doubt, the United States is also showing a growing interest in all percutaneous techniques for the treatment of herniated disc (the lecture on $O_2$-$O_3$ was preceded by talks on percutaneous nucleotomy, IDET, and nucleoplasty) given their excellent results and minimal invasiveness. There is an ongoing rise in the number of percutaneous treatments carried out, currently amounting to 150,000 a year. Most of these treatments are undertaken by orthopaedic surgeons and* anaesthetists*, with only 20% done by radiologists. This is a worrying figure for us radiologists and neuroradiologists given the recent difficulty recruiting young graduates to even the diagnostic specialty.*
*In spinal interventions, as in endovascular procedures, in-depth clinical and diagnostic assessment of patients is essential. The outcome of treatment is often determined not only by accurate technical procedure, but equally by a correct selection of patients. It should be remembered that low back pain and sciatica are multifactorial and we can only intervene on one of them, albeit often the decisive element.*
*The italian group on this tour was composed also by Luigi Manfrè a moderator at some of the meeting's sessions, and Matteo Bonetti, Editor of our journal* Rivista Italiana di Ossigeno-Ozonoterapia*: in a very pleasant atmosphere.*
*The ASSR website is available as a link through www.asnr.org.*

*Au revoir until the next ASSR meeting scheduled in Las Vegas next February.*

*Mario Muto*


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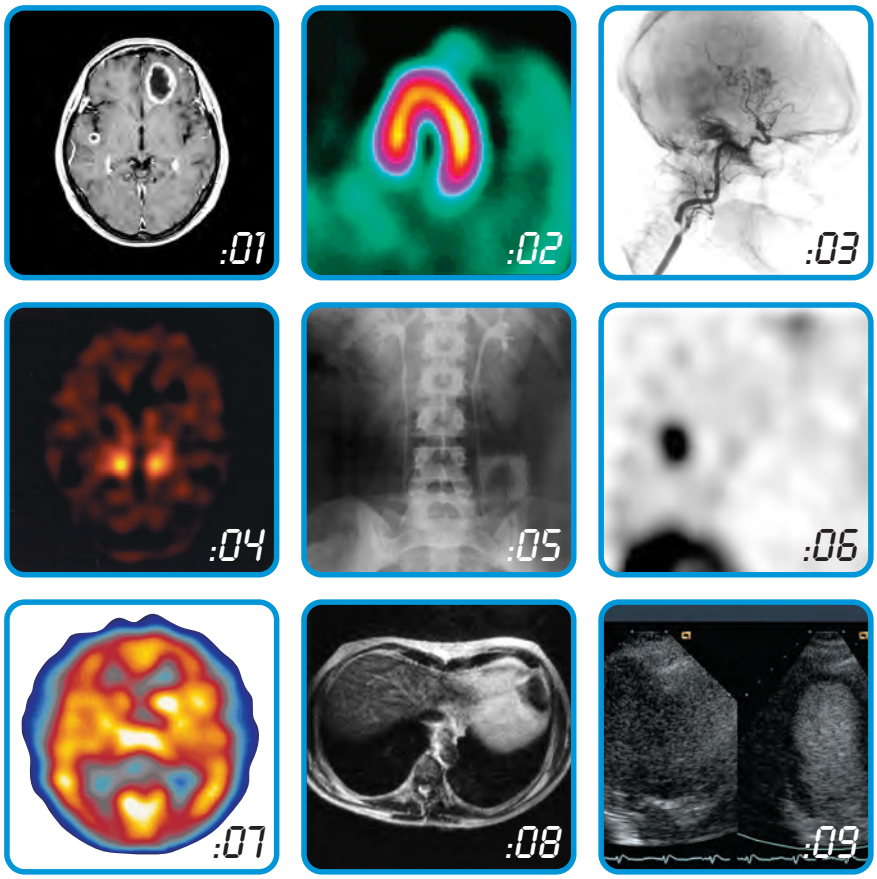


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# Percutaneous Treatment of Lumbar Disc Herniation by Oxygen-Ozone Injection
## A Clinical Study of 322 Cases

WANG ZHU YING, JIANG CAI MEI, WANG ZHI MIN

*The Second Hospital of Shan xi Province, China*

**Key words:** oxygen-ozone, lumbar disc herniation, curative effect

**SUMMARY** – We studied the clinical effect of oxygen-ozone treatment of lumber disc herniation. Oxygen-ozone was administered by percutaneous injection (35-yong/ml), 6-15 ml into the intralumbar disc, and a few patients needed re-injection 48 hours later. We treated 323 patients with 433 discs with a total effective rate of 77.7%. Treatment of lumber disc herniation by oxygen-ozone was simple, safe and effective. With minimal trauma, oxygen-ozone not only oxidizes the proteoglycan in the nucleus, leading to its contraction, but also has an anti-inflammatory effect and alleviates pain. No complications of treatment have been encountered so far.

### Introduction

The application of ozone ($O_2$-$O_3$) in the treatment in lumbar disc herniation is a therapy devised in Europe, but not yet widely used in clinical practice in China. Animal experiments [1] have confirmed the technical usefulness and safety of the treatment. The mechanism of the treatment is ozone oxidization of the proteoglycan in the nucleus, leading to its contraction, and at the same time ozone alleviates symptoms quickly [3-5]. We applied this technique in 600 patients with lumbar disc herniation two years ago, and 323 cases were followed up for three to 12 months.

### Material and Method

Of 323 cases with lumbar disc herniation, 185 patients were men, 138 women, 19-76 years old, mean age 46 years; the longest disease history was 22 years, the shortest five days. Clinical assessment: 97 cases had pain only in the lumbar spine; 158 cases had pain in lumbar spine with numbness in one or both legs; 68 cases had pain or numbness only in the legs. All patients underwent CT or MRI scans. Of 323 cases, 11 were in L2-3, 41 in L3-4, 217 in L4-5, 193 in L5-S1. 41 cases involved three kinds of disc hernation for each patient, 177 cases involved two and 105 cases involved only 1.

*Apparatus*: Ozonizer (Shanxi RuiBo Corp. ROG-C2), X-ray machine with C type arm, ozone appropriation No. 6 needle.

*Operation methods*: In a sterile surgical operating room, the patient lies on the surgical bed face down with a cushion under the lower abdomen. After local anaesthesia, under the C type arm X-ray surveillance, the disc was punctured with the needle, keeping it 40-45° to the middle line of the body. The tip of the needle reached the middle of the disc, checking the point of needle position accuracy without error and injecting into density as 35- 45 μg/ml of combined air 6-15 ml including $O_2$-$O_3$ and air, then withdrawing the needle to the fibrous ring and injecting 5-10 ml. The skin wound can be glued to seal after injection . After treatment, the patients were kept lying supine for four to six hours, and then told to rest in a firm bed for three days.

After the operation, patients should be given intravenous antibiotics, and 20% mannitol 250 ml, dexamethasone 5 mg for three days.

## Results

Short-term outcome: After injection of ozone, symptoms disappeared immediately at 17 cases (5.26%), according to the improvement of the symptoms and the Macnab standard, the effect can be divided into Excellent, Good, Satisafactory and Poor. The total effective rate was 60.05%.

*Table 1*

| **Cases improved in the first week immediately 1 day, 3 days, 7 days** | | | | |
|---|---|---|---|---|
| Excellent | 17 | 41 | 76 | 91 (28.17%) |
| Good | 29 | 64 | 87 | 103 (31.88%) |
| Satisfactory | 96 | 101 | 83 | 66 (20.43%) |
| Poor | 181 | 117 | 77 | 63 (19.50%) |

Every patient had a file in the hospital, and was followed by phone for three to 12 months, the final results were assessed by Macnab curative effect standard: excellent: 127 cases (39.31%); Good: 124 cases (38.39%); Satisfactory: 49 cases (15.17%); Poor: 23 cases (12.69%) ; the total success rate was 77.7%.

The condition of the fibrous ring is closely related to the curative effect. The curative effect was significantly higher in the group with broken fibrous ring than in the unbroken ring group.

*Table 2* **Fibrous ring condition**

| | excellent | good | satisfactory | poor | total |
|---|---|---|---|---|---|
| Complete | 97 | 71 | 17 | 6 | 191 |
| Not complete | 30 | 35 | 22 | 17 | 132 |

The curative effect of patients whose herniation was 30% of vertebral tube width or less was better those above 30%.

*Table 3* **Fibrous ring condition**

| Degree of herniation | excellent | good | satisfactory | poor |
|---|---|---|---|---|
| Less or equal 30% | 59 | 61 | 28 | 17 |
| Above 30% | 32 | 42 | 38 | 46 |

## Discussion

*Mechanism of therapy*

1) *Oxidization of proteoglycan*. The normal nucleus consists of proteoglycan, collagen fibers and nucleus cells. The proteoglycan is one of the major components of the macromolecular material in the nucleus and the main factor maintaining the osmotic pressure and water in the nucleus. After the injection of ozone, the proteoglycan is oxidized directly [2], and this is thought to destroy the amino acid and CH group in the proteoglycan complex, losing fixing charge density. Osmotic pressure then decreases and the water is lost [6].

2) *Destruction of the nucleus cell*. Animal experiment [1] confirms that ozone can degenerate the cells, which are then lysed ending finally in death. The necrosis was more severe in the repeat-injection group.

3) *Anti-inflammatory effect*. Pressure on the spinal dura mater and blood vessels around the nerves caused by the lumbar disc herniation is thought to block the venous circulation leading to tissue edema. Meanwhile the herniation will release some chemical substance triggering an immune response. An aspetic inflammation study [3,4] shows that ozone functions in the following ways: a) stimulating the over expression of anti-oxidized enzyme; b) stimulating the release of cell-reactive factors and immune-inhibitors; c) stimulating endothelial cells to release NO and PDGF to cause blood vessel dilation and improve the inflammation.

4) *Pain relief*. The herniation mechanically compresses the nerve root and stimulates nerves extensively distributed in the small joint, intervertebral disc surface and nearby tissues. At the same time the substance released by the herniation will sensitize the nerve and stimulate the muscles to spasm, causing pain in the lumbar spine or legs [5]. The ozone shrinks the herniation, releasing the pressure on the nerve and decreasing the inflammatory response with an alleviation of pain.

5) *Factors involved in the curative effect*. Published data showed [7,8] that the success rate of ozone in the treatment of lumbar disc herniation was around 76%. The success rate in our group was 77.7% consistent with literature reports. The factors related to the curative effect of the ozone treatment include general factors, such as choosing the indication before surgery; consistency between imaging features and clinical assessment; the technical level of the doctor; the standard of curative effect evaluation; the time of follow-up and the patient's mental state, etc. Our results suggest that the curative effect was closely related to the fibrous ring

condition. The curative effect was significantly higher in the group with a broken fibrous ring than in the unbroken ring group. This may be because ozone not only oxidizes the proteoglycan inside the disc, but also has anti-inflammatory functions, decreasing the inflammatory response and alleviating the pain. The larger the herniation, the harder the treatment.

*Indications and contraindications*

*Indications*: Clinical performance is waist backache and/or neuralgia without severe nerve function impairment confirmed by CT or MR findings of mild or moderate disc herniation and consistent with the clinical position assessment; FBSS after surgery.

*Contraindications*: Lumbar disc herniation combined with severe nerve function impairment; severe stenosis of the vertebral canal; calcification in the herniation; herniation exceeding 30% of the vertebral canal; Free herniation inside the vertebral canal; with displacement of vertebrae; with surgical risk and mental disorder.

*Complications and management*

As far as we know, there have been no serious complications. Only a few patients had mild pain in the lumbar spine or leg after the injection of ozone, which disappeared automatically in several minutes without intervention. Only eight cases had mild respiratory impairment; dyspnea and cornea stimulates similar to the typical respiratory symptoms of allergy to ozone. These symptoms on leaving the ozone environment, inhaling oxygen and calming the patient. No nerve injury, infection or serious allergy occurred.

*The advantage of ozone treatment*

This method not only has the same advantages as interventional therapy, such as minimal trauma, preservation of the normal configuration, few complications, very little pain, good success rate and rapid recovery, etc., but also has the following particular advantages: a) The ozone can not only decrease the pressure inside the disc and cause the contraction effectively, but also improves inflammation and alleviates pain. This is the advantage that other minimally invasive treatments do not offer. b) The ozone can strongly destroy the nucleus, but with no obvious negative effect on the surrounding tissues. As ozone is very instable, it is readily decomposed to become stable oxygen, and hence does not lead to pollution or damage tissues. c) The surgical method is simple, with no obvious injury or pain and minimal discomfort. The treatment can be performed at the outpatients' clinic. d) Ozone has the function of disinfection, thereby reducing disc infection after surgery. e) The equipment for ozone treatment is simple, and the technique can be easily grasped and diffused.

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# Use of FAT/SAT Magnetic Resonance Sequences with Gadolinium in the Pre-Treatment and Follow-up Assessment of Patients Undergoing Oxygen-Ozone Therapy

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**Key words:** MR, fat saturation sequences, medical oxygen-ozone, intraforaminal infiltration

**SUMMARY** - We assessed the usefulness of magnetic resonance imaging (MR) after gadolinium administration with and without the fat saturation technique (FAT/SAT) in the diagnostic work up and follow-up of patients undergoing oxygen-ozone therapy. We selected 220 candidates for intraforaminal infiltration of $O_2$-$O_3$ from September 2002 to January 2005 and undertook MR scans after paramagnetic contrast administration before and after oxygen-ozone treatment. Intravenous contrast administration was very helpful in disclosing disease unrecognized in standard neuroradiological imaging in 18% of cases. This proved essential in planning the interventional procedure to be implemented and also allowed us to monitor the degree of soft herniated disc dehydration during follow-up. Our findings are in agreement with the latest international literature showing that T2 and T1 weighted sequences with fat suppression can yield additional information with respect to standard neuroradiological scans of the spine. This information improves clinical classification and patient selection. Additional information was also obtained from follow-up MR scans which helped us to plan the most appropriate maintenance therapy for our patients after treatment.

## Introduction

We have over 15 years' experience of spinal interventional procedures using CT-guided intradiscal and/or intraforaminal or paravertebral injection of oxygen-ozone. Accurate preoperative diagnosis is essential in planning spinal interventions to ensure the patient receives maximum therapeutic benefit [6-12,16].

In view of this and recent literature reports [1-5,8], we inserted MR imaging with T2 and T1 FAT/SAT MR sequences into our preoperative diagnostic and follow-up protocols.

## Materials and Methods

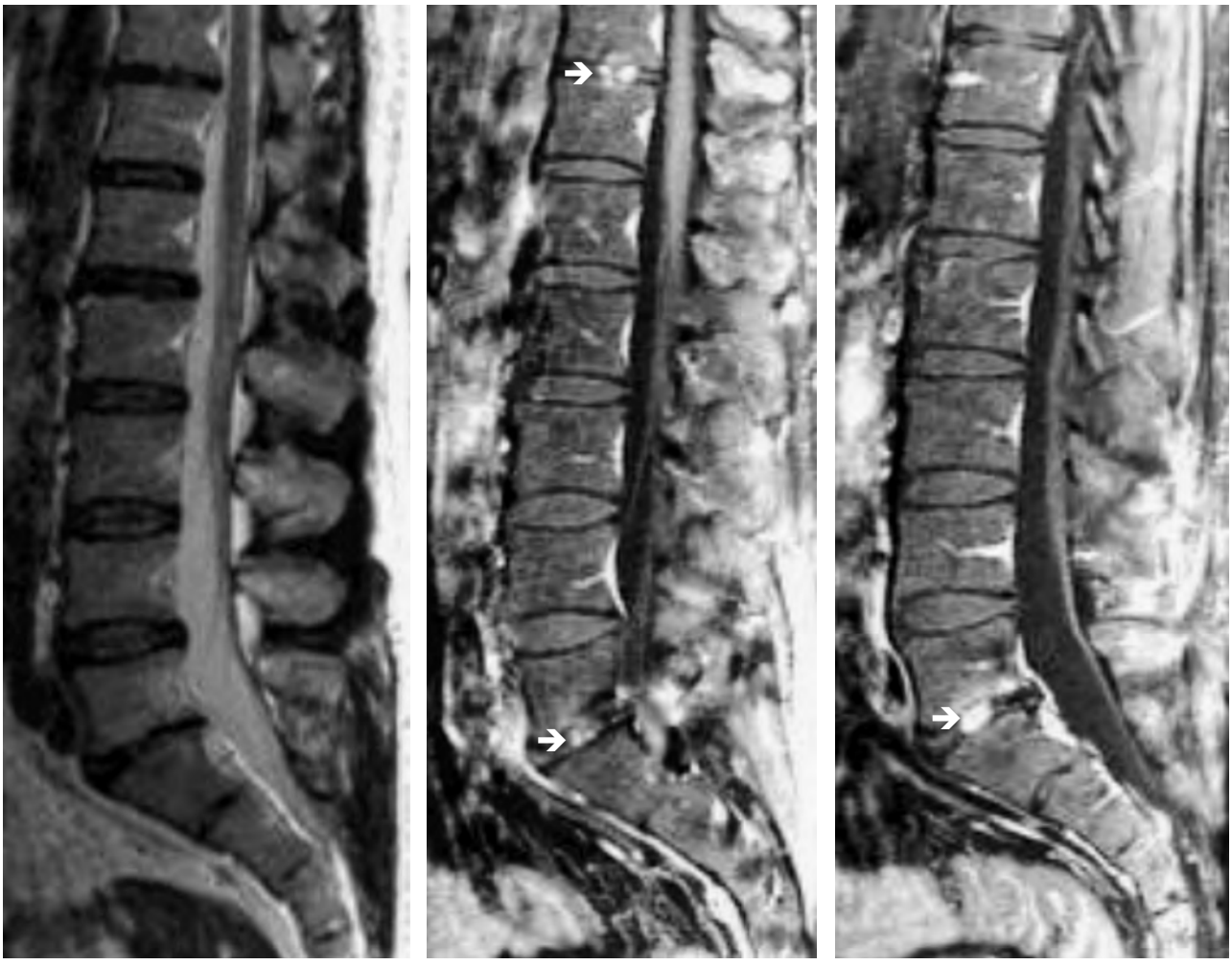
Between September 2002 and January 2005, 220 patients (134 men and 86 women aged from 18 to 82 years; average age 52.6 years) with low back pain and/or sciatica caused by lumbosacral degenerative disease and/or herniated disc were referred for oxygen-ozone infiltration.

Before treatment all patients underwent MR imaging of the spine using T2-weighted Fat-Saturation (FAT-SAT) sequences and T1-weighted FAT-SAT sequences after gadolinium administration at the Neuroradiology Service of Brescia Hospital.

Of the 220 patients 205 also had long-term MR follow-up. MR follow-up monitoring was not required in 15 patients as they had opted for a different treatment after the initial MR scan.

Patients were examined on a 1 Tesla MR system (Philips Gyroscan) using the following sequences:

– *Sagittal TSE T1*
  *TR 400, TE 11, FOV 325 × 325, Matrix 384 × 512, Av 3, Thk 4, TA 4.24*
– *Sagittal TSE T2*



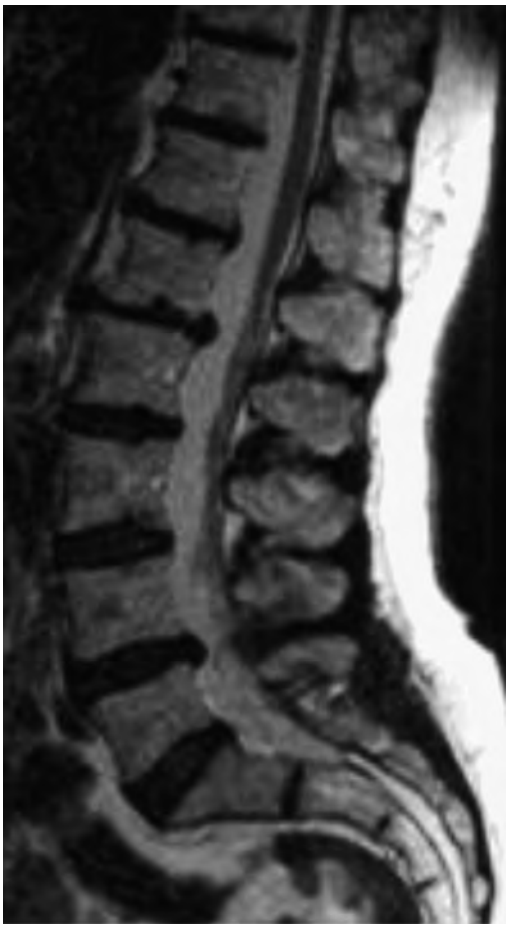
A B C

Figure1 Aseptic discitis. A 46-year-old patient with chronic low back pain. (A) Sagittal T2 MR scan. (B-C) Sagittal MR scan after gadolinium administration showing pathological contrast enhancement of the L5-S1 nucleus pulposus corresponding to aseptic discitis (arrows). Note also a second focus of contrast uptake by the D11-D12 intervertebral disc with similar meaning (arrows).

*TR 3500, TE 120, FOV 345, RFOV 80%, Matrix 368 × 512, Av 3, Thk 4, TA 1.51*

– *Axial SE T1*
*TR 800, TE 13, FOV 220 RFOV 85%, Matrix 256 × 512, Av 4, Thk 4, TA 2.15*
– *Sagittal TSE T2 FAT SATURATION*
*TR 2500, TE 10, IR 160, FOV 325 x 325, Matrix 304 × 512, Av 3, Thk 3, TA 5.30*

Intravenous paramagnetic contrast medium (gadolinium 0.5 mol/1) was administered to all patients. Oxygen-ozone infiltration was done in the day hospital using the same infiltration technique used for discography. Treatment starts with a CT scan to mark the injection site on the patient's skin followed by measurement of the distance between this point and the disc or root canal depending on the approach selected. Local anaesthesia is then applied using ethyl chloride spray. We always use a 22G needle varying in length. Further CT scans are done to establish correct needle placement and 3 cc of oxygen-ozone mixture at 25mg/ml is injected for both intradiscal and intraforaminal infiltration. The needle is then withdrawn a few mm and 7-8 cc of gas mixture are injected into the



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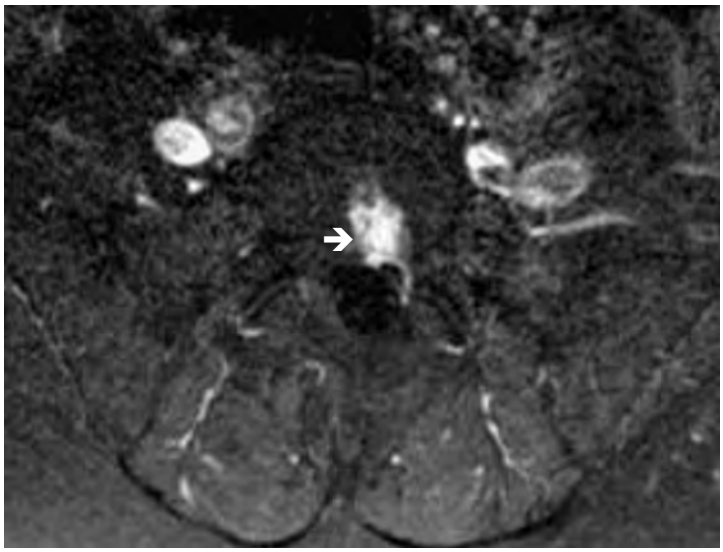

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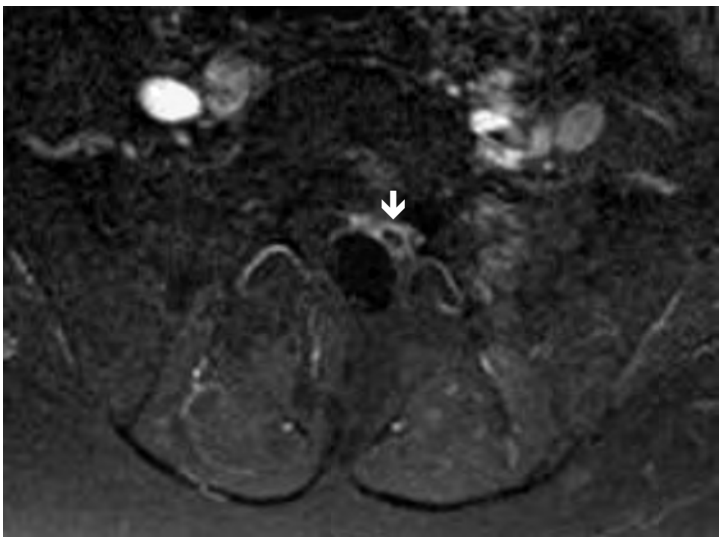


C

D

Figure 2 Patient with "bar-like" back pain and left low back pain and sciatica. (A) Standard MR scan (sagittal T2) fails to display significant changes accounting for the patient's symptoms. (B-C-D) After paramagnetic contrast administration enhancement of the D11-D12 and L5-S1 discs is evident (arrows) corresponding to aseptic discitis associated with periradicular uptake at the origin of the left S1 nerve root indicative of an inflammatory response (radiculitis) (arrows).

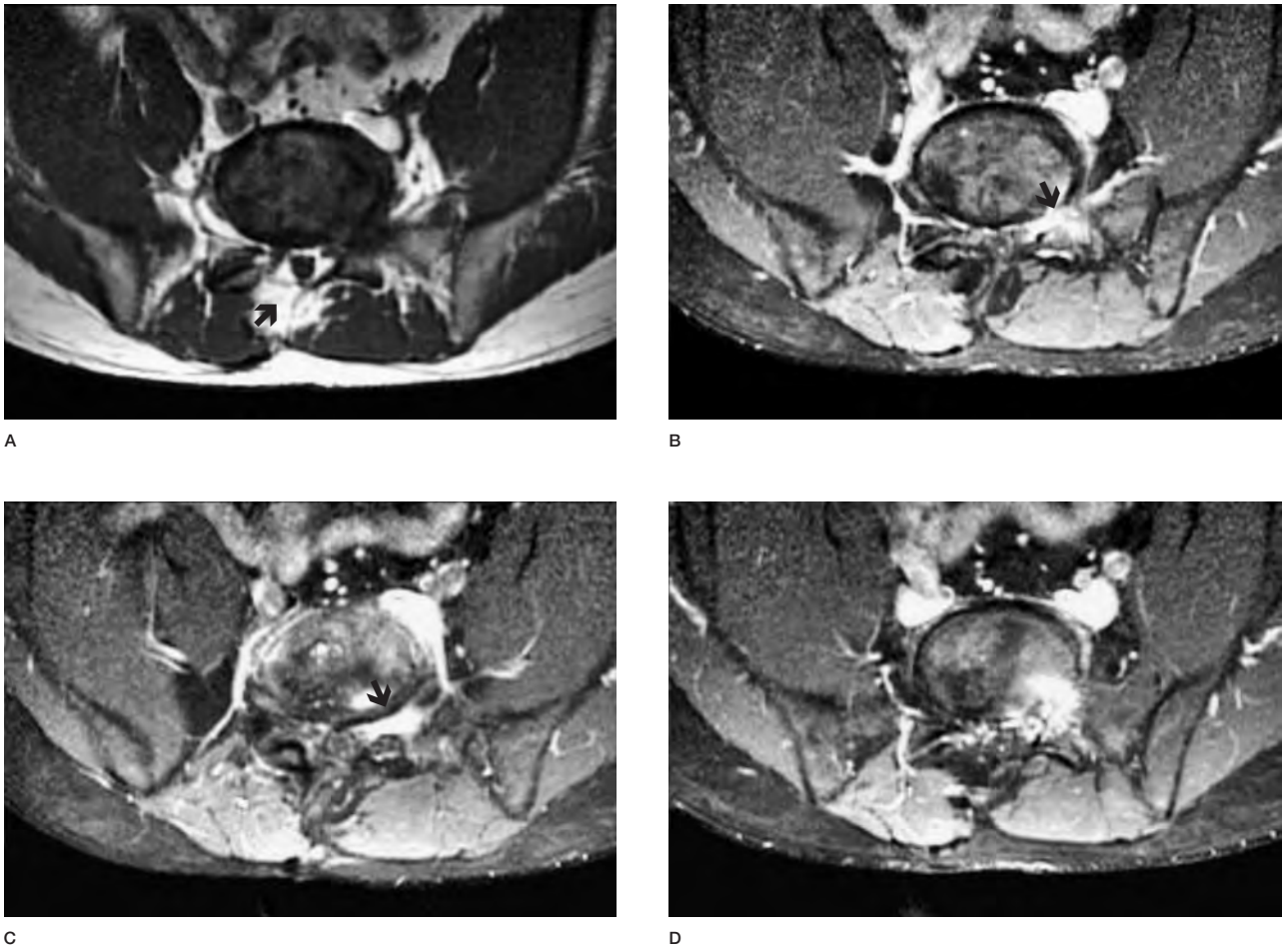


Figure 3 Patient with left low back pain after L5 right laminectomy and flavectomy. (A) Axial T1 MR scan without contrast administration showing the outcome of previous surgery with the surgical incision in the right L5 lamina (arrow). (B-C) After contrast administration the intraforaminal stretch of the L5 and the S1 nerve roots are enhanced as if from radiculitis (arrow). (D) Enhancement of the S1 superior end plate and left sacral wing due to inflammation secondary to post-surgical instability with overloading of the S1 hemisoma and sacral wing.

facet joint. A final CT scan is done to display the correct distribution of the oxygen-ozone mixture. Patients are clinically monitored for two hours after the procedure and then discharged.

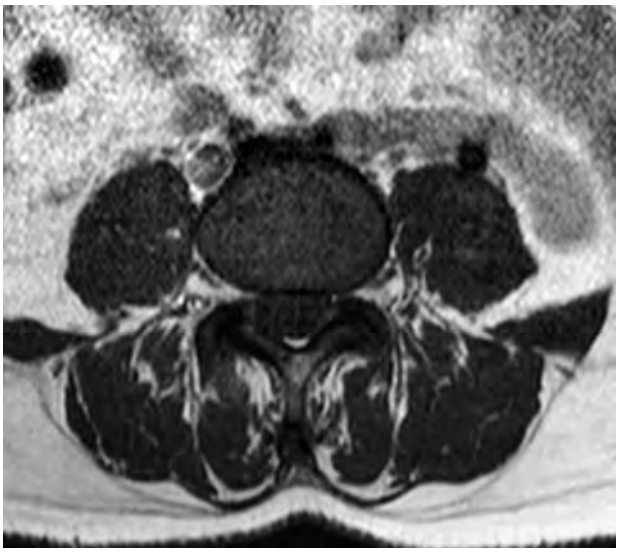
## Results and Discussion

Patients with low back pain with or without sciatica due to nerve root compression are treated by CT-guided infiltration of a medical oxygen-ozone gas mixture.

In the light of recent literature reports on the use of contrast administration in MR imaging of the spine [2], we inserted the fat saturation sequences in our protocol of MR imaging before and after oxygen-ozone infiltration [1-5,13-15,17]. This technique saturates the fat signal in almost all available sequences from Spin Echo to Gradient Echo, with any type of contrast T1, T2 or T2*.

The use of T1 FAT-SAT sequences in our series of 220 candidates for intradiscal and/or periganglionic infiltration of oxygen-ozone disclosed findings not documented by standard CT and/or MR scans in 36 cases (18 %).

In particular, MR sequences with contrast administration revealed aseptic discitis with enhancement of the nucleus pulposus in 16 patients, thereby identifying the exact level to be treated (figure 1). In addition, more than one disc showed pathological contrast uptake in four of these patients (figure 2) yielding a perfect correlation between the patients' symptoms and neuroradiological findings as they had all complained of low back pain and sciatica with concomitant "bar-like" pain. Neuroradiological evidence of pathological en-



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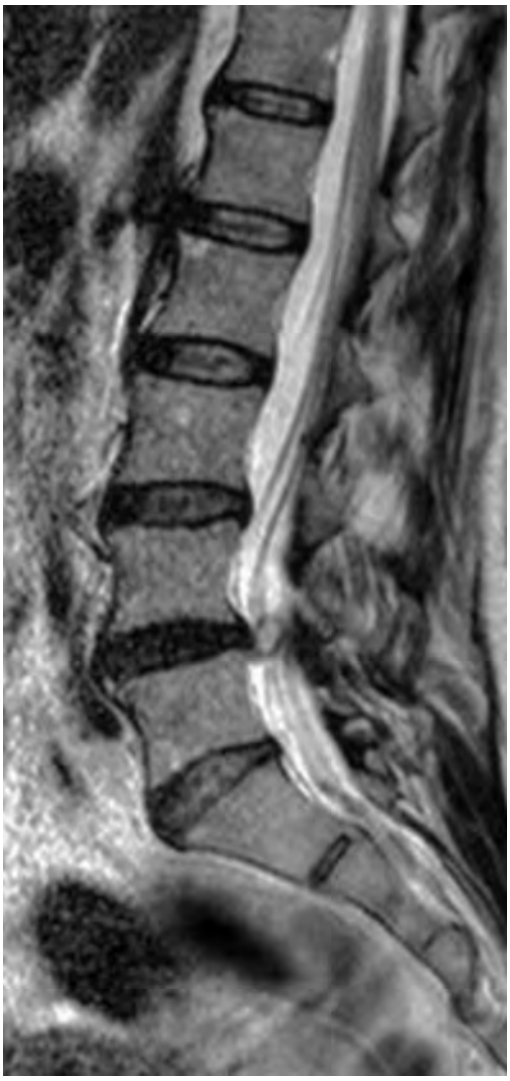

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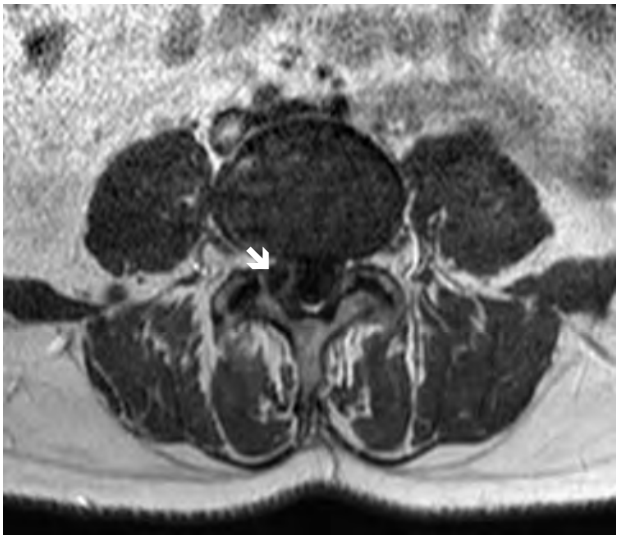

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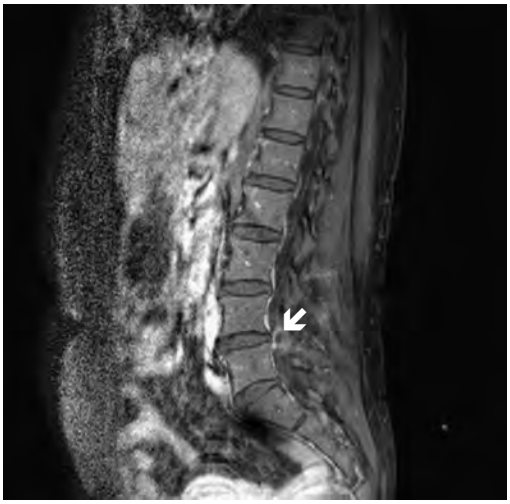
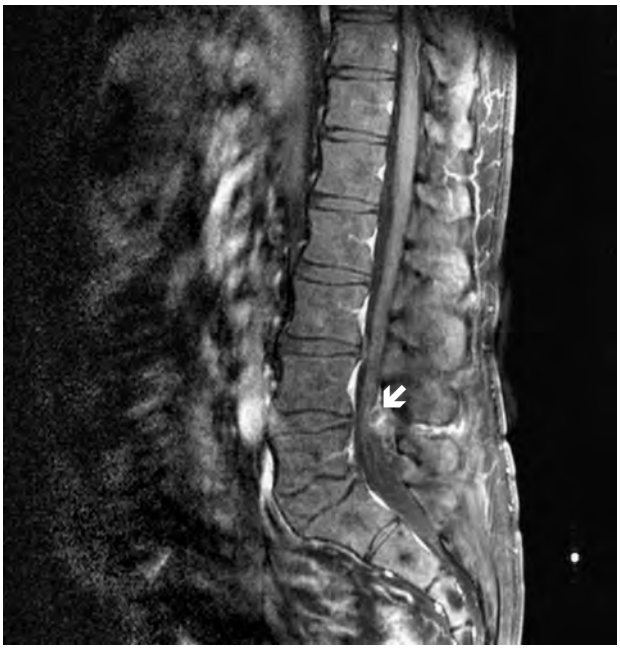


D

Figure 4 Synovial cyst. Standard MR scan (A) T1 axial view and (B) T2 sagittal view suggesting a possible synovial cyst. MR scan after gadolinium (C-D) T1 SE axial view and T1 Fat/Sat sequence giving more detail of the cystic lesion (arrows).



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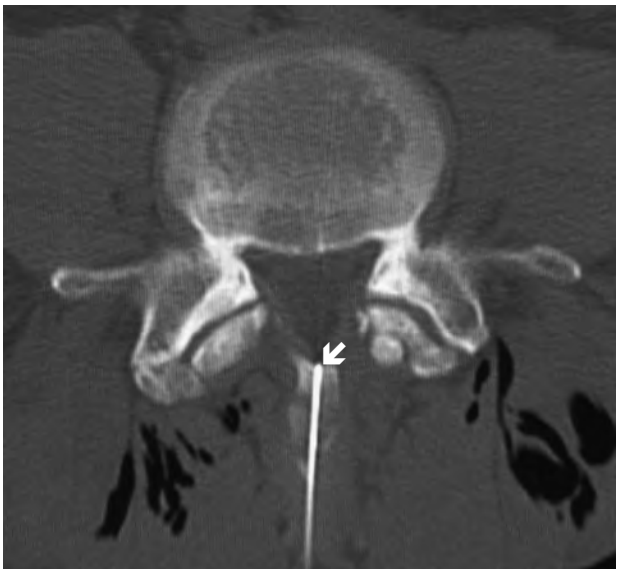

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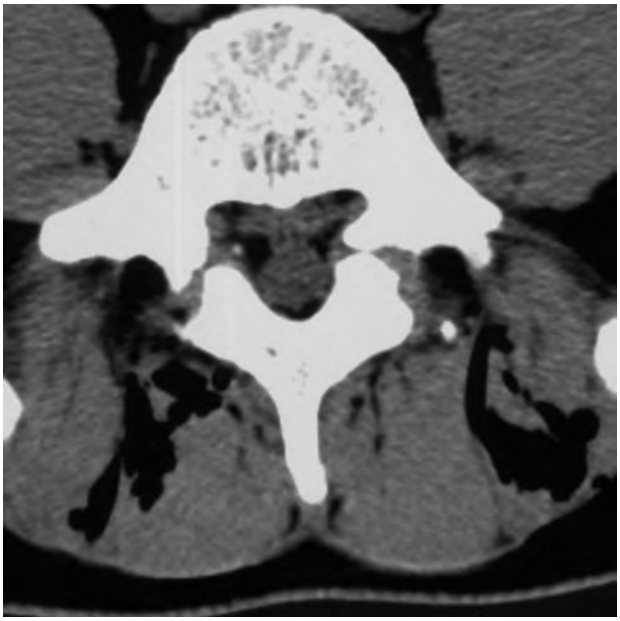


C

Figure 5 L4-L5 synovial cyst and Meyerding's I degree listhesis of L5 over S1. (A) Sagittal T2 FAT-SAT MR scan showing the synovial cyst (arrow). (B) CT-guided emptying of the cyst showing correct needle placement (arrow). (C) Oxygen-ozone infiltration into the points of isthmic lysis.

hancement at the dorsolumbar intersection accounted for the back pain correlated to aseptic discitis mechanically induced by posture. None of these findings had been visible in standard images.

In five patients who had undergone repeated surgery for recurrent herniated disc MR scans with contrast showed intense enhancement of both the vertebral bodies and the intervertebral disc, revealing spondylodiscitis as responsible for the painful symptoms (figure 3).

Seven patients proved to have synovial cysts: in one (figure 4) the finding had never been reported and accurate diagnosis led to a different therapeutic approach. In specific cases the cysts were emptied (figure 5) and filled with steroid.

T2 FAT-SAT and T1-weighted FAT-SAT sequences after contrast administration disclosed pathological enhancement of the facet joints in four patients (figure 6). This finding had also been overlooked in standard imaging tests and its identification led to an adjustment of treatment opting for steroid infiltration into the facet joints.

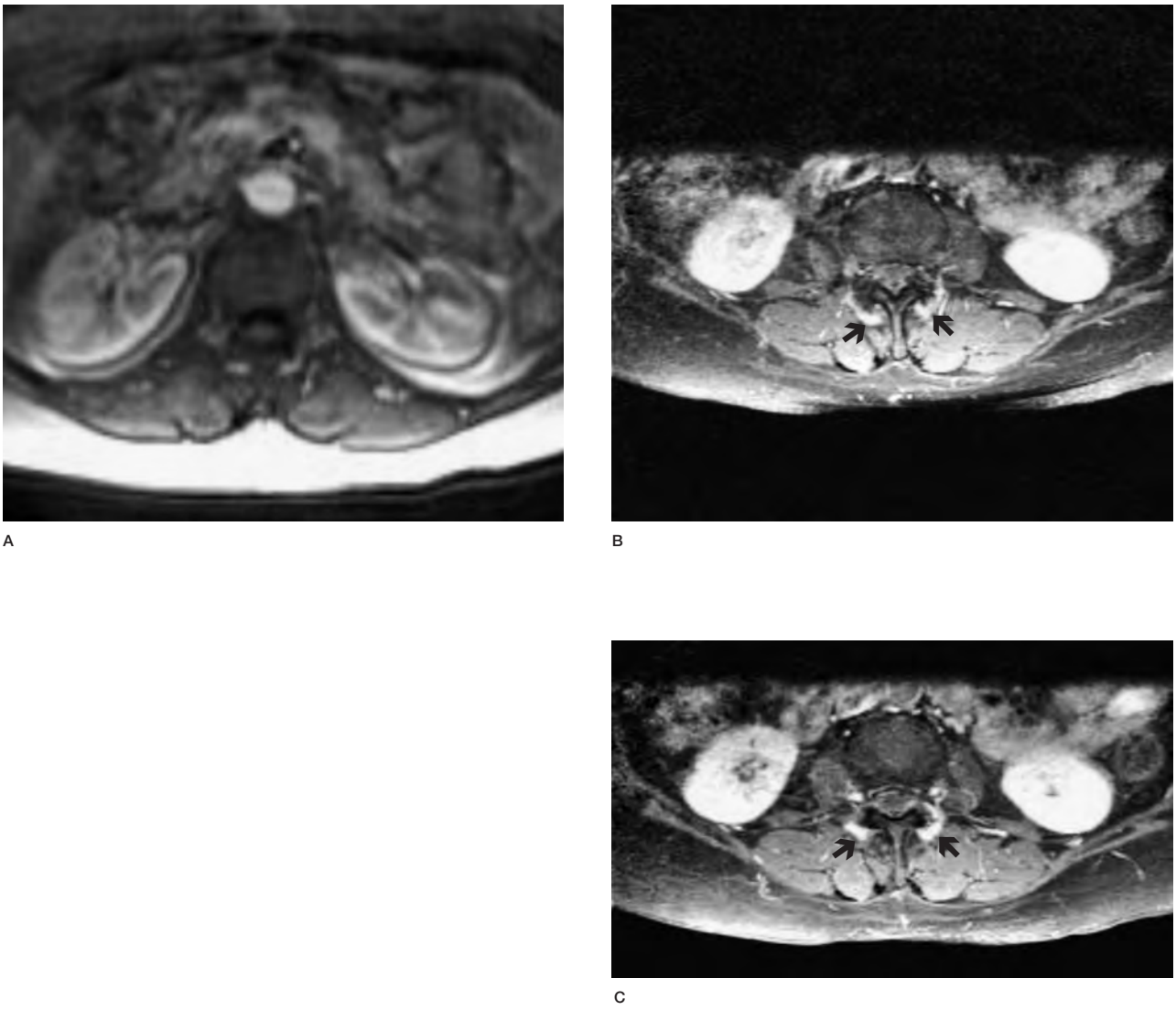


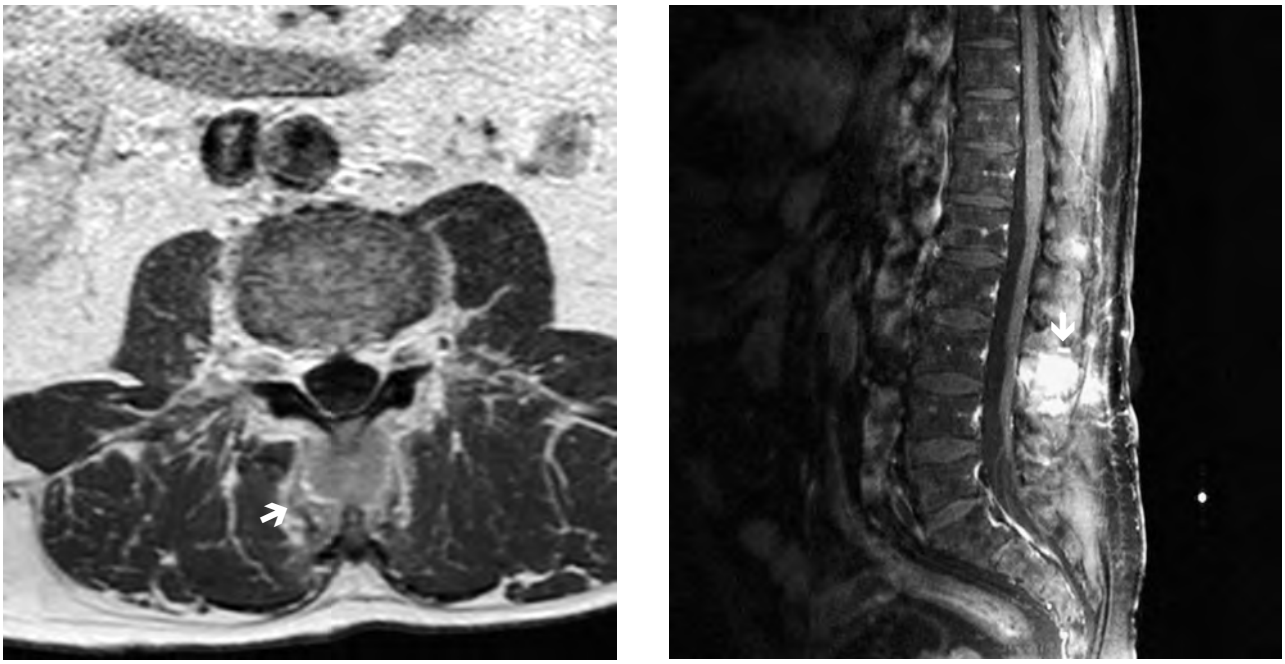

Figure 6 (A) Non significant standard MR scan. (B-C) MR scan after gadolinium shows pathological enhancement in the facet joints (arrows). This finding led us to change our therapeutic approach opting for bilateral infiltration of steroid into the facet joints.

One patient with severe back pain exacerbated by finger pressure on the L3 and L4 spinous apophyses was diagnosed to have a metastasis of the L3 spinous apophysis involving the L3-L4 intervertebral ligament, a finding unrecognized in standard scans (figure 7).

We also had one patient with severe back pain uncomplicated by sciatica and completely negative standard CT scans. In this cases MR with gadolinium administration disclosed a rare meningioma of the conus medullaris region.

CT scan over the last three intervertebral spaces in a 68-year-old patient with severe back pain documented mild lumbar protrusions, readily treatable by oxygen-ozone infiltration. MR scans with contrast administration, done because of the discrepancy between his symptoms and the CT findings, disclosed osteostructural disruption of the L2 vertebral body and initial interest of the left L1 hemisoma, subsequently found to be metastases from prostate cancer (figure 8).

Gadolinium administration in a further case dis-



A B

Figure 7 Metastasis of the L3 spinous apophysis. (A) Axial T1 SE MR scan with contrast administration showing the tumour recurrence (arrow); (B) Sagittal MR scan with Fat/Sat sequences confirms the lesion and yields information on tumour extension and involvement of the intervertebral ligament (arrow).

closed pathological contrast uptake by the L3-L4 and L4-L5 intervertebral ligaments. In this case the painful symptoms were completely resolved by oxygen-ozone infiltration into the intervertebral ligaments. Of the 220 patients enrolled in our study, 205 underwent neuroradiological follow-up for periods between one and four months after treatment using T2 FAT-SAT and T1 weighted FAT-SAT sequences with contrast administration. Long-term follow-up with T1 FAT-SAT and gadolinium administration in 84 treated patients (38%) showed strong contrast enhancement of the tissue around the herniation indicative of an inflammatory response and evidence of the rapid healing mechanism in the disc after infiltration. One 48-year-old patient with a large paramedian extruded herniation at L5-S1 associated with Meyerding's 1st degree listhesis of L5 over S1 was treated by ozone therapy with an excellent outcome and complete dehydration of the herniated disc. Follow-up MR scan with gadolinium three months after treatment disclosed enhancement of the nucleus pulposus as due to mechanically induced aseptic discitis hence secondary to the listhesis (figure 9)

## Conclusion

Candidates for spinal interventional procedures require an in-depth diagnostic work up to establish what, when, how and if to treat. The true cause of the patient's pain ("what") must be sought, avoiding diagnostic errors leading to treatment of what in fact is only an accessory finding and ignoring the root of the problem. Good examples are the synovial cyst, spinous apophysis metastasis, and meningioma encountered in our patients. The timing of treatment ("when") is crucial to have as accurate information as possible on when the pathological event arose. Planning the treatment, "how" to reach the spine, selecting the access routes and infiltration points depend on detailed diagnostic classification (the state of the paravertebral muscles, integrity of the peduncles, etc.). Lastly, the "if": when is it truly worth implementing an oxygen-ozone intervention? It is important to weigh up the risk-benefit ratio for the patient or simply acknowledge that the situation is so impaired that the patient's quality of life will not be improved, i.e. whether the procedure will be useful or not. Nowadays the answers to all these ques-

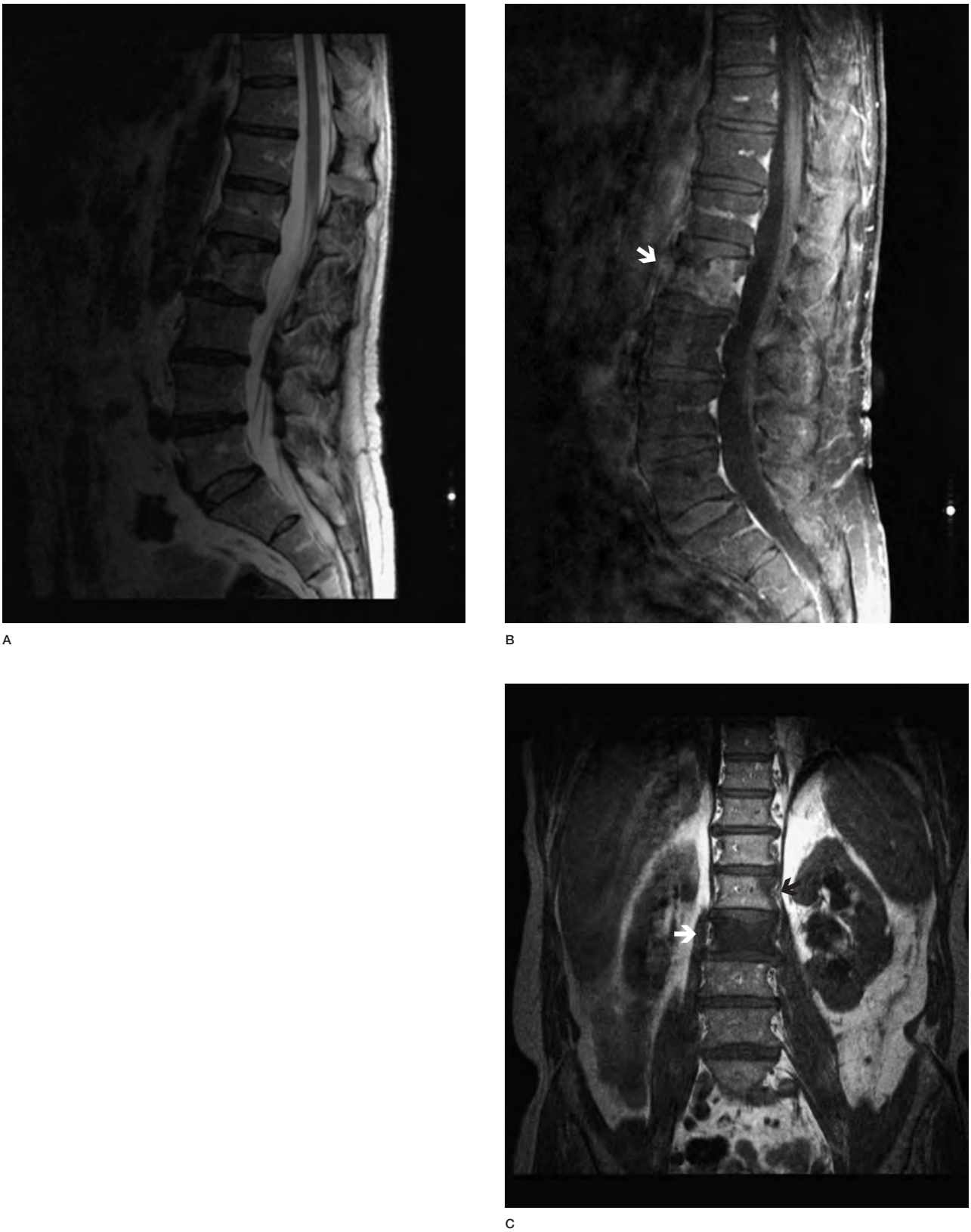
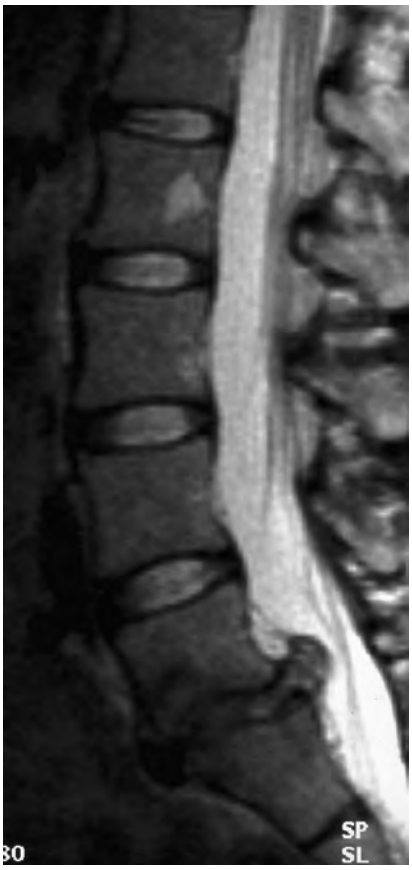
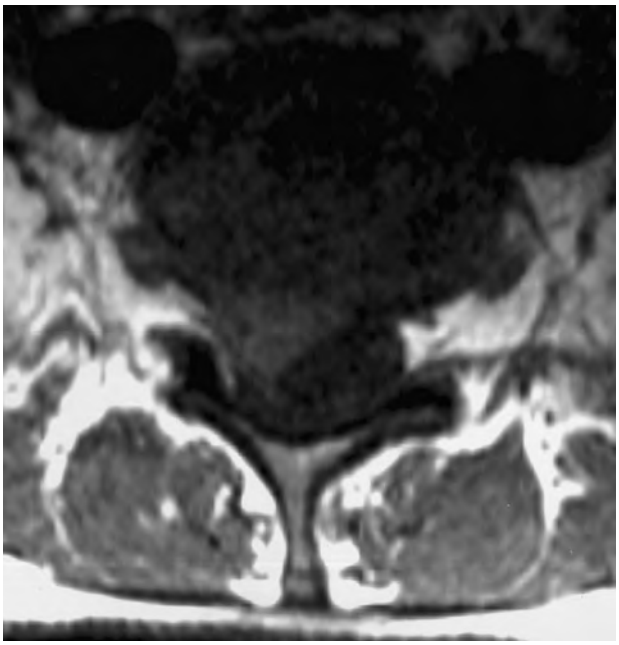


Figure 8 L1 and L2 metastases from prostate carcinoma. (A) MR scan without contrast suggests osteostructural disruption of the L2 vertebral body. (B) Sagittal T1 Fat/Sat MR scan after gadolinium administration shows blurred pathological enhancement of the body of L2 (arrow). (C) Coronal MR scan confirms the metastasis in L2 (arrow) and reveals a second lesion in the left hemisoma of L1 (arrow).




A



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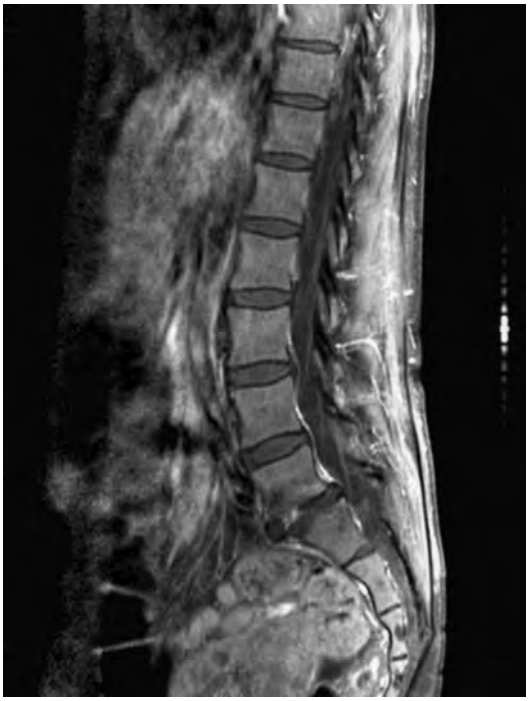

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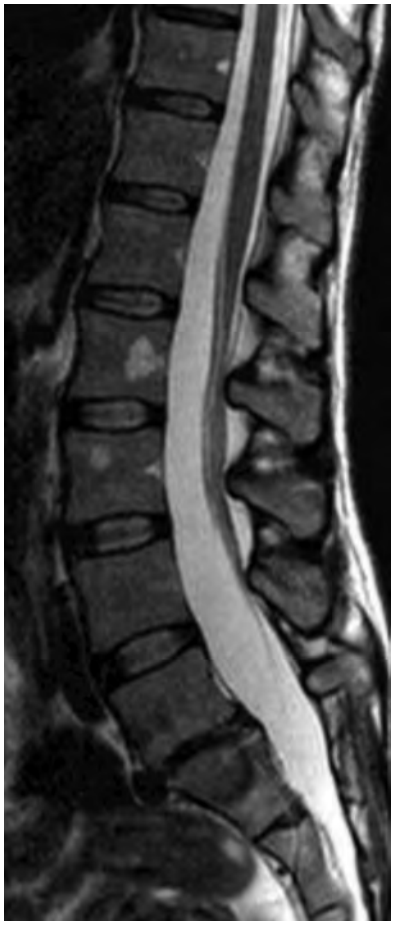

D

Figure 9 48-year-old patient with a large paramedian extruded herniation at L5-S1 associated with Meyerding's I degree listhesis of L5 over S1, successfully treated by oxygen-ozone therapy with complete dehydration of the herniated disc. Follow-up MR scans with gadolinium three months after treatment showed enhancement of the nucleus pulposus as if from mechanically induced aseptic discitis, hence secondary to the listhesis.

tions are best furnished by neuroradiological diagnostic imaging. In our experience, MR scans with T2 and T1 FAT-SAT sequences and contrast administration before and after oxygen-ozone treatment offer adjunct information in the diagnostic approach to these patients.

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# $O_2$-$O_3$ Therapy in Tendinopathies and Entrapment Syndromes

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**Key words:** $O_2$-$O_3$, tendinopathies, entrapment syndromes

**SUMMARY** – We compare the results obtained after local administration of oxygen-ozone ($O_2$-$O_3$) with those of anti-inflammatory mesotherapy in patients with painful shoulder, tendinopathies and entrapment syndromes. $O_2$-$O_3$ was significantly more effective than mesotherapy in relieving painful shoulder and pubic pain without side effects which did occur in patients treated by mesotherapy. Oxygen-ozone therapy is a valid treatment for inflammatory and degenerative diseases of the musculoskeletal apparatus.

## Introduction

Many therapeutic protocols have been advocated for the drug management and/or physiotherapy of tendinopathies and pain caused by compression of neurovascular and musculotendinous structures [4,5,6,7,9,10,15,17].

We describe our experience using oxygen-ozone to treat painful shoulder, tendinopathies and entrapment syndromes, comparing our findings with those of mesotherapy with traditional anti-inflammatory drugs. Our aim was to establish whether correct implementation of $O_2$-$O_3$ therapy in these conditions attenuates the inflammatory response with an improvement in clinical symptoms.

## Materials and Methods

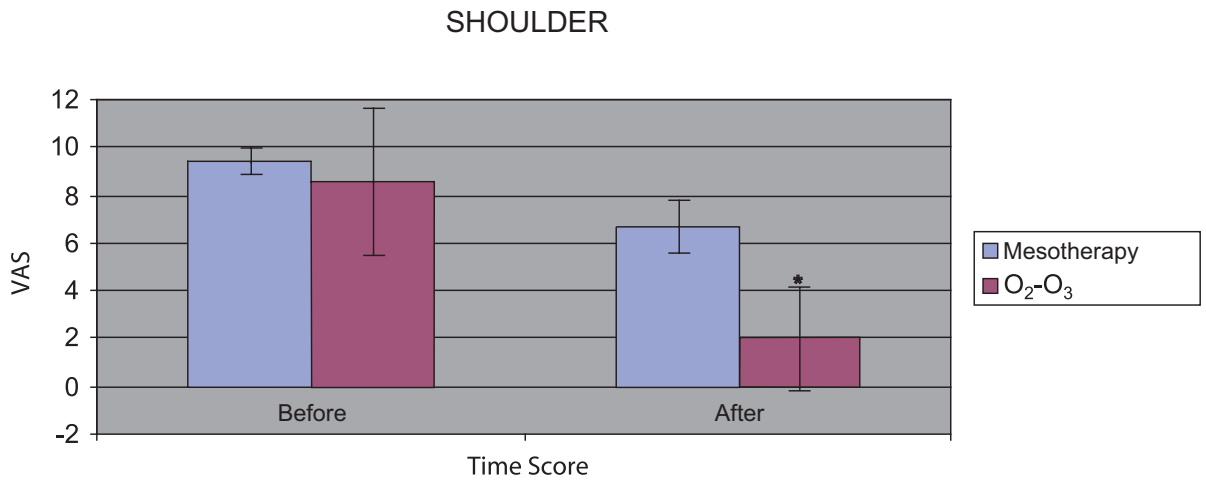
We enrolled patients with different types of painful shoulder, tendinopathies and carpal tunnel syndromes of the upper and lower limbs. For painful shoulder we conducted a randomized prospective study on patients with supraspinatus tendonosis and tendinitis of the long head of the biceps muscle presenting a Visual Analogic Scale (VAS) ≥7 before treatment. Patients with cuff rupture were excluded.

The cohort treated by $O_2$-$O_3$ therapy comprised 83 patients (27 men and 56 women) with an average age of 61 years, whereas the control group undergoing anti-inflammatory mesotherapy comprised 40 patients with a male:female ratio of 14:26 and an average age of 60 years. Prior to treatment both groups underwent history-taking, clinical examination, VAS measurement and routine instrumental tests for the shoulder (X-ray and ultrasound).

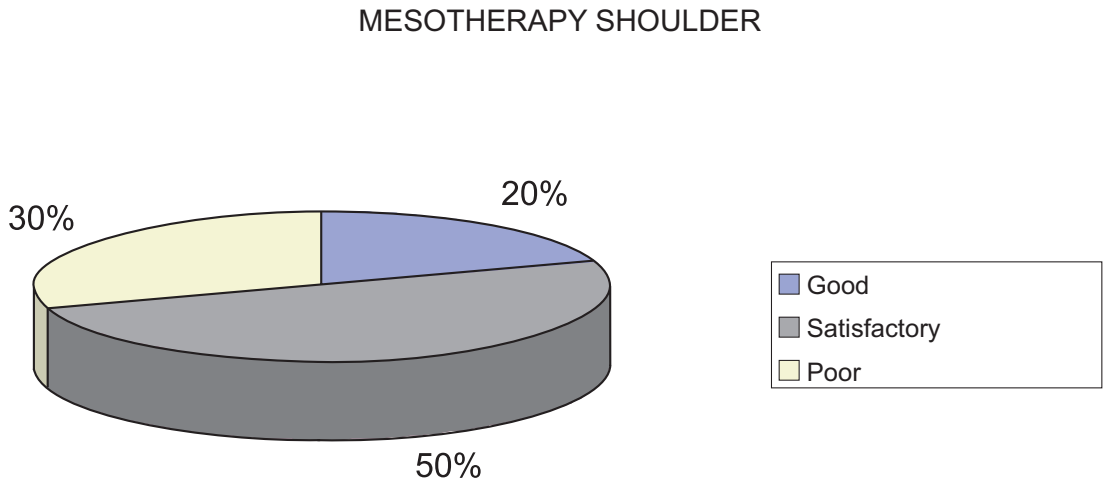
The group treated by $O_2$-$O_3$ received six infiltrations of 10 ml $O_2$-$O_3$ at a concentration of 6-10 micrograms/ml injected twice weekly using a 25G needle into the periarticular region at the point of maximum pain. Anterior or posterior intra-articular access was reserved to 25 patients presenting X-ray evidence of degenerative arthropathy of the shoulder. They received 10-15 ml $O_2$-$O_3$ at a concentration of 15-20 μg/ml injected once a week using a 22 G needle.

The group treated by anti-inflammatory mesotherapy received several injections into the painful site using a 30 G needle and a cocktail of 1 ml ketoprofen lysin salt, 1 ml betamethasone, 1 ml lidocaine and 7 ml saline solution for a total of ten sessions twice weekly. Clinical examination and VAS were used to evaluate both groups after treatment.

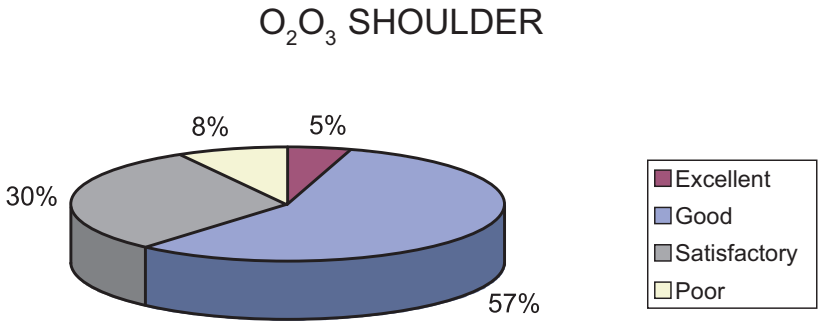
We also tested the outcome of $O_2$-$O_3$ therapy and mesotherapy on the painful wrist and hand (carpal tunnel syndrome, De Quervain's tenosynovitis, Dupuytren Syndrome contracture, tenosyn-




Graph 1




Graph 1A




Graph 1B

ovitis of the extensors), painful heel and foot (metatarsalgia, plantar fasciitis, peroneal tenosynovitis, Morton's neuroma, Achilles tendinitis, posterior tibialis tenosynovitis), pubic pain (abductor insertion tendonitis), painful knee (tendinitis, patellar tendinopathy) and painful elbow (medial and lateral epicondylitis). All patients underwent history-taking, clinical examination and ultrasound investigation before treatment and all has a VAS ≥7.

The cohort treated by $O_2$-$O_3$ comprised:

- Wrist and/or hand: n=54, M:F=12:42, average age = 62 years;
- Heel and/or foot: n=22, M:F=11:11, average age = 60 years;
- Pubic pain: n=15, M:F=9:6, average age = 45 years;
- Knee: n=36, M:F=22:14, average age =40 years;
- Elbow:n=11, M:F=7:4, average age =43 years;.

The cohort treated by mesotherapy comprised:

- Wrist and/or hand: n=22, M:F=10:12, average age = 62 years;
- Heel and/or foot: n=16, M:F=10:6, average age = 60 years;
- Pubic pain: n=10, M:F=7:3, average age = 45 years;
- Knee: n=13, M:F=9:4, average age =35 years;
- Elbow: n=10, M:F=8:2, average age =40 years.

Patients with painful wrist or hand treated by $O_2$-$O_3$ received six weekly infiltrations of 5 ml $O_2$-$O_3$ at a concentration of 6 micrograms/ml using a 25 G needle injected along the sheath of the tendons involved (De Quervain's tenosynovitis, Dupuytren Syndrome contracture, tenosynovitis of the wrist extensors) and on the line of the wrist sulcus, on the ulnar side with respect to the median line of the palmar fascia (carpal tunnel syndrome).

Patients with painful heel or foot received six twice weekly infiltrations of 5-10 ml $O_2$-$O_3$ at a concentration of 10-15 μg/ml using a 25 or 30 G needle injected along the sheath of the tendons involved (Achilles tendinitis, posterior tibialis or peroneal tenosynovitis) or on the medial side of the heel at the point of maximum pain (calcaneal sulcus), or along the medial surface of the sole (plantar fasciitis) or into the intermetatarsal space involved (Morton's neuroma or metatarsalgia).

Patients with public pain received a minimum of six up to a maximum of ten twice weekly infiltrations of 5 ml $O_2$-$O_3$ at a concentration of 6-10 μg/ml using a 30 G needle injected into the painful area.

Patients with knee and elbow tendinopathies also received six twice weekly infiltrations of 5-10 ml $O_2$-$O_3$ at a concentration of 10-15 μg/ml injected along the sheath of the tendon involved.

Patients treated by mesotherapy received the same cocktail given to patients with painful shoulder. At the end of treatment all patients underwent clinical examination with VAS assessment. Statistical analysis was done using the T-Test ($p<0.05$).

## Results

As shown in Graph 1, patients with painful shoulder treated by $O_2$-$O_3$ had a statistically significant improvement with respect to those who received mesotherapy with a greater reduction of VAS from an initial value of 9.4 to a final value of 2.9, whereas mesotherapy patients went from an initial VAS value of 9 to a final value of 6.

We further classified the outcome in terms of pain reduction into excellent (> 90% pain reduction), good (between 70 % and 90%), satisfactory (between 40 and 70%), and poor (< 40%).

Among the cohort treated by $O_2$-$O_3$, an excellent outcome was noted in four (4.82%), good in 47 (56.63%), satisfactory in 25 (30.12%) and poor in seven (8.43%). Among the cohort treated by mesotherapy there was no excellent outcome, but only satisfactory in half the patients, good in 20% and poor in 30% (graphs 1A and 1B).

No statistically significant differences were found in the patients with painful wrist or hand, tendonitis of the knee and epicondylitis / epitrochleitis treated by $O_2$-$O_3$ or mesotherapy since the improvement in symptoms was similar in both groups (graphs 2, 2A, 2B, 5 , 5A, 5B, 6, 6A, 6B).

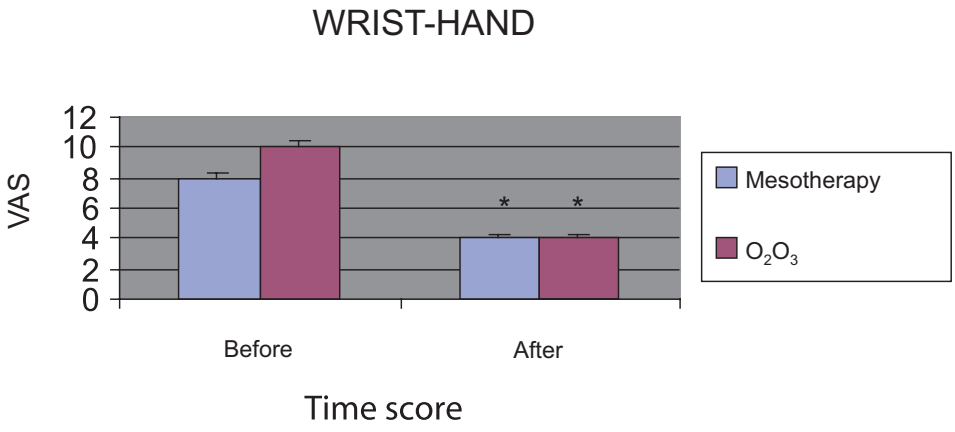
Instead, patients with public pain treated by $O_2$-$O_3$ benefited more from treatment than those who received mesotherapy although the improvement did not reach statistical significance (graph 4, 4A and 4B).

Mesotherapy proved slightly more effective than $O_2$-$O_3$ in patients with painful foot but a higher percentage of good outcome was noted in the group treated by $O_2$-$O_3$ (graphs 3, 3A and 3B).

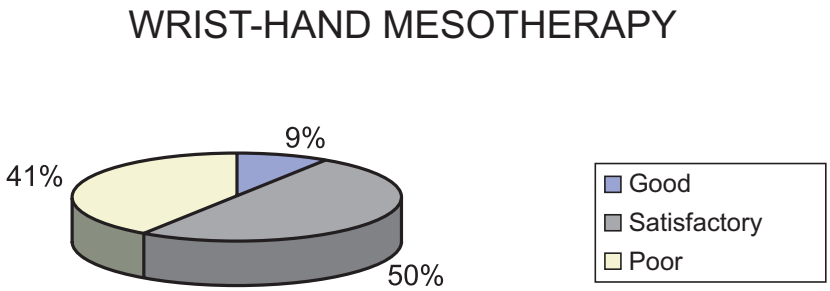
In addition, seven patients (14% of the whole population) treated by mesotherapy with anti-inflammatory drugs presented side effects consisting of pain at the site of injection, allergic reactions and recurrence of pain several hours after treatment. No side effects were encountered in the cohort treated by $O_2$-$O_3$ .

## Discussion

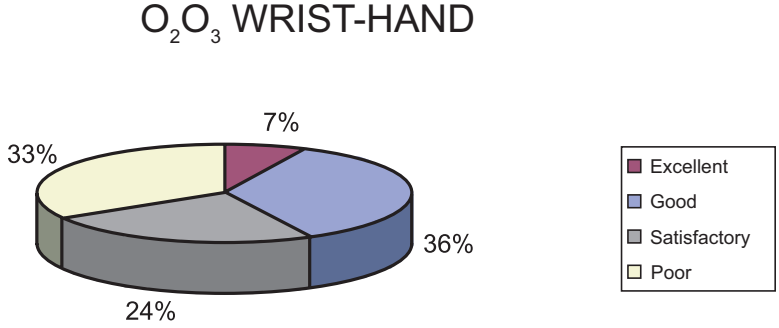
Rotator cuff lesions are caused by a variety of extrinsic (microtrauma, subacromial impingement, shoulder instability) and/or intrinsic factors (avascularity, degeneration) [13]. The tendons of the rota-



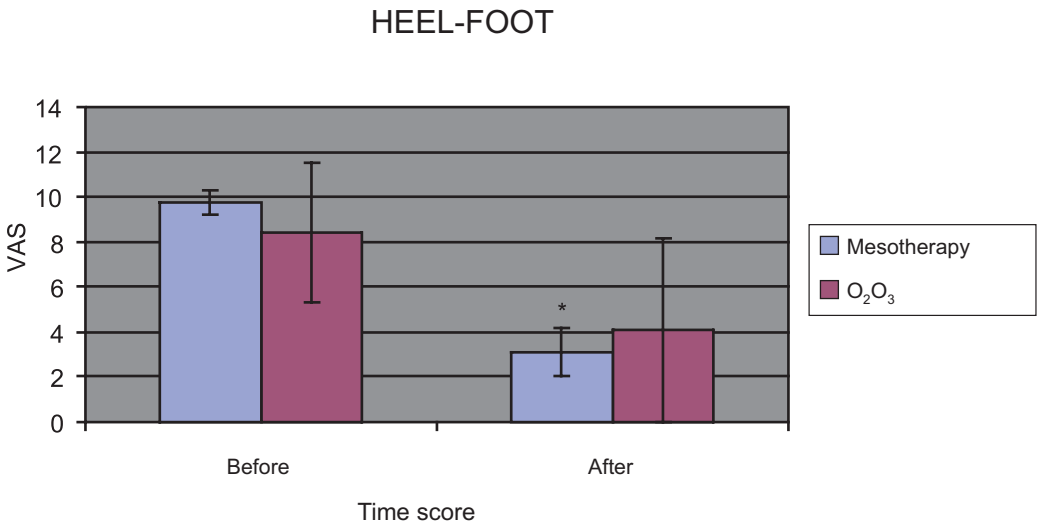

Graph 2



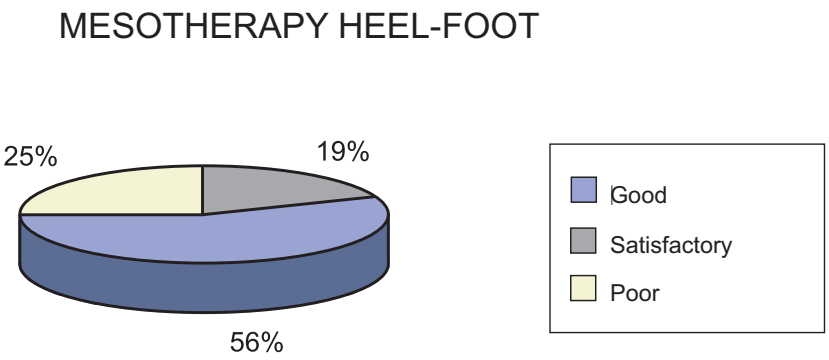

Graph 2A



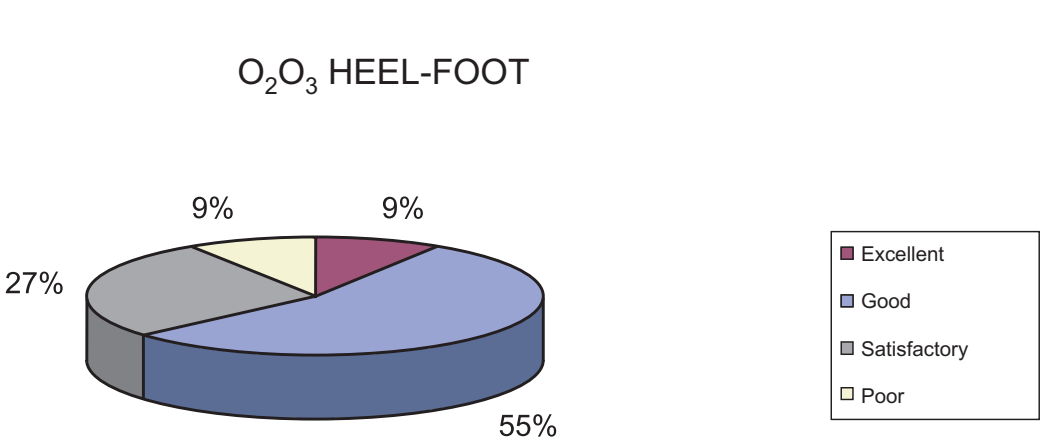

Graph 2B



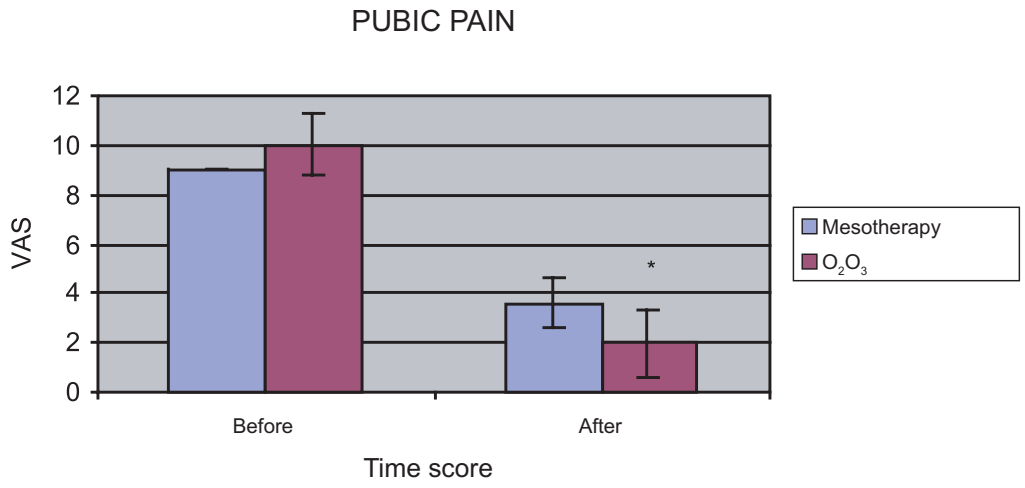

Graph 3



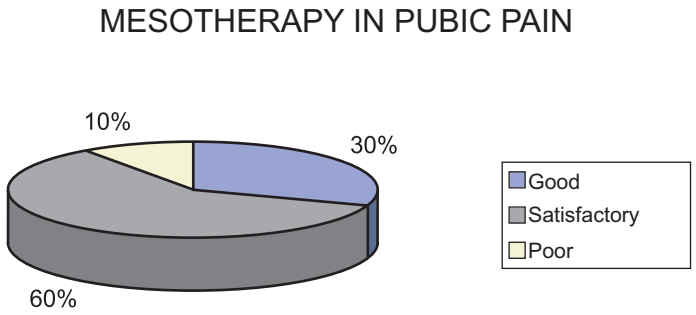

Graph 3A



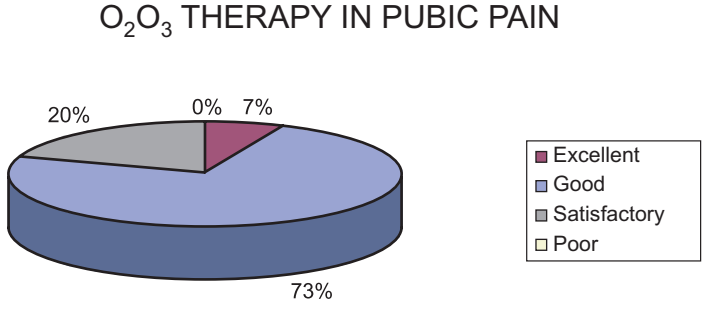

Graph 3B



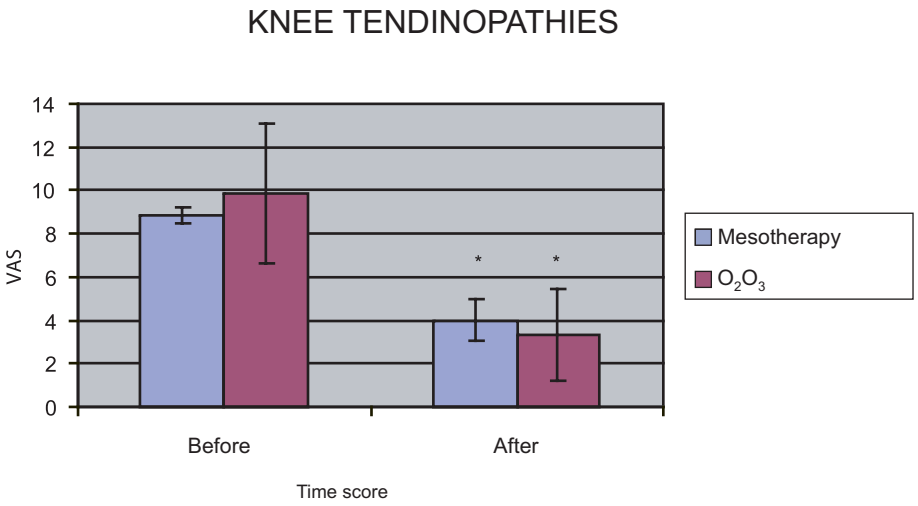

Graph 4



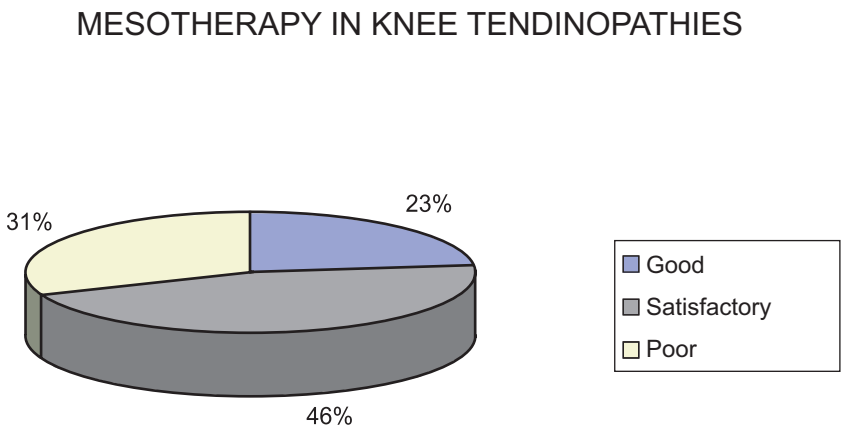

Graph 4A



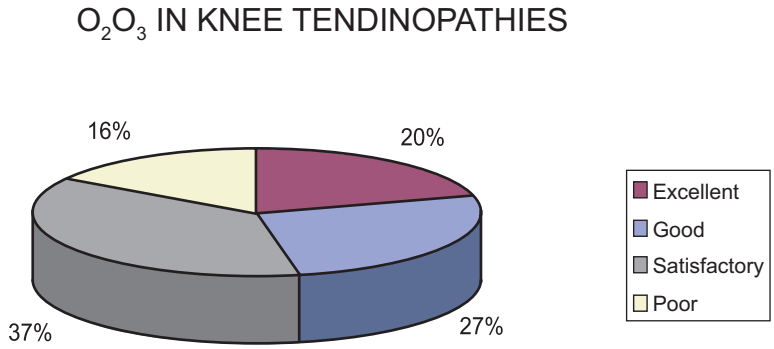

Graph 4B



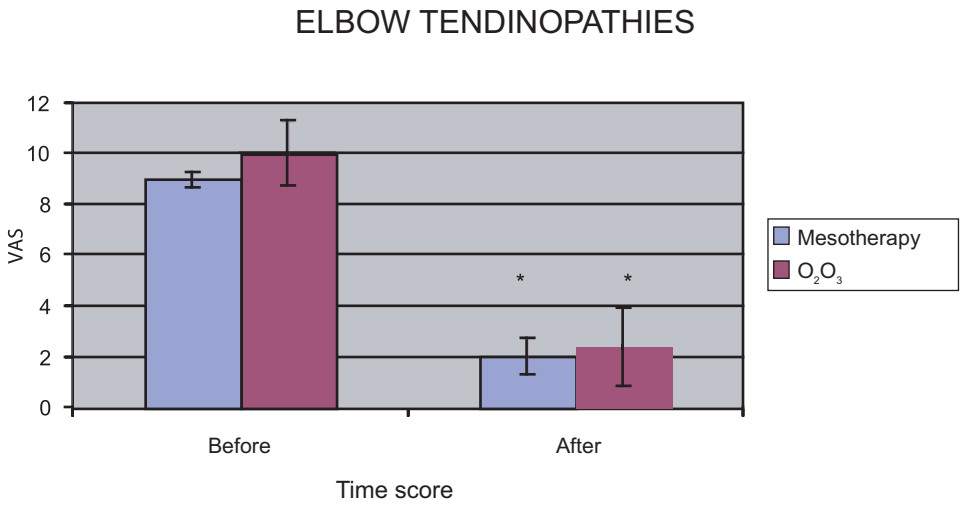

Graph 5



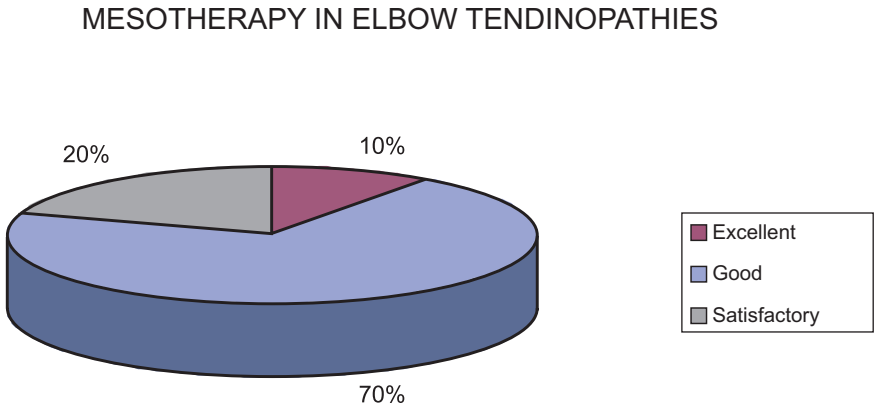

Graph 5A



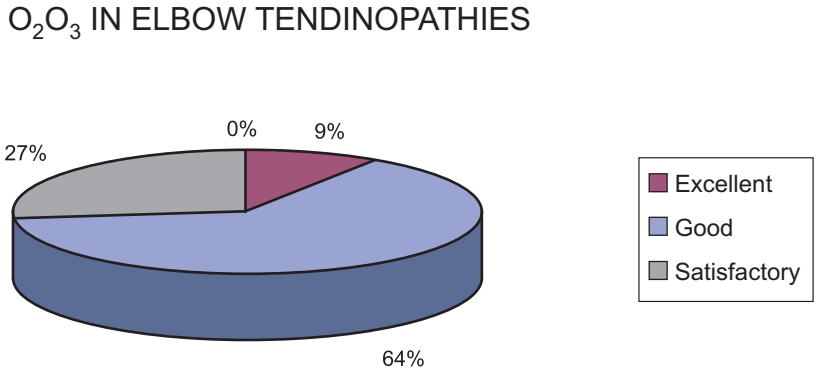

Graph 5B




Graph 6




Graph 6A




Graph 6B

tor cuff may be affected by tendonitis, calcific tendinopathies, lesions involving the joints and bursitis up to complete rupture. The supraspinatus portion of the cuff is most commonly affected (51-82%) by tendinitis [3,12,14,16].

Calcific deposits result from local avascularity which is thought to induce primary degeneration of the tendinous fibres and hence hyalinosis/fibrillation and maceration/detachment up to tenocyte necrosis with intracellular accumulation of calcium crystals. Clinically, pain is encountered at the insertion of the deltoid muscle or irradiates along the arm, worsening at night, with a painful arc between 70° and 110°, immobility and acute borsal pain during rupture of the deposits.

Before embarking on our study, we reviewed literature reports on $O_2$-$O_3$ therapy. In particular, Gjonovich et al. (2002) infiltrated a maximum of 35 ml $O_2$-$O_3$ mixture (12-15 micrograms/ml) in painful shoulder complicated by rotator cuff lesions, finding an excellent percentage of positive results (67%) with good pain control and excellent recovery of joint function [6]. Ikonomidis et al. (2002) effectively treated post-traumatic shoulder syndrome by infiltrating an $O_2$-$O_3$ mixture (6 micrograms/ml) every three days with injections of 10 ml into the subacromial deltoid bursa and 5 ml into the most painful point.

This treatment was repeated for a total of six sessions in association with daily stretching and rest exercises. The patients did not need steroid injections or NSAIDs [9].

Tendinopathies and enthesopathies are characterized by intrinsic degeneration of tendon tissue and enthesis caused by inflammatory degenerative disease of the synovial or peritendinous sheaths [1].

Clancy and Leadbetter's classification includes 1) Paratendinitis: with involvement of the peritendinous tissues; 2) Paratendinitis with degenerative inflammatory diseases of the peritendinous tissues and tendon body; 3) Tendinosis: degenerative and involutive intratendinous disease; 4) Tendinitis: intratendinous inflammatory disease.

These conditions are also caused by a variety of intrinsic (age, sex, obesity, abnormal morphotype, impaired tendon elasticity, muscle imbalance) and extrinsic factors (level of sports training, execution and preparation of athletic movement, training schedule, environmental conditions, type and quality of materials). Clinically, tendinitis may be acute (<2 weeks.) or chronic (>6 weeks) presenting with aspecific signs of local inflammation or tendinosis, often asymptomatic and characterized by nodules along the tendon body.

Ultrasound is a useful diagnostic investigation, possibly completed by colour-power doppler, X-ray and in some cases MR or CT scans.

Among the entrapment syndromes treated, tarsal tunnel syndrome presents with burning pain under the foot, hallux and heel, often associated with impaired plantar flexion of the toes. Morton's neuroma is caused by interstitial fibrosis compressing the digital nerve just before it divides into its two terminal branches [8,11,18,19]. In this condition patients complain of a sharp pain in the forefoot shooting through to the toes exacerbated by loading and irradiating into the interdigital space. Clinical examination may disclose a small lump at the base of the toes, digital pain on compression with a palpable click on transverse metatarsal compression. Ultrasound may confirm the diagnosis, but MR scan yields more information.

Carpal tunnel syndrome consists in entrapment of the median nerve in the carpal tunnel at the wrist together with the superficial and deep flexor tendons of the fingers resulting in painful tingling in the wrist and hands mainly affecting the thumb, index and middle fingers with weakness of the tenar eminence, namely the abductor pollicis brevis and longus, Clinical examination discloses positive Phalen manoeuvre and Tinel's sign. Clinical diagnosis can be confirmed by EMG and ultrasound and X-ray examination of the wrist.

Trenti et Al (2002) tested $O_2$-$O_3$ therapy in calcific tendinopathies. Peri-articular infiltration of 14 ml $O_2$-$O_3$ mixture (17-20 micrograms/ml) using a 27 G needle proved an effective treatment for pain with a recovery of joint function, especially when the treatment was combined with shock waves (six sessions in 45 days) [17].

Ikonomidis et Al (1989) combined $O_2$-$O_3$ therapy with infiltrations of steroid in acute tendinitis. After infiltration with a mixture of local anaesthetic and glycocortisone, they injected an $O_2$-$O_3$ mixture (10-15 micrograms/ml) into the same site in two to three sessions over three days. They also suggested topical injection of an $O_2$-$O_3$ mixture (10-15 micrograms/ml) over the tendon twice a week for four to five sessions combined with a programme of stretching exercises [10].

Our experience demonstrated a greater efficacy of $O_2$-$O_3$ therapy compared with mesotherapy in the treatment of painful shoulder and public pain with a statistically more significant improvement after $O_2$-$O_3$ and no side effects. Instead, no significant differences were found in the treatment of painful hand and wrist, knee, elbow, heel and foot.

## Conclusions

Our comparison between $O_2$-$O_3$ therapy and anti-inflammatory mesotherapy disclosed a statistically more significant improvement of painful

shoulder and public pain after $O_2$-$O_3$. A similar outcome was encountered in the other disorders treated but results did not reach statistical significance. Given its ready administration, lack of side effects and effective anti-inflammatory and analgesic action, $O_2$-$O_3$ is a valid treatment for inflammatory and degenerative disorders of the musculoskeletal system.

The differences in methods of treatment and $O_2$-$O_3$.

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# The Use of Hydrogen Peroxide as a Medical Drug

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**Key words:** hydrogen peroxide, ozone, ROS, LOPs, oxidative stress, macular degeneration

**SUMMARY** – Since 1993, a diluted solution of hydrogen peroxide ($H_2O_2$) has been administered intravenously in many ischaemic and neoplastic patients in the USA and Canada as a bio-oxidative therapy. However, to date no biochemical study has defined the behaviour and fate of $H_2O_2$ diluted in either human blood or a 5% glucose solution. Our study aimed to define the stability of $H_2O_2$ *in vitro* and *in vivo* and to compare the generation and stability of reactive oxygen species (ROS) and lipid oxidation products (LOPs) when blood is treated with either ozone or $H_2O_2$. In addition, we evaluated the therapeutic effect of the gluco-peroxide solution in age-related macular degeneration (ARMD) patients with encouraging results. There is a general consensus that $H_2O_2$ is one of the most important physiological messengers and because it could activate multiple cell targets, $H_2O_2$ could become a useful medical drug particularly in countries with scant medical resources.

## Introduction

During the last 35 years reactive oxygen species (ROS) have come of age and, if not the direct cause of several human pathologies, they certainly maintain chronic oxidative stress. More recently the concept that cells can regulate redox-sensitive signal transduction pathways and transcriptional regulatory processes through a physiological generation of ROS has gained a wide consensus. Needless to say, excessive and continuous release of ROS during chronic inflammation are partly responsible for cell degeneration and death.

Although hydrogen peroxide ($H_2O_2$) is not a radical molecule, it has oxidizing properties and can act as a second messenger in several biological processes. $H_2O_2$ modulates protein phosphorylation through cysteine oxidation of nuclear factor kB (NFkB) [1], AP-1 [2], and T-cell serum response factor[3] are all involved in ROS signalling mediated by hydrogen peroxide. A fairly low concentration of $H_2O_2$ (121 microMole) stimulates fibroblast proliferation [4], neoangiogenesis [5,6] and activates lymphocytes [7]. $H_2O_2$ can also stimulate IL-8 production in leukocytes [8,9] and in cultured endothelial cells to a level that can induce angiogenesis [10]. Moreover it is important for the transduction of signals by PDGF [11], insulin [12], leukotriene B4 [13] and TNF-alpha [14]. We found that ozonation of human plasma triggers a reaction leading to release of $H_2O_2$ and lipid oxidation products (LOPs) [15,16] so that ozonated serum briefly added to human endothelial cells in culture induces a significant and steady increase in nitric oxide (NO) production [17]. Interestingly, addition of $H_2O_2$ (20-40 microMole) to the same cell system rapidly increases the release of NO, that is further potentiated by L-Arginine (20 microMole) addition and totally blocked by the NO synthase inhibitor NG-nitro-L-arginine methyl ester. Moreover, Brown [18] and Thengchaisri and Kuo [19] have suggested that $H_2O_2$ induces endothelium-dependent vasodilation through activation of cyclooxygenase-dependent prostaglandin $E_2$ formation. Hydrogen peroxide can be produced inside the cell and also in the extracellular space by a membrane bound NADPH oxidase. It readily diffuses through the plasma membrane and acts as a second messenger inside the cell. "Physiological" concentrations of $H_2O_2$ can trigger several biochemical pathways (reviewed in Bocci [15,16] without

deleterious effects because the normal cell has an efficacious antioxidant capacity that rapidly reduces it to water. When $H_2O_2$ is produced extracellularly or added to a cell culture system a gradient of $H_2O_2$ is rapidly established across the plasma membrane [20]. Stone and Collins [21] demonstrated that this gradient is the result of $H_2O_2$-scavenging enzymes (catalase, GSH-peroxidase) and results in the steady-state intracellular concentration being about tenfold less than the extracellular concentration. This result is important because the intravenous (IV) infusion of a low and calculated concentration of $H_2O_2$ results in a marked dilution in the plasma pool with partial inactivation and in intracellular levels able to exert biological effects on blood and endothelial cells without aggravating the concomitant oxidative stress. In 1888 Love [22] perceived that "hydrogen peroxide could be used as a topical remedial agent". He had a wonderful insight into a problem that was clarified only some eighty years later showing that phagocytes can only defeat pathogens when they deliver ROS ($O_2^-$, $H_2O_2$, HOCl and $NO^\cdot$) [23]. Only in 1993 did Farr [24] promote the intravenous (IV) administration of an aqueous solution of $H_2O_2$ diluted in a isotonic glucose in a few illnesses and founded bio-oxidative therapy, included by the NIH (Bethesda, MD, USA) among the complementary medical approaches. Clinical studies in ischaemic and neoplastic patients have subsequently been reported by Urschel [25], Sasaki [26], Nathan and Cohn [27] and Symons [28]. However no scientific evaluation on the stability and pharmacokinetics of $H_2O_2$ and derivatives has been carried out and we present our results.

## Materials and Methods

### *Materials*

Analytical grade $H_2O_2$ 30% was purchased from Fluka GmbH, Switzerland and stored in the cold room. Twice crystallized, aqueous solution catalase from bovine liver and all the materials not specified below were purchased from Sigma Aldrich srl, Milan, Italy. Anticoagulants for human use were either heparin (calcium salt) or 3.8 % sodium citrate solution (1 ml per 9 ml of blood). Sterile apyrogenic glucose solution 5% in 250 ml glass bottles was purchased from Galenica Senese, Siena, Italy.

### *Ozone generation and measurements*

Ozone was produced from medical grade oxygen using electric corona arc discharge with a modern ozone generator (Ozonosan PM 100K, Hansler GmbH, Iffezheim, Germany) which allows the gas flow rate and ozone concentration to be controlled in real time by photometric determination as recommended by the Standardization Committee of the International Ozone Association. Tygon tubing and ozone-resistant disposable syringes were used throughout the reaction procedure to ensure containment of ozone and consistency in concentration.

### *Ozone delivery to human blood*

A predetermined volume (usually 5 ml) of oxygen-ozone gas mixture at various ozone concentrations within the therapeutic range (20-80 μg/ml of gas per ml of blood or plasma) was collected with a syringe and immediately introduced into a second, 10 ml syringe, via a multidirectional stopcock containing an identical volume of either plasma or blood samples obtained from normal donors at the Siena Clinical Blood Centre. The final gas pressure remained at normal atmospheric pressure. Ozone is a very reactive gas so that rapid and precise handling is required to ensure reproducible results. In order to avoid foaming, samples were gently but continuously mixed with the gas phase for ten minutes, i.e. the period of time allowing the total reaction of ozone with blood. Afterwards they were dispensed into test tubes for analyses. Control samples were either used as such or mixed with an equal volume of oxygen. This control is necessary because oxygen accounts for at least 96% of the gas mixture. Ozonated autohaemotherapy (AHT) was performed [15] by adding 225 ml of blood into a neutral glass sterile bottle under vacuum to 25 ml of Na citrate (3.8%) solution. Next, 225 ml of gas mixture containing ozone at a concentration of 40 μg/ml per ml of blood (total dose: 9 mg) were added and, after the usual ten minutes gentle mixing, the oxygenated-ozonated blood was reinfused during the following 20 min into the donor (one of us, VB, has volunteered to do these autotransfusions since 1995). To evaluate the pharmacokinetics of thiobarbituric acid reactive substances (TBARS) and protein thiol groups (PTG) plasma level values, small blood samples were withdrawn before, at ten and 20 min infusion period and then at two, ten, 20 and 30 min during the post-perfusion period.

### *Preparation of the glucose solution containing hydrogen peroxide (gluco-peroxide solution)*

Using a sterile hood, a hydrogen peroxide solution at 15 % is prepared by diluting 30% reagent grade $H_2O_2$ with an equal volume of apyrogenic s-

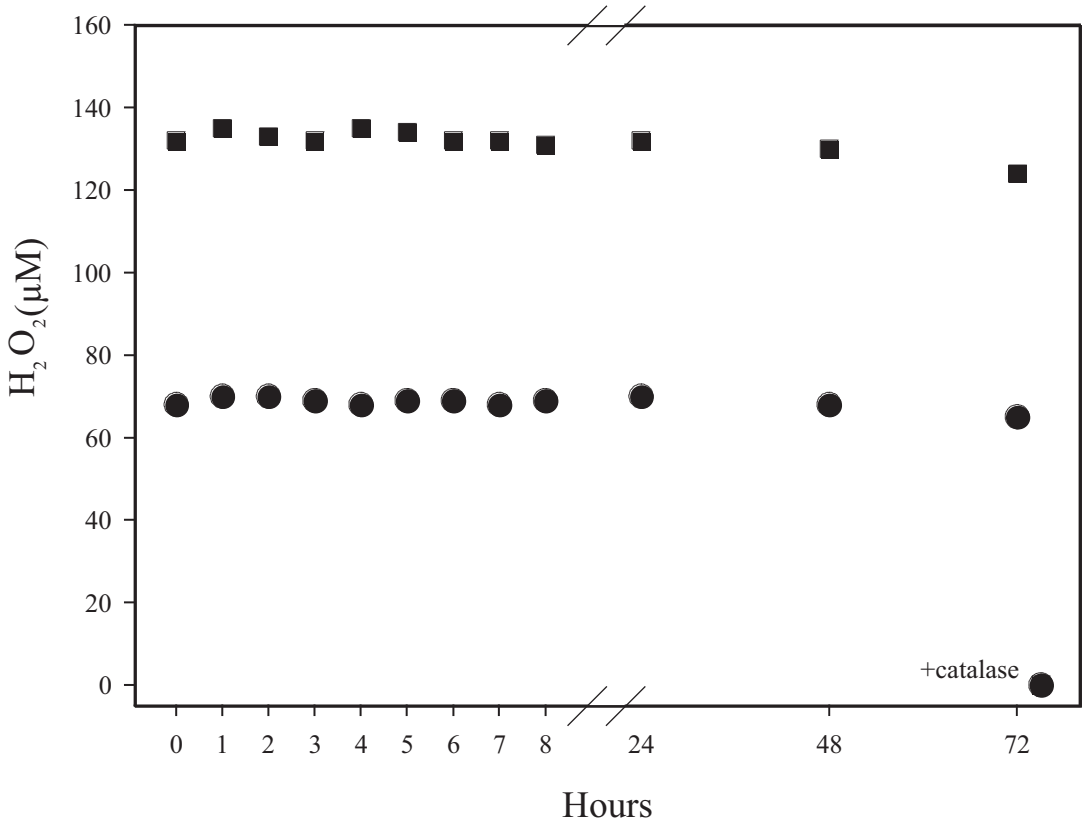


Figure 1 Stability of two solutions (68 and 132 microMole) of $H_2O_2$ kept at +21 °C in 5% glucose solutions. Average of two determinations.

terile bidistilled water. The final solution is prepared by injecting 0.5 ml of the 15% $H_2O_2$ solution into the 250 ml flask of 5% glucose solution via a sterile mini-spike plus particle filter (Ref. 4550234, B. Braun, Melsungen, Germany). During preparation, either glass or polypropylene disposable sterile syringes are recommended, avoiding the use of a metal needle.

The final $H_2O_2$ concentration is equivalent to 0.03% (8.8 mM) and the solution is isotonic and suitable for direct slow (20 min) IV infusion via a G-23 or a G-25 angiocath (plastic catheter). $H_2O_2$ *should never be diluted into saline to avoid the risk of HOCl formation*.

The $H_2O_2$ solution for topical use has a concentration of 3.5% (12 volumes). According to Farr [24], the final $H_2O_2$ concentration in the gluco-peroxide solution can vary from 0.03% (8.8 mM) to a maximum of 0.15% (44 mM) which must be infused at a slow rate.

The pharmacokinetic study presented here was carried out in duplicate using a 0.12% (35.2 mM) concentration infused within 20 min without any side effects (VB volunteered for the analysis). While we followed Farr's formulation, we refrained from adding both Mg and Mn chloride which may alter $H_2O_2$ stability.

*Therapeutic effect of the gluco-peroxide solution in ARMD patients.*

Owing to a lack of suitable venous accesses for blood collection, women with ARMD have the only option to be treated with the gluco-peroxide solution via a small, visible vein in the back of a hand. After being fully informed about this new experimental therapy and signing an informed consent form, this therapy has been so far performed in six women (age: 71±11) at the "Misericordia Medical Clinic" Taverne d'Arbia, Siena by VB as a physician. In order to induce tolerance, we adopted the strategy: start low, go slow. Thus $H_2O_2$ concentration in the glucose solution was 0.03% for the first week (two treatments), then 0.06% for the second week, 0.09% for the third week and finally 0.12% for the fourth and following three weeks. Results are reported in Section 6. Provided that the solution is injected slowly, even the final concentration does not cause any venous irritation.

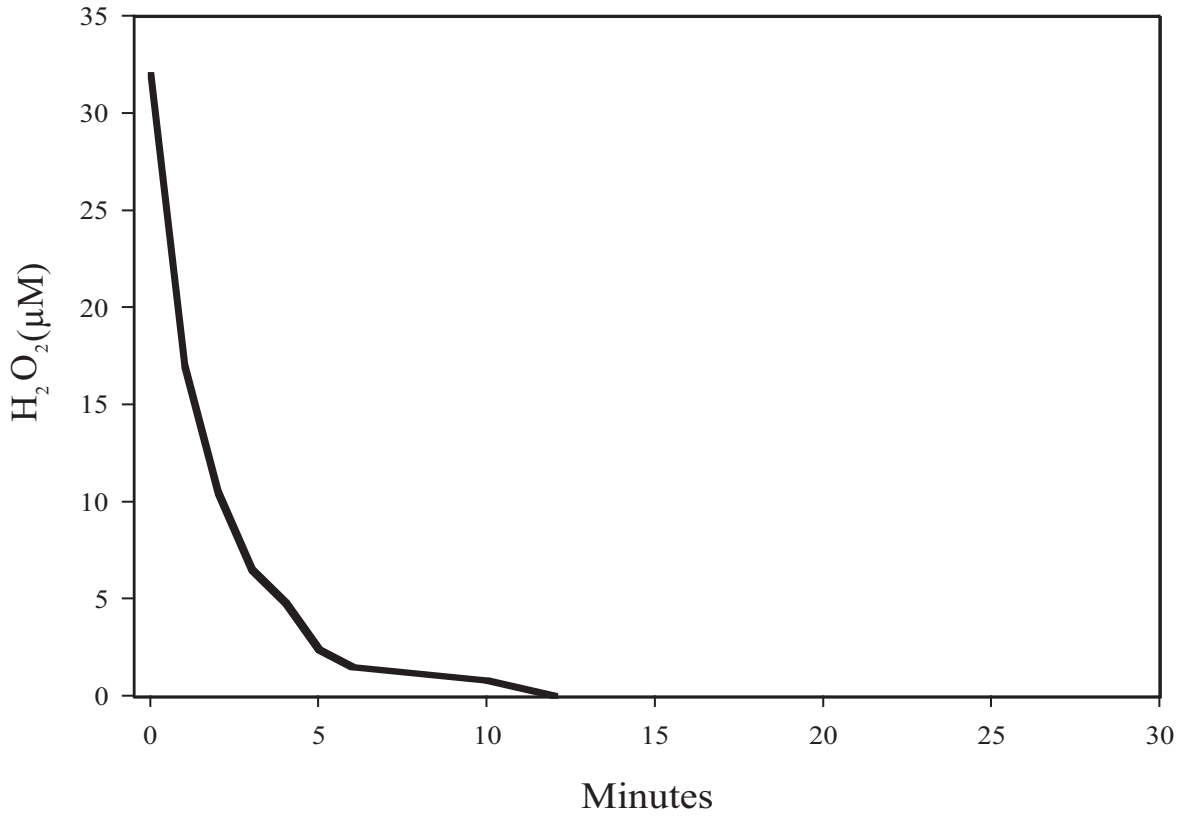


Figure 2 Rapid decay at 21 °C of $H_2O_2$ diluted in human plasma. The half-life is about 1 min.

*Biochemical determinations*

a) Hydrogen peroxide was measured in the gluco-peroxide solution and human plasma by the enzymatic method described by Green and Hill [29]. When necessary, catalase (20-40 Units) was added to the solution under test.
b) Total antioxidant status (TAS) in plasma samples was determined according to Rice-Evans and Miller [30]. Values are reported in mM terms.
c) The thiobarbituric acid assay completed with butanol extraction was carried out in plasma as described by Buege and Aust [31]. Values are expressed as microMole of TBARS relative to a malonyldialdehyde (MDA) standard.
d) PTG were measured in plasma according to Hu [32] using procedure 1 with 5,5'-dithio-bis(2-nitrobenzoic acid, DTNB) dissolved in absolute methanol. Values are reported as mM.
e) The haemoglobin determination was performed using 20 microLitres of original blood and an equal volume of plasma collected after the ozonation. Samples were mixed with 5 ml of the cyanide-methahaemoglobin reagent (Sclavo Haemoglobin test kit). Optical density, read spectrophothometrically at 540 nm, was converted to haemoglobin according to a standard curve and referred to as a percentage of total haemoglobin.

*Statistical analysis*

Whenever possible, results were expressed either as an average of two determinations or as means ± SD. Statistical evaluation of the experimental data was performed with Student's *t*-test for paired samples with ≤0.05 as the minimal level of significance ($P \leq 0.05^{+}$).

## Results

1) *Stability of the gluco-peroxide solution*

Figure 1 shows that the repeated titration of two solutions at different $H_2O_2$ concentrations, kept at +21°C, shows no practical change in concentrations up to three days. The final addition of catalase lowers the titres to zero within a few minutes. A sample of the $H_2O_2$ solution (68 microMole) kept at +4°C remains equally stable for three days (data not shown). The gluco-peroxide solution, prepared in the late morning is infused in patients

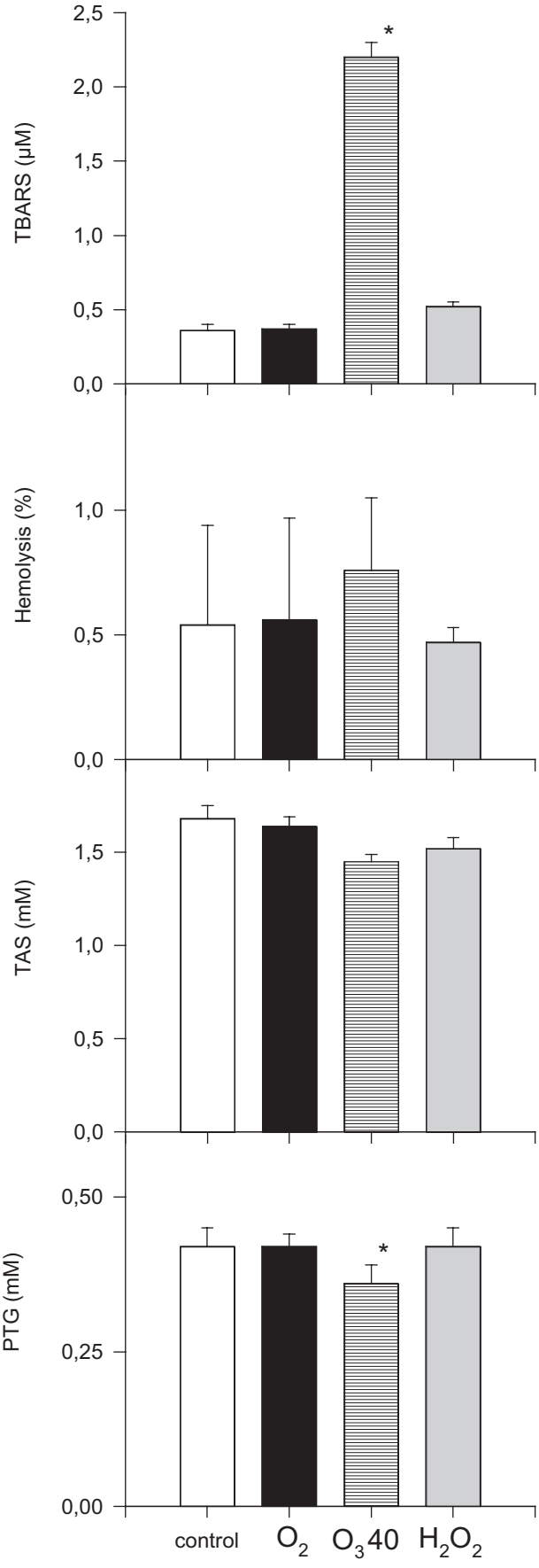


Figure 3 Three human blood samples were exposed to air (control) or $O_2$, or $O_2$-$O_3$ with an ozone concentration of 40 mcg/ml or to $H_2O_2$ (0.12%) for 1 min. TBARS, TAS and PTG levels varied significantly (+P<0.05) only after ozone exposure.

in the afternoon or otherwise discarded. For current medical use the hospital and private pharmacists are qualified to preparing the solution.

2) *Instability of hydrogen peroxide in human plasma*

Addition of the gluco-peroxide solution to human plasma anticoagulated with Na citrate leads to a very rapid disappearance of the $H_2O_2$ titre. The half–life is estimated to be about one min (figure 2). The reduction of hydrogen peroxide is mainly due to the presence of physiological amounts of uric and ascorbic acids and traces of antioxidant enzymes (catalase and GSH-peroxidase). Addition of both 3-amino-1,2,4-triazole and N-ethylmaleimide delays but does not block the disappearance of $H_2O_2$.

Addition of the gluco-peroxide solution to human blood leads to such an extremely rapid disappearance of the $H_2O_2$ titre that it is technically impossible to detect it even 90 s after addition. Besides the presence of antioxidants, the erythrocyte mass mops up $H_2O_2$ almost instantaneously.

3) *Peroxidation of human blood by either ozone or* $H_2O_2$

Three human normal blood samples (5 ml each) anticoagulated with Na citrate were either treated

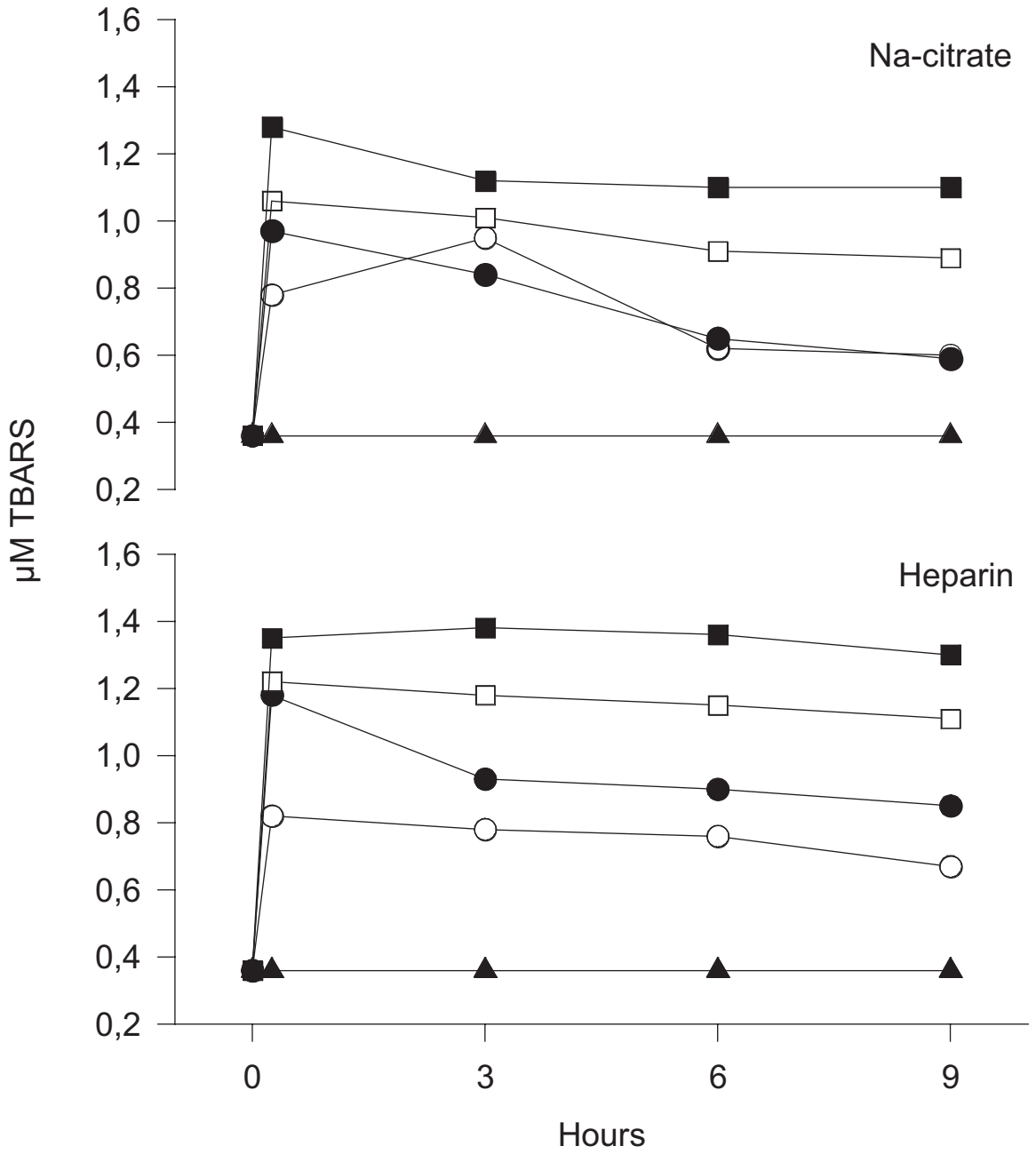


Figure 4 Kinetics of TBARS mean values measured in two normal human plasma samples before (0 time) and immediately after ozonation up to 9 hours with ozone concentrations of 10 (○), 20 (●), 35 (□) and 70 (■) mcg/ml per ml of blood. Controls are samples exposed to $O_2$ only (▲). All samples were incubated at +37 °C.

with 5 ml gas containing an ozone concentration of 40 mcg/ml (total dose: 0.2 mg ozone) or supplemented with a gluco-peroxide solution so that the final concentration of $H_2O_2$ was 0.06% (17.6 mM).

Figure 3 compares the peroxidation (TBARS), haemolysis, total antioxidants (TAS) and protein oxidation (PTG) values measured after addition of either ozone or $H_2O_2$. Within the previously defined therapeutic window [15,16], the ozone concentration of 40 mcg/ml per ml of blood is in the middle range and yet, in comparison with control and simply oxygenated samples, it appears to modify the blood sample significantly more than the gluco-peroxide solution. Indeed the generation of LOPs is far higher after ozonation than after $H_2O_2$ addition and this was expected as $H_2O_2$ is only one compound of the many generated during the reaction of ozone with blood components.

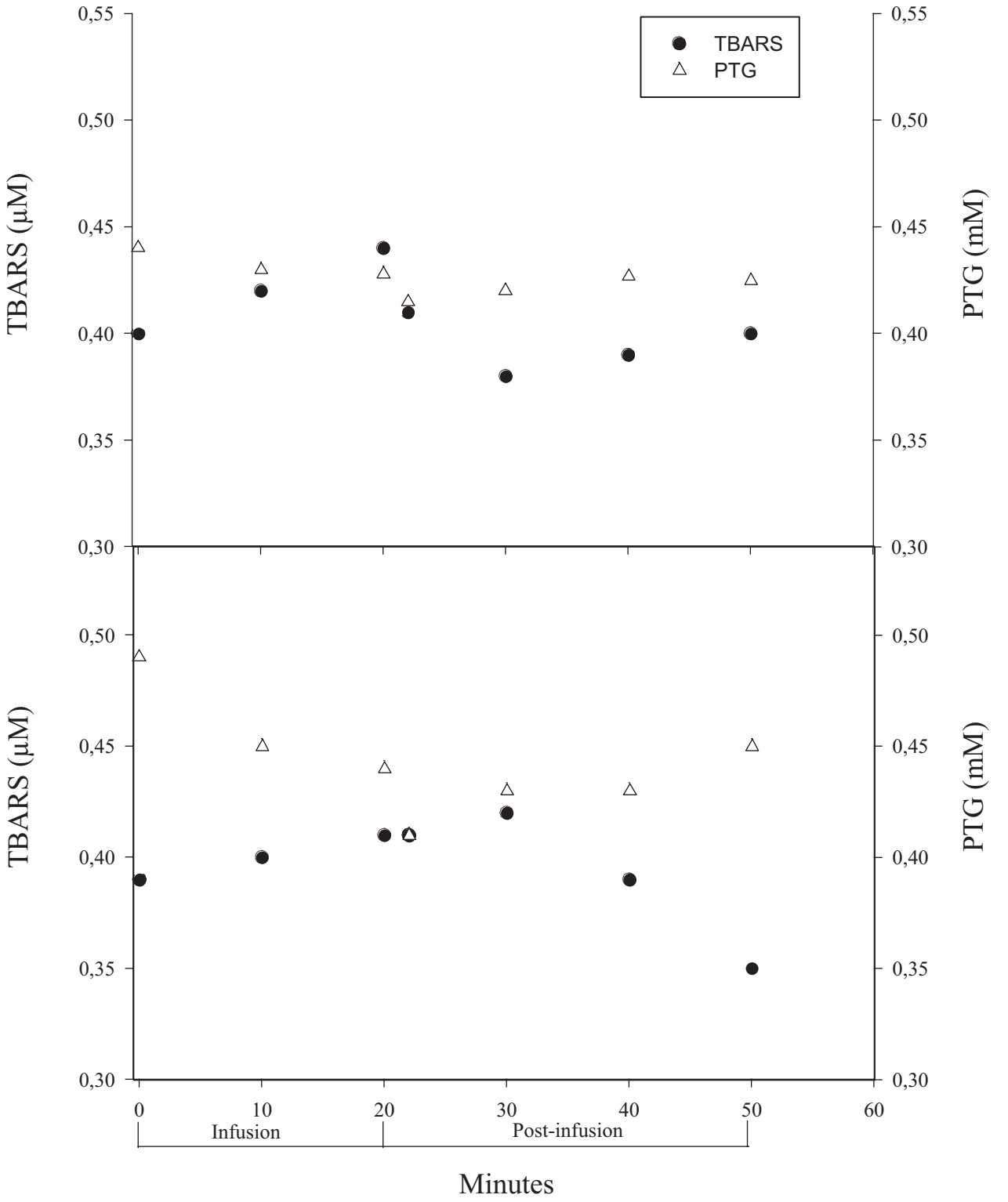


Figure 5 A e B Kinetics of LOPs *in vivo*. (A) In the case of ozonated blood, TBARS levels in plasma increases slightly only during the infusion period and thereafter they fluctuate within normal values. (B) The infusion of the gluco-peroxide solution does not modify T-BARS levels. In both cases, PTG values are hardly modified.

4) *Stability of LOPs in vitro*

$H_2O_2$ as a typical marker of ROS disappears very rapidly from body fluids either after its addition or after ozonation of human plasma ex vivo. On the other hand, LOPs (a heterogeneous mixture of MDA and alkenals) appear to be stable in vitro, even when incubated at +37°C at pH 7.3. Figure 4 shows that different concentrations of these compounds decay slowly in vitro and this result helps to explain why they are toxic in static tissue cultures even at 1 microMole concentration.

5) *What is the fate of LOPs in vivo*?

A preliminary result [33] has now been amply confirmed after infusion in one volunteer of either ozonated blood or the gluco-peroxide solution. However, both types of infusions have already been practiced in hundreds and thousands of patients.

If LOPs remained stable in the circulation during a 20 min infusion, we would have measured their progressive increase in serial plasma samples collected during the infusion. Figure 5A clearly shows that TBARS hardly increased during the infusion of ozonated blood and returned to normal levels during the next 30 min. Infusion of the gluco-peroxide solution did not affect TBARS values either during infusion or thereafter (figure 5B). likewise, the kinetics of PTG values does not show any modifications. Neither type of infusion caused any acute or chronic side effects.

6) *Effect of a treatment cycle of the gluco-peroxide solution in age-related macular degeneration patients.*

With the exception of a palliative effect of oral supplementation of antioxidants and zinc, there is no orthodox ophthalmological therapy for the atrophic form of ARMD. Unavoidably this disease more or less rapidly progresses to blindness. However, since 1995, we have found that due to retinal ischaemia combined with retinal pigment epithelium and photoreceptors degeneration, the early and not too advanced stages of this disease can benefit from a cycle of 14-16 treatments in two months (twice weekly) of oxygenated-ozonated autohaemotherapy (AHT). Mean distance visual acuity was significantly improved in ARMD patients whereas no significant improvement was observed in the control (oxygen only) group [15,16].

Unfortunately a sizable proportion of women have poor venous accesses which impede the AHT treatment. The gluco-peroxide solution can nonetheless be infused via small veins visible on the back of the hand. So far, in close collaboration with the ophthalmologist, we have performed a full cycle (14 treatments during seven weeks) in six women. The ophthalmologic control performed at the end of the cycle disclosed an increase in visual acuity from 0.15 to 0.23 (an average increase of 53%) in four women. The improvement was minimal in one woman and none in another probably owing to irreversible photoreceptors degeneration. Considering that there are no other therapeutic options, the improvement in visual acuity, though modest, is highly appreciated by patients because they become more independent and report a better quality of life. The fact that they show an excellent compliance during the successive maintenance therapy is the best demonstration of the therapy's value. No control arm (5% glucose solution only) could be carried out because although treatments are free of charge, it would be unethical. There are no side effects and the majority of patients currently report feeling well during the course of therapy.

## Discussion

Today $H_2O_2$ is acknowledged as one of the crucial ROS and an early and effective ozone messenger. By activating glycolysis, ATP and 2,3-DPG formation in erythrocytes, these biochemical changes lead to improved oxygen delivery in ischaemic tissues [15,16]. In lymphocytes, the transient increase in $H_2O_2$ in the cytoplasm activates a tyrosine kinase, which, by phosphorylating IkB·, detaches it from the inactive complex NFkB-IkB allowing rapid migration of the heterodimer to the nucleus resulting in the successive synthesis of several proteins [15]. Even a minimal activation of platelets enhances the release of growth factors [34,35] and, on endothelial cells, $H_2O_2$ determines an increased production of NO [17-19]. Thus direct infusion of the gluco-peroxide solution triggers a number of biochemical pathways that can eventually result in therapeutic effects.

From our data (figure 5), it appears that the infusion of this solution barely increases the plasma levels of peroxidation end-products, while this aspect is slightly more evident after the infusion of ozonated blood into the donor. The fact that TBARS and PTG plasma levels remain practically unmodified is due firstly to judicious dosages, secondly to the lower oxidizing property of $H_2O_2$ in comparison to ozone, thirdly to the prompt reducing activity of blood antioxidants and fourthly to the association of a number of processes (dilution in body fluids, neutralization, enzymatic detoxification and excretion of LOPs) operating simultaneously and effectively *in vivo*. These considerations explain why the use of either ozonated blood or the gluco-peroxide solution is never accompanied by any acute or chronic toxicity. We have calculated that by virtue of the protective processes described, the final circulating levels of LOPs dur-

ing and after reinfusion of ozonated blood remain at submicromolar levels. This result is important [36] because the transitory presence of LOPs is likely to be responsible for the upregulation of antioxidant enzymes (SOD, GSH-peroxidase, G-6PD) we demonstrated in erythrocytes *in vivo* during a therapeutic cycle of ozone therapy [15,16,33,37,38]. This paradoxical result has a great practical validity and is due to repeated, calculated, acute oxidative stresses able to induce a positive response similar to the phenomenon of small, repeated ischaemic heart-conditioning effects.

*We emphasize that hydrogen peroxide should never be added to physiological solution (saline) owing to the risk of forming caustic* OCl-. *Moreover we condemn the infusion of ozonated saline in vitro as well as in patients: this practice has become common in Russia and, regrettably, is also used by a few charlatans in Italy without understanding that they can harm the patient by infusing an irritant as powerful and toxic as* OCl-.

Work in progress aims to compare laboratory and clinical results by testing the classical HAT and the gluco-peroxide solution in vasculopathies, ARMD, infectious and degenerative diseases. This rationale behind this line of work is that $H_2O_2$ is one of the most important early ozone messengers. However the question whether $H_2O_2$ is as effective as ozonated blood autotransfusion remains open because late products, like LOPs, appear to be scarcely generated *in vivo* owing to rapid reduction of hydrogen peroxide. Needless to add, although gluco-peroxide infusion does not present the risk of direct gas administration, it must be performed slowly to avoid any risk of oxygen embolism and potential venous irritation. *A clear disadvantage to bear in mind is that the gluco-peroxide solution cannot be used in diabetics*. Nonetheless we feel that this approach deserves to be pursued because it has the following advantages: A) ozone generators, with all their problems and cost, would become superfluous. B) The cost of the gluco-peroxide solution is almost negligible: the preparation of the solution is simple and well standardized, it is far more stable than ozone and can be transported and administered anywhere. C) One needs only reagent grade $H_2O_2$ (30%), a few ampoules of sterile bidistilled water, the 5% glucose solution flask, a few plastic disposable tools and, with good care and a little experience there is no need for electricity or a sterile hood. The advantage is that this therapy could be performed in poor countries in remote corners of our planet to alleviate serious diseases. We should not forget that the majority of the Earth's population receives minimal medical assistance.

## Acknowledgements

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# New Data regarding the Use of Oxidative Stress (Ozone Therapy) in the Former Soviet Union Countries

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**Key words:** oxygen-ozone, oxidative stress

**SUMMARY** – Ozone therapy is a well established medical practice in treating several pathologies by the "Russian method" also. The main difference between the "West Europe method" and the method used in the republics of Former USSR ( as well as in Cuba etc) is ozonization of normal saline and intravenusly drop by drop infusion with a very specific instumentation instead of extra corporal blood ozonization. The authors travelled far away to the medical academy of Nizny Novgorod Russia present the several indications and methods of ozonotherapy instructed to them by masters of their kind with the russian ozonators.

The oxidative stress in biological systems, applied in the form of oxygen free radical ($O_3$), which is produced in specific medical appliances (ozone generators) and it is administered in the form of $O_2/O_3$ mixture on all membranes and extracellural macromolecules, has a therapeutical effect only when it is implemented under specific protocols. Pioneers in this kind of therapy are Germans and Swiss who first manufactured the medical ozone generators. The Russians, 30 years ago, manufactured ozone machines and introduced the ozone therapy method (oxidative stress) in their national health system, creating a school of their own.

In the antipode of German-Swiss school which is established in European countries (Italy, Spain, Greece etc) and the Middle East (Israel, Egypt, Jordan etc), is the Russian school and their technologically and scientifically dependent countries as Kazakhstan, Sri Lanca, Cuba etc. [1]

The basic research and biochemical Russian discoveries do not differ at all from the European (German) school and at some points they are more expanded regarding the biochemistry of free radicals. Nowadays, the method of choice for the therapeutic effect of systematic oxidative stress of a patient is the use of ozonized normal saline in the form of slowly dropped infusion on the contrary of autologous blood auto transfusion (major autohemotherapy) which is used in western countries.

In the Russian school, they ozonize a certain amount of normal saline (200 ml) for 15 minutes. The preselected concentration of $O_2/O_3$ in Internal Medicine, is estimated regarding patient weight * and its health condition. The flow rate of $O_3$ into the ozone generator is steadily 1 lt/min. The catalyst eliminates the bubbles that pass trough the saline (figures 1, 2).

The maximum amount of $O_3$ daily administered per dose, is usually 4-5 mgr and should never exceed 8-10 mgr. If we exceed these rates, the over coagulation syndrome starts. That is why we take into consideration the prothrombin time (PT, INR), the bleeding time test and the coagulation time rate of the patient, before starting therapy [6].

* 1 Kgr of body weight is correspondent at 20 μgr $O_3$/lt $O_3$-$O_2$ for many internal diseases. It means that a patient of 100 kgr total weight has to get a concentration of 2000 mgr $O_3$/lt or 2 mgr $O_3$/lt or 2 μgr $O_3$/ml [8].

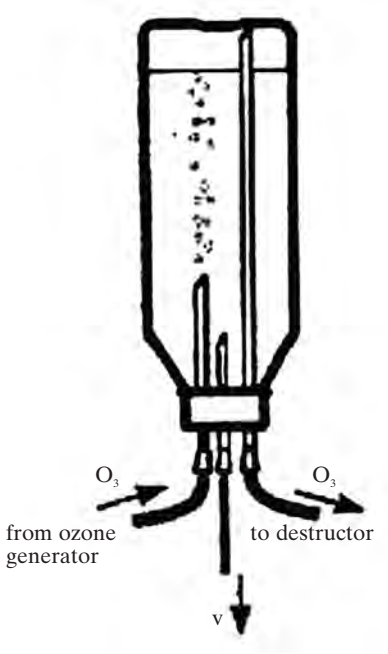


Figure 1 Ozonitation of physiological salina for intravenous infusion, if physiological saline is available in glass bottles.

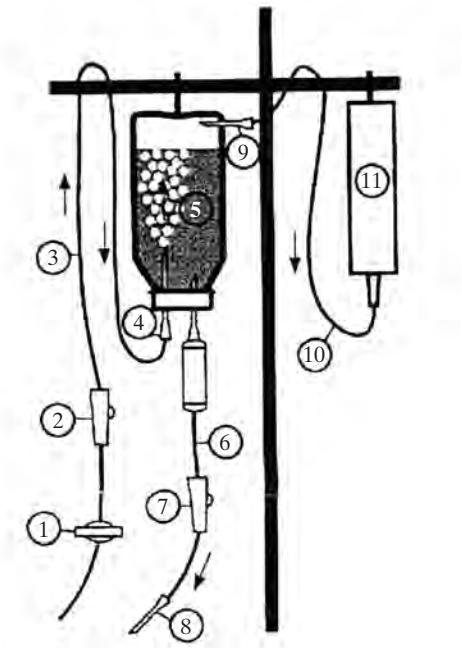


Figure 2 To be used, if physiological saline is available in plastic containers. 1) Hydrophobic Filter Preventing Solution. 2) Leakage into the Ozone Generator. 3) Roller Clamp of Ozone Transfer Tubing. 4) Ozone Transfer Tubing. 5) Needle (d=1,2 mm). 6) Container 250 ml with 0,9% NaCl Infusion Solution. 7) Infusion Set. 8) Roller Clamp of Infusion Set. 9) Venous Puncture Needle (G22-G24). 10) Needle (d=1,5 mm). 11) Connection Tubing to Destructor for Removal of Residual Ozone. 12) Destructor. Basic produced concentration of gas mixture $O_2/O_3$ at 1 lt/min $O_2$ supply, in patients of 100 KGR total body weight.

| | | |
|---|---|---|
| ONCOLOGY<br>Under chemotherapy or radiotherapy<br><br><br>100-200 μgr/lt | GYNECOLOGY<br>Dystocia, ecla mpsia, automatic abortion<br>400-500 μgr/lt<br>Gynecological infections<br>600-800 (έως 1500) μgr/lt | NEUROLOGY<br>Dystonia, migraine<br>500 μgr/lt |
| RHEMATOLOGY<br>Autoimmune disorders, Chronic infections<br><br><br>2000-2500 μgr/lt | CARDIOLOGY<br>Acute myocardial infraction<br><br><br>800 μgr/lt | INTERNAL MEDICINE<br>ages 25-60 years<br>1000-1200 μgr/lt<br>ages over 60 years<br>1500-1800 μgr/lt |

The free radicals which are produced in the ozonized normal saline are shown at the chemical reactions below (NaCl does not react with $O_3$ under normal conditions):

$O_3 + H_2O \rightarrow 2OH' + O_2$ (OH radical)
$O_3 + OH' \rightarrow HO_2' + O_2$
$O_3 + HO_2' \rightarrow OH' + 2\ O_2$
$OH' + OH' \rightarrow H_2O_2$
$O_3 + H_2O_2 \rightarrow OH' + HO_2' + O_2$
$OH' + HO_2' \rightarrow H_2O + O_2$

When we are treating patients who have cellular destruction, since there are more antioxidant molecules extracellurally, we have to administer greater amounts of $O_3$ at the saline we infuse intracorporarly [9]. The method used from the Russians regarding minor auto transfusion of autologe blood (minor autohemotherapy), is replica of western countries (5-10 ml blood +10 ml $O_2/O_3$, 10-20 μgr/ml) [12].

There is a great research and experience of Russians about ozone therapy for different kind of

pathological conditions like: ischemic brain infractions [2], atherosclerosis, diabetes mellitus, cardiac failure, ischemic myocardial disease, hypertension, gastro duodenum ulcer [5], obstructional peripheral arteriopathy, chronic colitis, chronic cholecystitis, chronic pancreatitis, psoriasis [7], neuro-dermatitis, and herpes.

The use of $O_3$ through the rectum (rectal insuflation) in the concentration of 1500-2500 μgr/lt (1 lt total amount) substitutes, very well, the intravenous therapy with ozonized normal saline at non-oncological patients.

The external ulcers therapy with $O_2/O_3$ atmosphere is applied for 20 minutes without continuing gas irrigation. We simply stuff the bag with $O_2/O_3$ in a concentration of 6000 μgr/lt in infected suppurative ulcers, 2000 μgr/lt in non infected ulcers when fresh granulating tissue is needed to be developed and 1000 μgr/lt in ulcers under epithelialization. Treatment is always combined with ozone intravenous therapy [10]. Progress in wound cleansing and healing depends on the specific patient and may thus last for periods between a few weeks and several months.

The ozonized double distilled water is produced by 10 lt $H_2O+O_2/O_3$ 10000 μgr/lt that passes through the glass pot for 20 minutes approximately in a flow rate of 1 lt/min. The ozonized water is used for drinking or regional application and for cavity and ulcer washing [11]. In the refrigerator the half time of ozonized water is about five days kept always in glass containers.

The ozonized oil (sunflower oil or olive oil) is ozonized for 60 minutes with 5000 μgr/lt gas (internal use) or for 60 minutes with 10000 μgr/lt gas (external use) in a flow rate of 1lt/min.

Ozone therapy helps the chronically suffered patient because it also improves the drug response of the cells [13]. Nowadays, hyperthyroidism is not considered as contraindication for ozone therapy.

In the field of hypertension, $O_3$ helps via its activity at the endothelium of the vessels by producing NO (which is reduced at the hypertensive patients) into the endothelium cells. The newly produced NO decreases platelets' aggregation rate (PAR) and it causes distention onto the previously closed capillary vessels (normally, the erythrocyte passes throw only 1/3 of the capillary vessels). By this way the diastolic blood pressure is decreased whereas the peripheral oxygen supply is increased. The dosage of normal saline used, which contains a certain amount of $O_2/O_3$, used for ozonization in internal medicine is 200 ml. It is treated with 20 μgr/lt/Kgr of body weight for 15 minutes extracorporaly and then it is infused intravenously for about 20 min [8].

Ozone therapy is also applied in bronchial asthma and chronic bronchitis as the higher amount of NO, after ozonization, into the organism leads to bronchodilatation. Furthermore, it has high bactericidal action, reduces hypoxia and increases phagocytosis and TNF onto the lungs.

The use of hydro-colon therapy as a preventive method for all the diseases and as a method for the management of constipation, chronic immunodeficient and autoimmune diseases [3], dermatitis and allergies, is expanded in the former Soviet Union countries. The contraindications for hydrocolon therapy are the presence of diverticulae and polyps, the acute large intestinal hemorrhage and Crohn's disease. The therapeutical pressure of warm water that is introduced into the colon during hydro-colon therapy is 50-60 mbar. At each colon washing the total amount of water is 2-3 lt. At each session, the total amount of water used is 30-40 lt (10-15 washings). Thus, the duration of the total procedure is approximately 30-40 minutes. At the end of each session, the colon washing is finished using ozonized water (5 lt at first, 20 lt to the latest sessions). The total number of hydro-colon therapy sessions is 5-6, every 3 days.

The intravenous ozone therapy is applicable to all the diabetic patients. Ozone alters insulin action and reduces hyperglucosemia via the Pendose Phosphate pathway. By this way, there is a better response to the classical drug therapy and better managing in the diabetes mellitus complications (peripheral neuropathy, microangiopathy). The beneficial outcome lasts for over 6 months [4].

Furthermore, Russian cosmetology is advanced. Ozone therapy is applied in cellulitis, alopecia, wrinkles and telangiectasiae.

Russians measure the effectiveness of ozone therapy using a chemoluminometer by which the produced scavenging curves of the laboratory - produced oxidative stress in various biological fluids of the patient, are proportional (and by this way diagnostical) to the antioxidative deposits of the specific fluid.

Nowadays, the medical academies of Moscow and N. Novgorod (where the authors of this presentation have been educated), are organizing seminars and educate health professionals of various medical specialties. They are considered as pioneers in the field of ozone therapy because they have a great research outcome and many scientific papers are announced at international congresses or published in international medical journals.

Oxidative stress of living tissues is a useful therapeutic tool in all hospitals of the former Soviet Union countries. Technologically implicated industries (at least five of them) are continuously cooperating with hospital clinics and medical academies.

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# Total Clinical and Radiological Resolution of Acute, Massive Lumbar Disc Prolapse by Ozonucleolysis
## The First Indian Case Report

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**Key words:** lumbar discal hernia, oxygen-ozone treatment

**SUMMARY** – Direct injection of ozone (ozonucleolysis) has been proven to be a safe and effective alternative to open surgery for patients suffering from disc herniation in many centres around the world [1,2,3,4,5]. From August 2003 to July 2004 45 patients with discogenic radiculopathy who had failed to respond to an average of twelve weeks of conservative treatment were treated by ozonucleolysis. Percutaneous injection of the disc(s) or foraminal injection of gas was performed in a prone position using a posterolateral approach in an out-patient setting. Over a three-week period, one injection of 4ml intradiscal ozone oxygen mixture at 29 mcg% conc. was followed by twice weekly injections of 10ml of $O_3O_2$ in the pararadicular region. 88% had a successful outcome (55% excellent, 33% good) and 12% were failures measured on the Odom scale.6 There was no ozone related morbidity and no patient had to be hospitalized for any complication related to the procedure. We present two case reports from India of patients with massive lumbar disc herniation treated by ozonucleolysis who made a full recovery.

### Case Report 1

A 40-year-old male cook presented on 25/11/2003 with a work-related incapacitating low back and left leg pain with paresthesia and mild foot weakness of two-month duration. He had failed to respond to physical therapy, rest and analgesic and anti-inflammatory medications.

Straight leg raising was limited to 45 degrees with a moderate (3/5) weakness in left extensors of great toe and ankle and left L5 sensory loss. MRI scans (figure 1) showed a massive central protrusion, slightly more to the left, nearly occupying the entire canal. The patient refused surgical decompression and the option of ozonucleolysis was chosen after a detailed discussion.

*Course*

On 28/11/2003, ozonucleolysis (ozone discectomy) was performed using 4 ml intradiscal and 12 ml foraminal $O_3O_2$ mixture at a concentration of 29 mcg% under real time fluoroscopic navigation as recommended by Leonardi [7]. This was followed by twice weekly IM (pararadicular) $O_3O_2$ injections for three weeks.

There was a rapid resolution of symptoms. In two weeks the patient was asymptomatic. Straight leg raising was normal, motor strength in the left leg had returned to normal with recovery of sensory function.

A follow-up MRI scan (figure 2) on 17/04/2004 showed a near total resolution of the disc prolapse. He remained free of any complaints attributed to his back or leg and was without any neurological deficit.

On his last follow-up on 18/01/2005 he was working full time and remains fully asymptomatic.

### Case Report 2

A 39-year-old woman presented on 1/11/2003 with an unyielding back and severe left leg pain during a golf swing of two weeks duration. She

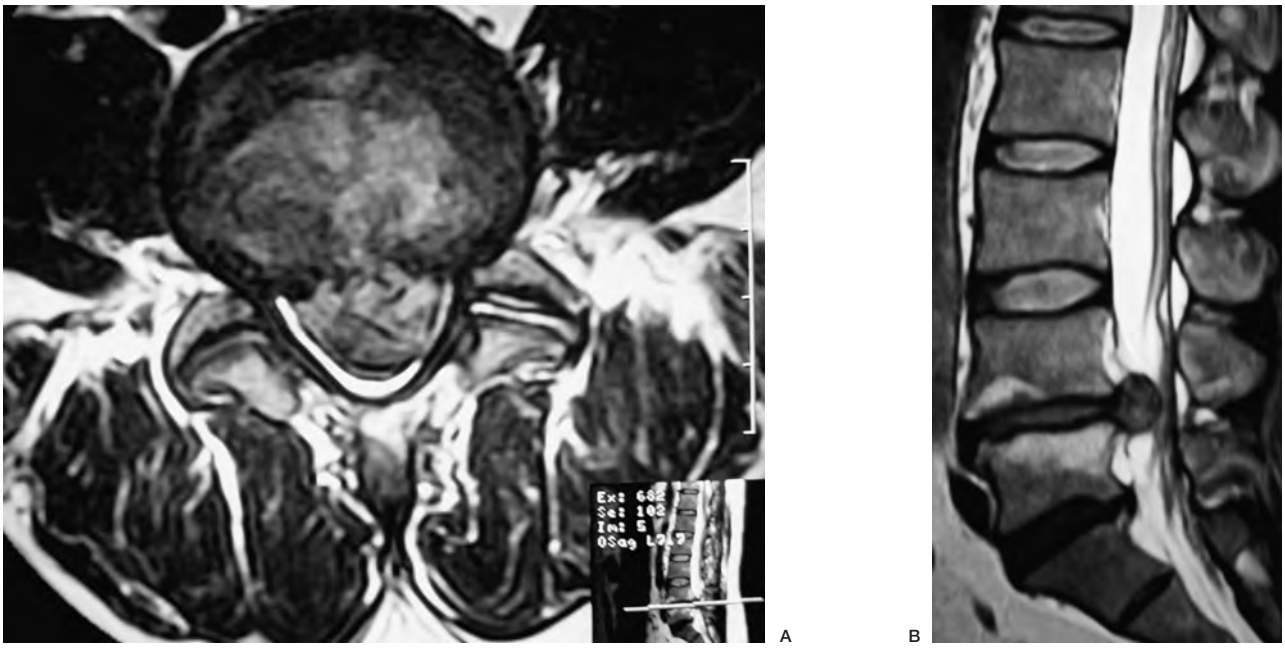


Figure 1 T2 weighted MRI image demonstrating a massive L4-5 disc prolapse nearly occupying the entire canal.

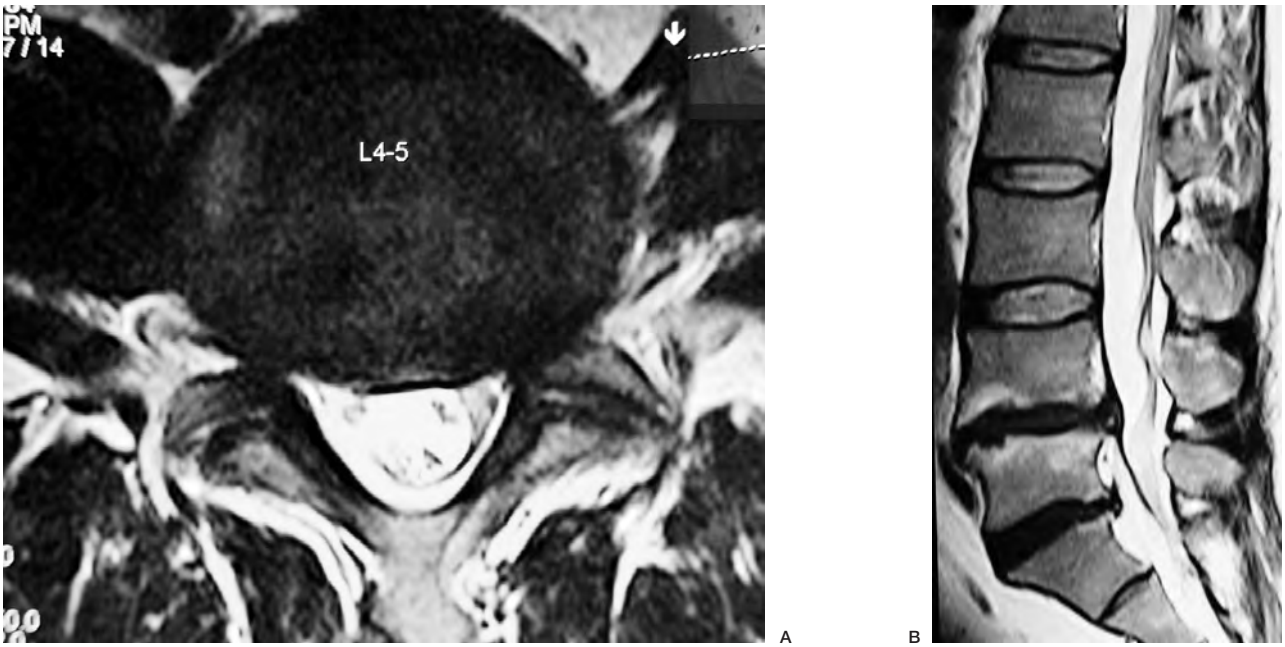
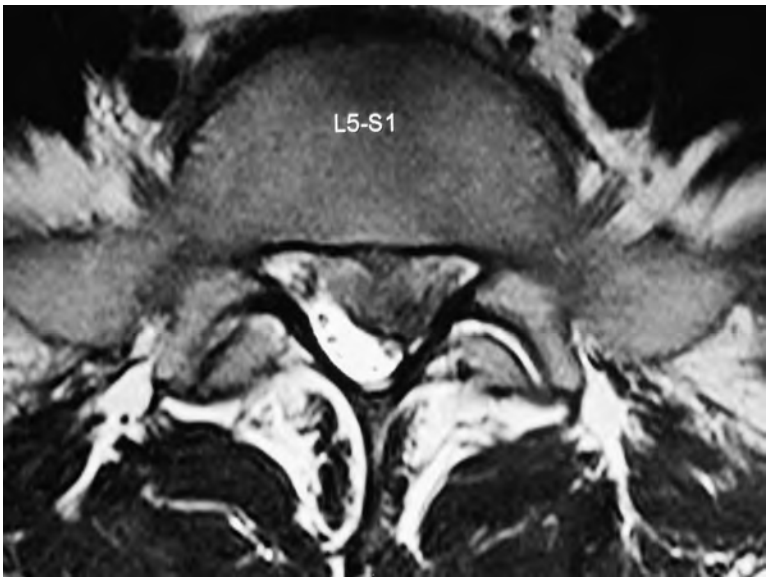



Figure 2 T2 weighted MRI image demonstrating near total resolution of disc prolapse.

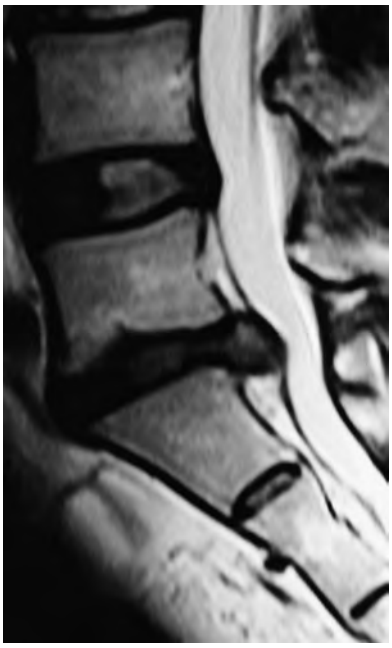
had a history of back pain for which an epidural steroid injection had been given five months earlier with a successful outcome. On examination straight leg raising was limited to 30 degrees with absent left ankle reflex and S1 sensory loss. MRI scan (figure 3) showed a large left paracentral protrusion at left L5S1 level.

*Course*

On 6/11/2003, ozonucleolysis (ozone discectomy) was performed using 4 ml intradiscal and 12 ml foraminal $O_3O_2$ mixture at a concentration of 29 mcg% under real time fluoroscopic navigation. This was followed by twice weekly IM (pararadicular)

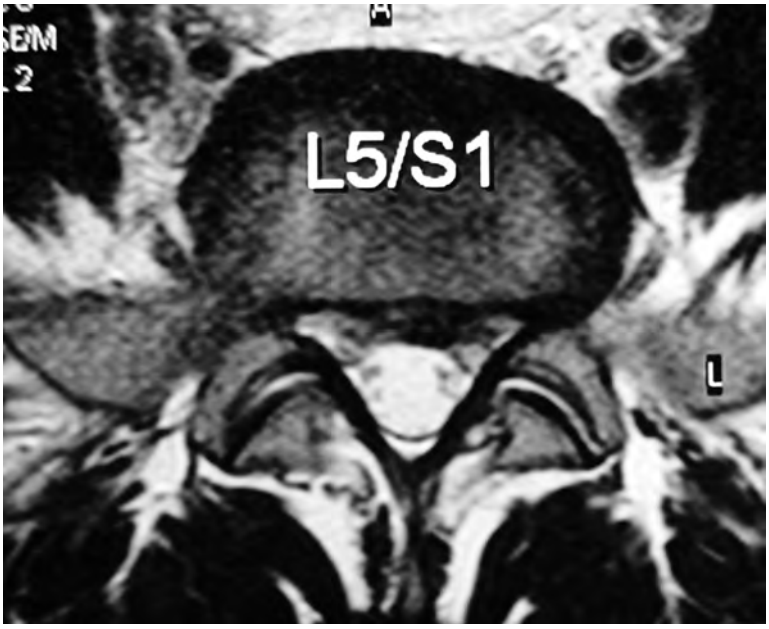



A



B

Figure 3 T2 weighted MRI image demonstrating a large left paracentral extrusion at L5S1 level.

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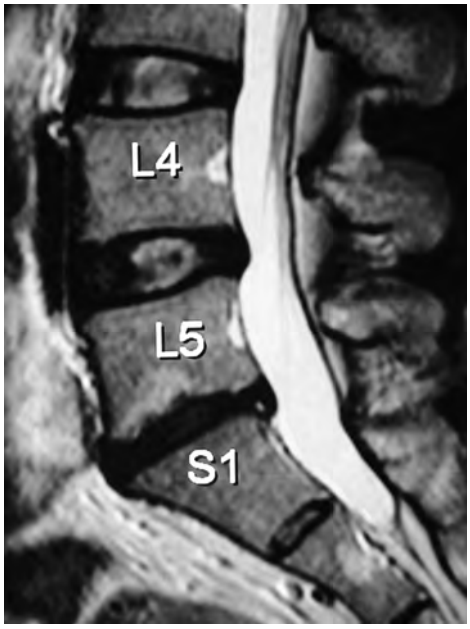


B

Figure 4 T2 weighted MRI image demonstrating near total resolution of disc extrusion.

$O_3O_2$ injections and physical therapy for three weeks. She became asymptomatic in four weeks and resumed playing daily golf in three months. A follow up MRI scan (figure 4) shows total resolution of disc extrusion. On her last follow-up on 1/15/2005, she remained asymptomatic. She plays an 18 hole round of golf six days a week.

## Discussion

Since disc prolapse was first observed by Dandy [8] and subsequently described in detail by Mixter and Barr [9] over 70 years ago, its treatment has confounded clinicians and investigators due a relatively high failure rate and complications associated with

the various treatment options [10,11,12]. Outcome studies of lumbar disc surgery document a success rate between 49 and 90% and re-operation after lumbar discectomy ranging from 4% to 15% [13,14,15,16,17,18]. Reasons for this failure have been variously attributed to several factors including dural fibrosis [19], arachnoidal adhesions20, muscle and fascial fibrosis and mechanical instability resulting from the partial removal of bony and ligamentous structures required for surgical exposure and decompression [21,22,23,24,25]. There has been a surge of interest in finding alternative means of nerve root decompression while maintaining structural stability. Several refinements of root decompression have been developed including the use of magnification and introduction of various less invasive procedures like percutaneous automated discectomy, percutaneous laser discectomy, arthroscopic discectomy, and chymopapain chemonucleolysis, amongst others [26,27,28]. Chemonucleolysis held an early promise with a success rate of about 80% that was nearly equal to that seen in the best surgical interventions [29,30]. The procedure fell out of favor due to rare but severe complications of anaphylaxis from intradiscal chymopapain [31]. Injection of ozone for discogenic radiculopathy was developed in pursuit of finding safe and effective less invasive alternatives, free of the toxic effects seen with chymopapain [2,3,32,33 34].

In 1989, Verga injected ozone-oxygen mixture into the paraspinal region with a good outcome [34]. Muto suggested intradiscal injection of ozone for disc hernia in 1998 [5]. He injected ozone inside the disc under CT imaging. Leonardi popularized the use of fluoroscopic navigation with excellent results [7].

Successful outcomes from ozone injection have been reported by practitioners from various European centres [2,3,4,5,32].

Striking in all these cases is the near absence of procedural complications. Over 30,000 cases of ozone injections performed without a serious complication establishes a formidable safety record for the procedure [34].

Our cases establish the efficacy of disc injection of ozone as a valid alternative to surgical decompression even in cases when a massive disc prolapse presents with radiculopathy without any clinical findings of cauda equina syndrome.

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# Ozone Chemyonucleolysis vs Microdiscectomy
## Prospective Controlled Study with 18 Months Follow-up

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**Key words:** lumbar disc herniation, chemonucleolysis, ozone, percutaneous surgery, microdiscectomy

**SUMMARY** – This prospective control study with 18 months follow-up was designed to disclose the differences in outcome between intradiscal ozone chemonucleolysis and microdiscectomy in patients with non-contained lumbar disc herniations. Forty-five patients were enrolled on the basis of precise inclusion and exclusion criteria and divided into two treatment groups selected by the patients themselves. The patients were followed by Visual Analogic Scale (VAS), Roland-Morris Disability Questionaire (RMDQ) and Overall Patient Rating Scale (OPRS). Disc herniation volume morphology was evaluated for five months by control MRI scanning. Twenty-seven patients (90%) in the chemonucleolysis group showed a statistically significant improvement in pain ($P<0.001$, Wilcoxon test) and function ($P<0.001$, Wilcoxon test) and the same was true for 14 patients (93.3%) in the microdiscectomy group. The mean satisfaction with the treatment on OPSR was 79.3% for the chemonucleolysis group and 82.1% for the microdiscectomy group. There were no major complications related to procedures. This study indicates that patients from both groups achieved a statistically significant improvement in pain and disability at 18 months follow-up and that there is no statistically significant difference in results between the two treatments.

### Introduction

Lumbar disc herniation is a pathologic condition most commonly responsible for low back pain and nerve root compression, and the major reason for lumbar surgery [25]. MOST patients with lumboradicular symptoms from a disc herniation will get better spontaneously and the herniation will eventually disappear in a few months without any treatment [16]. In a number of reports on the long-term outcome of lumbar discectomy for lumbar disc herniation the success rates were fairly consistent (between 76% and 93%), although evaluation methods varied, and approximately 10-12% of the patients underwent revisions [1,9,21,22,33]. Many authors agree that peridural scar formation with tension on neural tissue plays an important role in a substantial proportion of patients with gradually increasing symptoms after primary successful surgical treatment [10,11,27].

For these reasons a number of minimally-invasive percutaneous techniques have been developed. These techniques share the common principle of of acting directly on the disc content without accessing the spinal channel. Two main types of percutaneous treatments have been devised: mechanical removal (endoscopic discectomy, automatized discectomy, laser discectomy) and chemical disruption of the nucleus pulposus (chymopapain, collagen, hydrocortisone, aprotin).

In the last decade, experimental studies showed that epidural application of autologus nucleus pulposus can induce marked morphological and functional changes in the nerve roots due to the increased endoneural fluid pressure of the nerve root and decrease of blood flow in the dorsal root ganglia with a concomitant increase in its excitability and mechanical hypersensitivity [28,32], all in the absence of mechanical compression. Phospholipase A2, tumor necrosis factor a, metalloproteinases and other substances were found in great quantities in the degenerated nucleus pulposus. These were found able to cause nerve root injury by partial demyelination that increases nerve root mechano-sensitivity making the nerve root more susceptible to mechanical pressure. The mechanical

factor may then trigger hyperexcitability and the ectopic nerve impulses in primary afferent axons that cause neuropathic paresthesia and pain [8,23].

Medical ozone is a trivalent form of oxygen used in medical treatment from the early 20th century, mostly in European countries. In 1885 The Florida Medical Association published *Ozone* by Dr. Charles J. Kenworthy, M.D. detailing the use of ozone for therapeutic purposes. In 1911, Dr. Noble M. Eberhart published "*A Working Manual of High Frequency Currents*" *(New Medicine Publishing Co, chapter* IX*)* on the use of ozone for medical purposes. Numerous other medical reports describe the use of ozone in the treatment of different human diseases *(for a comprehensive review one should search the web pages at www.iaqara.us/mccabe/)*. Experimental studies performed to date indicate that ozone, at appropriate doses and concentrations, dissolves in the interstitial water and generates the formation of reactive oxygen species (ROS). These act differently when they are present in the nucleus pulposus, where they oxygenate proteoglycans and glycosaminoglycans. Indeed, histological studies demonstrated that the intradiscal application of ozone at high concentrations produces hydrolysis of the matrix, water release and consequently cell shrinkage [14,18]. However, ozone released in surrounding fluids apparently causes a "paradoxical effect" such as the induction of antioxidant enzymes which suppress the production of pro-inflammatory cytokines and inhibit the synthesis of prostaglandins, bradykinins and other algogenic compounds [3,26].

This prospective controlled study compared the results of ozone chemonucleolysis and microdiscectomy in patients with non contained lumbar disc herniations with 18 months follow-up.

## Patients and Selection Criteria

From September 2001 till December 2002, 45 patients, 22 women and 23 men, aged between 19 and 77 years (mean 45 ± s.d.14.2) were enrolled in the study on the basis of the following inclusion and exclusion criteria.

Inclusion criteria:
- Acute or subacute pain for at least one month non responsive to pharmacological treatment.
- Non-contained disc herniation at levels between L3 and S1;
- level of disc herniation corresponding to the level of symptoms;
- confirmation of pathology by MRI scanning.

Exclusion criteria:
- moderate to severe motor palsy (Fisher < 4);
- contained disc herniation;
- other spinal pathologies such as tumours, lyses, fractures, deformities, stenosis, instability, etc.;
- previous spinal surgery;
- use of drugs or history of mental disease.

A physician not involved in the treatment gave all the patients a detailed explanation of both procedures, the possibilities of success and the risk factors entailed, and each patient independently chose which treatment to receive by signing an informed consent form.

On the basis of this kind of randomization, the patients were divided into two groups:
1) the first group, comprising 30 patients, 16 women and 14 men, underwent ozone chemonucleolysis treatment;
2) the second group, comprising 15 patients, 6 women and 9 men, underwent standard microdiscectomy.

Six patients in the ozone chemonucleolysis group (20%) underwent multilevel treatment while 24 patients (80%) underwent single level treatment. All the patients in the microdiscectomy group were operated at just one level. The symptom duration for both groups ranged from 21 to >365 days with a mean duration of 203.9 days (s.d. ± 129.6.) The straight leg raising test was positive for all patients with a mean angle of evocation being 51.3° (s.d. ± 20.5°). None of the patients had major motor dysfunction. All the patients had an MRI image positive for non-contained disc herniation whose outer diameter was larger than ~4 mm.

## Procedures

### *Percutaneous Technique*

The procedure was performed in the operating theatre under moderate sedation. No preventive antibiotic therapy was given. The patient was prepared by the anaesthesiologist with pharmacological sedation half an hour before the procedure and then brought to the operating room and positioned in lateral decubitus leaving the affected side upwards with legs folded. The operating table was also folded to assume an upwards convex shape. This facilitated the surgeon's access to the lower discal space (L5-S1) even in patients with a high iliac crest or major spondylo-arthrosic deformities. A Beckton-Dickinson, Chiba type 22 G, 27 cm needle was inserted by the standard posterolateral, extra-articular percutaneous approach. The whole procedure was performed under continuous fluoroscopic control. Once in place, the position of the needle was confirmed by laterolateral, oblique and anteroposterior imaging. The ozone-oxygen mixture was produced in real-time by a medical o-

zone generator Ozonline E 80 (Medica srl) CE certified. The gas concentration range was ~30 μg $O_3$/ml $O_2$ in quantities between 10-15 ml for a single level. The syringe used was a Terumo type –50 ml. A bacteriological Millipore filter was positioned between the syringe and the needle before infiltrating the gas mixture inside the disc space. The ozone-oxygen mixture was infiltrated inside the disc space at an approximate velocity of 10 ml/min. The gas mixture inside the disc space appeared on the fluoroscopic image as positive contrastography. Some of the gas mixture escaped from the disc space and ran into the epidural space in cranial and caudal directions. During gas infiltration the patient was sedated by Propofol. The patient was discharged the next morning. For the first two days patients were recommended not to assume the sitting position but walking was encouraged. Return to work was permitted seven days after surgery.

*Microdiscectomy*

The procedure was performed in a standard microsurgical fashion. Antibiotic therapy (3rd generation cephalosporin) was administrated on the same day as surgery and then continued for five days afterwards. The patients were given a spinal anesthesia and positioned on the operating table in the knee-chest position. A median 2-3 cm incision was made and the paravertebral musculature of the affected side was removed from the spinous process until reaching the interlaminary space. The yellow ligament was incised followed by standard approach to the disc space.

The herniated material was removed and just a small part of the disc itself was excised as much as necessary to have the entrance space through the anulus free of detached disc material. Then rigorous haemostasis was performed and the wound was closed in a standard three-layer fashion. The patient was allowed to get out of bed 12 hours later and discharged the day after the surgery. Sitting was not allowed for the first five days post-surgery. Return to work was permitted two weeks after the procedure.

*Follow-up*

Patients were followed prospectively by compilation of pre and post-procedure questionnaires. Pain was evaluated by Visual Analogue Scale (VAS). Dysfunction and disability were followed by self-administrated Roland-Morris Disability Questionnaire (RMDQ). Overall treatment satisfaction was evaluated by a 100 point Overall Patient Satisfaction Rating (OPSR).

The VAS was submitted to patients as a coloured scale divided into ten different shades of the same colour and each shade further divided into ten. The clearer the colour the lesser the pain and vice versa. The RMDQ used was in the form approved and validated for use in the Italian language. Pain Rating Scale of the same questionnaire was not used as it was found less valuable than the VAS evaluation for pain. The OPSR was used as a simple scale from 0 to 100 where the patient indicated the percent of his/her general sense of satisfaction with the treatment. The above ratings were made on the morning before treatment and then six, 12 and 18 months post-procedure.

Fifteen randomly chosen patients from the ozone chemonucleolysis group of treatment underwent control MRI between three and five months after the procedure. Volume reduction was measured by an independent observer and expressed in % of volume reduction.

*Statistical Method*

Statistical analysis was performed using STATA 7.0 software (Stata Corporation, USA). The significance of the difference of the VAS score and the RMDQ score at time 0 and 18 months was tested by non-parametric statistics (Wilcoxon sign-rank test).

## Results

Two patients dropped out of the ozone chemonucleolysis group because of aggravating symptoms and were operated upon: one three months and the other seven months after the pro-

Table 1 **Results and statistical significance at 18 months follow-up**

| Variable | N | Preprocedure value (T 0) | Postprocedure value (T 18) |
|---|---|---|---|
| VAS ozone | 30 | 5.3 ± 2.2 | 0.9 ± 1.0 |
| VAS microdiscectomy | 15 | 6.1 ± 3.1 | 2 ± 1.3 |
| RMDQ ozone | 30 | 9.1 ± 3.5 | 2.4 ± 2.7 |
| RMDQ microdiscectomy | 15 | 12.4 ± 4.3 | 2.1 ± 1.9 |

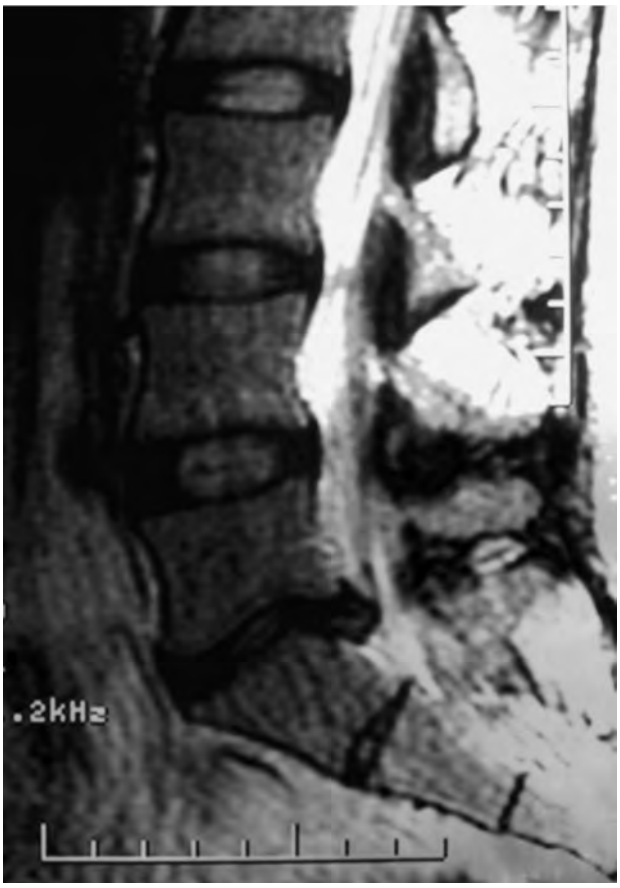


Figure 1

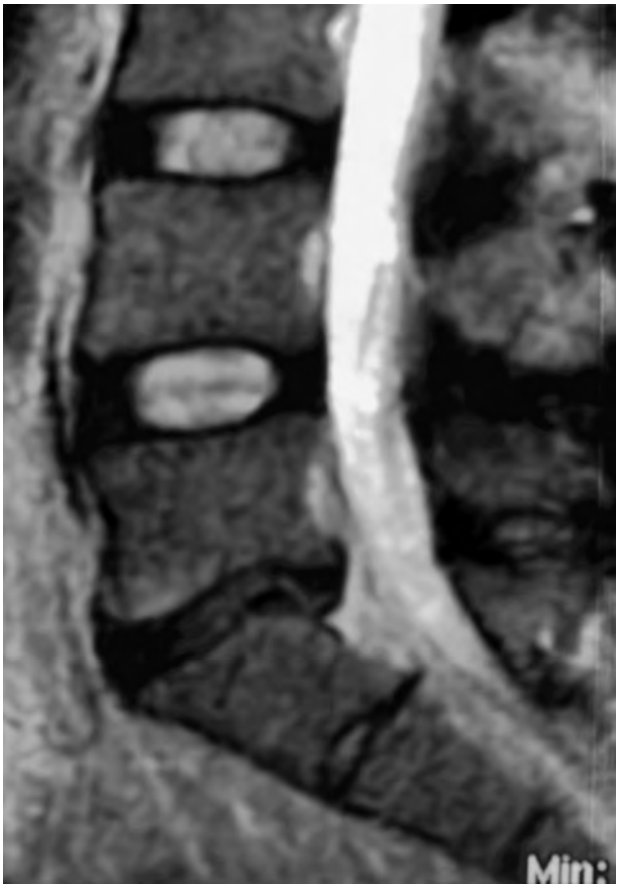


Figure 2

cedure. At 18 months follow-up 28 patients were available but the statistical analysis was performed on all 30 patients, regarding the two surgically treated patients as failures of the procedure. No patient from either group was lost to follow-up.

*VAS* – At 18 months follow-up, 27 patients (90%) in the ozone chemonucleolysis group showed improvement in pain, one patient (3.3%) remained unchanged whereas two patients (6.6%) had worsened (operated). The mean pre-treatment value for all patients was 5.3 ± s.d.2.2 and the overall mean 18 months follow-up value was 1.3 ± s.d. 1.6 with a change of 4.0 (95% CI = 2.9 – 5.0). The maximum improvement was seen inside the first two months.

At 18 months follow-up, 14 patients (93.3%) in the microdiscectomy group showed pain improvement whereas one patient (6.6%) had worsened. The mean pre-treatment value for all patients was 6.1 ± s.d.3.1 and the overall mean 18 months follow-up value was 2 ± s.d. 1.3 with a change of 4.1 (95% CI = 3.2 – 5.5). The maximum improvement was seen inside the first month.

Patients from both groups showed a statistically significant improvement in pain on 18 months follow-up ($p<0.001$). There was no statistically significant difference in pain improvement between the two groups of treatment ($p<0.001$).

*RMDQ* - At 18 months follow-up, 27 patients (90%) in the ozone chemonucleolysis group had improved in function, one patient (3.3%) remained the same whereas two patients (6.6%) had worsened (operated). The mean pre-treatment value for all patients was 9.1 ± 3.5 and the overall mean 18 months follow-up value was 2.2 ± s.d. 3.2 with a change of 6.9. The maximum improvement was seen inside the first three months.

At 18 months follow-up, 13 patients (86.6%) in the microdiscectomy group had improved in function, and two patients (13.2%) remained unchanged. The mean pre-treatment value for all patients was 12.4 ± 4.3 and the overall mean 18 months follow-up value was 2.1 ± s.d. 1.9 with a change of 10.3. The maximum improvement was seen inside the first three months.

Patients from both groups showed a statistically

significant improvement in function at 18 months follow-up ($p<0.001$). There was no statistically significant difference in function improvement between the two groups of treatment ($p<0.001$).

*OPRS* - Mean satisfaction with the treatment at 18 months was 79.3% ± 28.7 for the ozone chemonucleolysis group and 82.1% ± 31.2 for the microdiscectomy group.

Twenty-four patients (80%) in the chemonucleolysis group referred satisfaction equal to or greater than 80%, three patients (10%) referred satisfaction ranging from 50 to 80% whereas three patients (10%) were not satisfied with the treatment (two of these were operated upon by microdiscectomy). Twelve patients (80%) In the microdiscectomy group referred satisfaction equal to or greater then 80%, two patients (13%) referred satisfaction between 50 to 80% whereas one patient was not satisfied with the treatment.

Regarding satisfaction with treatment, there was no difference between the two groups.

*Morphological changes* (figure 1, figure 2) - Fifteen out of 30 patients from the ozone chemonucleolysis group, all of whom clinically improved, performed control MRI imaging. Eight of them had a substantial reduction, superior to 50%, of the herniation volume. Two patients showed volume reduction inferior to 50% whereas five patients had no substantial variation of the herniation volume. The mean volume reduction for 15 patients was 49% ± s.d. 42.5%.

## Discussion

As the equation large herniation = major symptoms, small herniation = minor symptoms is not always true, it seems quite natural to assume that clinical signs and symptoms of disc herniation are not caused only or mainly by mechanical compression but that biochemical factors play an important role in inflammatory sensitization and immune response in the peridural environment of the nerve root [15,20,25,31]. For the same reason it seems logical to presume that mechanical removal of herniated tissue may not always be needed and that reducing the inflammatory process could essentially be sufficient to treat the symptoms. This study partially confirms this hypothesis because although only eight out of 15 randomly chosen patients from the ozone chemonucleolysis group showed a substantial volume reduction of the herniated material, all 15 had a significant improvement in pain and function.

Ozone chemonucleolysis for degenerative disc disease is a relatively new intradiscal treatment started in Italy some ten years ago. Pioneering reports mainly in form of case reports or case series published in Italian scientific journals and a few recent articles published in international peer-reviewed journals indicate that by reducing pain and improving functional status the treatment is useful in patients with disc herniations [2,7,34]. Basic research on ozone activity conducted in several Italian universities found that the mixture of ozone and oxygen has a potent, dose-related, biological activity [5,6,24,29,30]. At high concentrations (30-70 $\mu g 0_3/ml 0_2$), it may cause alteration and destruction of tissue structures. At medium concentrations (20-30 $\mu g 0_3/ml 0_2$) it seems to affect the regulation of the immune system while at low concentrations (<20 $\mu g 0_3/ml 0_2$) it improves the microcirculation by increasing the oxygen delivery to tissues.

At the level of the intervertebral disc in disc-root conflict, the effects of the ozone mixture application appear mainly related to the reduction of inflammation. Moreover, the improvement of the local microcirculation with reduction of venous stasis and ischemia at nerve root level certainly plays an important role [13,19]. Histological studies performed on animal models, demonstrated that the intradiscal application of ozone at high concentrations produces degeneration of cytosol and cell shrinkage in the nucleus pulposus [14,18]. If applied in adequate concentrations, ozone produced no toxic effects either in vitro or in vivo [26]. The critical parameters such as the concentration range and dose and the gas volume must not exceed the antioxidant capacity at the site of injection. Enzymes such as superoxide dismutase, catalase and GSH-peroxidase prevent the accumulation of superoxide anion ($O_2$-) and hydrogen peroxide ($H_2O_2$). The risk of free radical formation is minimal because at pH 7.5 the predominant mechanism is ozonolysis favouring the production of peroxides. Experimental tests in animals and humans showed a lack of negative effects [17]. The data from this study and the findings of other physicians using this method essentially confirm the lack of adverse effects on short and long-term follow-up. Experimental studies also indicate that the adequate doses and concentrations of ozone to the human body have no mutagenic properties [4]. Special attention should be paid to patients with hyperthyroidism, unstable arterial hypertension, cachectic patients and those with favism due to either hypermetabolism or an enzymatic defect of G6PD.

The results of this prospective controlled study are encouraging, but we still do not know why herniation volume diminishes in some patients and not in others despite clinical improvement. Further randomized studies with larger groups of patients are needed to confirm these initial findings.

## Conclusion

This study indicates that there are no major differences in clinical outcome between ozone chemonucleolysis and microdiscectomy treatments in patients with non-contained disc herniations with predominant symptoms of pain and without neurological deficits. Treatment of disc herniation has to be proportionate to the severity of clinical signs and symptoms and the primary approach should not be surgical in patients with pain alone regardless of herniation volume.

Ozone chemonucleolysis may have a major impact on the treatment of symptoms of disc herniation as it seems to have a high clinical success rate and may also resolve the primary cause. It is a simple low-cost method both in terms of procedure and social cost with an almost total absence of risks and complications in short and long-term follow-up.

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# Oxygen-Ozone Therapy: CT -Guided Intraforaminal and Periganglionic Infiltration. Personal Case Series and Literature Review

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**Key words:** intraforaminal infiltration, oxygen-ozone, medical ozone, herniated disc

**SUMMARY** – We present our findings in a series of 275 patients with clinical features of low back pain complicated by sciatica caused by hernia-induced nerve root compression and treated by intraforaminal and/or periganglionic infiltration of an $O_2$-$O_3$ gas mixture between January 2004 and February 2005. We then reviewed major literature reports to compare our findings. Although our experience is limited, our results are in agreement with the latest series published with treatment success rates exceeding 80%. We propose CT-guided intraforaminal oxygen-ozone therapy as a valid alternative to surgery for herniated disc and the prime method of conservative management.

## Introduction

Low back pain with or without sciatica affects around 80% of the population at some time in their lives and is the prime cause of working days lost with a considerable impact on national health service spending.

Until 15 years ago, surgery was the treatment of choice but outcome was often disappointing and preference is now given to conservative management. Among the methods most commonly adopted in the last decade to tackle sciatic nerve pain induced by herniated disc or non-discal spine disease (osteophytosis, spondylolysis, facet joint syndrome, etc.) intraforaminal infiltration of an $O_2$-$O_3$ gas mixture has yielded promising results.

We compared the outcome obtained in our series of 275 patients treated by oxygen-ozone therapy with the latest cohorts reported in the literature [1-25].

## Materials and Methods

Between January 2004 and February 2005, 275 patients (156 men and 119 women aged between 21 and 76 years, average age 45.6 years) with low back pain and sciatica underwent CT-guided infiltration of an $O_2$-$O_3$ gas mixture after reading and signing their informed consent. On enrolment, clinical records were drawn up for all patients using the PC model presented by the Italian Federation of Oxygen-Ozone Therapy.

This document records the patient's name, date of birth, date of enrolment, date of treatment and clinical findings including pain characteristics and irradiation, any paraesthesias, Lasègue's sign, degree of sensitivity, lower limb reflexes, plantar and dorsal extension of the foot, dorsal extension of the big toe, etc. Before enrolment all patients had had a CT or MR scan and the results of preliminary neuroradiological findings were also recorded in the patient's electronic records. In addition, we noted the type of $O_2$-$O_3$ treatment administered specifying the needle used, the amount of gas mixture injected and its ozone concentration. All patients enrolled had low back pain and sciatica. Patients with bilateral pain or electromyographic features of neurogenic inflammation and/or denervation were excluded and advised to seek neurosurgical consultation. Duration of symptoms varied from one to 20 months. After disinfecting the region of interest, all patients underwent local anaesthesia with ethyl chloride spray. CT scan was used to pinpoint the site of infiltration which was pencilled onto the patient's

Table 1 **Assessment of therapeutic efficacy at the time of treatment and one week, three and six months later**

| | | Excellent | Good or satisfactory | Modest or poor |
|---|---|---|---|---|
| One week | | 241/275 (87.6%) | 31/275 (11.2 %) | 2/275 (0.7%) |
| Three months | | 238/275 (86.5%) | 34/275 (12.3%) | 2/275 (0.7%) |
| Six months | | 229/275 (83.2%) | 39/275 (14.1%) | 7/275 (2.5%) |

skin. We then measured the distance between this point and the root canal. A 22G Terumo needle (mainly 9 cm long, sometimes longer depending on the size of the patient) was inserted to around 2-3 mm from the canal near the ganglion of the affected nerve root (figure 1). Another CT scan was then done to check correct placement of the needle. The $O_2$-$O_3$ gas mixture was infiltrated by injecting 3 cc of the mixture at 25 µg/ml and then withdrawing the needle several millimetres and injecting another 5 cc of the mixture to involve the facet joint region.

Further CT scans displayed the distribution of the gas mixture in the root canal and facet joint. All treatments were done using equipment fitted with a photometric detector of the ozone concentration in the gas mixture (Alnitec Futura 2). All patients had short (one week)), medium (three months) and long-term (six months) clinical follow-up using McNab's method modified as follows (table 1):

a) excellent: resolution of pain and return to normal working activity carried out before pain onset
b) good or satisfactory: more than 50% reduction of pain
c) modest or poor: less than 70% reduction of pain

## Results

Current surgical techniques used to treat lumbar disc herniation by relieving root compression often fail to provide a definitive or lasting cure even in selected patients. In our series, we obtained a full clinical cure in around 85 % of patients confirmed at three and six month follow-up as 83.2% (figures 2-3). One CT-guided intraforaminal infiltration was sufficient in most patients leading to a complete disappearance of pain, whereas around 30% of patients had two to four treatment sessions over a period of time ranging from 30 days and three months after the first treatment. Only five patients subsequently required surgery. We emphasize that after treatment our patients were assessed by rehabilitation experts to establish the need for further treatments and patients, including cured cases, were always advised to undergo postural assessment as a preventive measure.

## Discussion and Conclusions

Recent research has clarified the mechanism underlying oxygen-ozoone therapy. Much credit for this is due to the Bologna school [26] whose work has shed light on the direct and indirect mechanisms of action of the oxygen-ozone mixture in therapeutic application for musculoskeletal disorders. In particular, the direct effect of the gas mixture on the mucopolysaccharide chains of the nucleus pulposus results in their oxidation and the release of water molecules with mechanical resolution of nerve root compression. This direct action is supported by the known indirect mechanisms of action, as explained by Prof. Bocci, i.e: its anti-inflammatory, analgesic, and eutrophic effects with reduction of disc degeneration and decongestion of the nerve roots [5,6]. This has also been confirmed by experimental studies [27]. In the wake of these findings, we embarked on oxygen-ozone therapy using the CT-guided intraforaminal technique, recruiting our first 275 patients. In agreement with different series published in the literature, we found this a relatively simple method combining precise control of the needle pathway with the curative effects of $O_2$-$O_3$. Treatment improved local circulation with a eutrophic effect both close to the damaged and compressed nerve root and in terms of muscular spasm. Cytokine and prostaglandin levels normalized with the anti-inflammatory analgesic effect with increased superoxide dismutase (SOD) and minimum oxidant reagents (ROS). Lastly, injection of the gas mixture close to the herniated material leading to faster dehydration or destruction of non vascularized tissue accounts for the good final outcome. The rapid resolution of pain without complications, straightforward application of the technique and complete control of infiltration under CT guidance make CT-guided oxygen-ozone therapy a valid alternative to surgery for herniated disc and the prime method of conservative management.

Figure 1 Correct placement of the needle in the ganglion region.

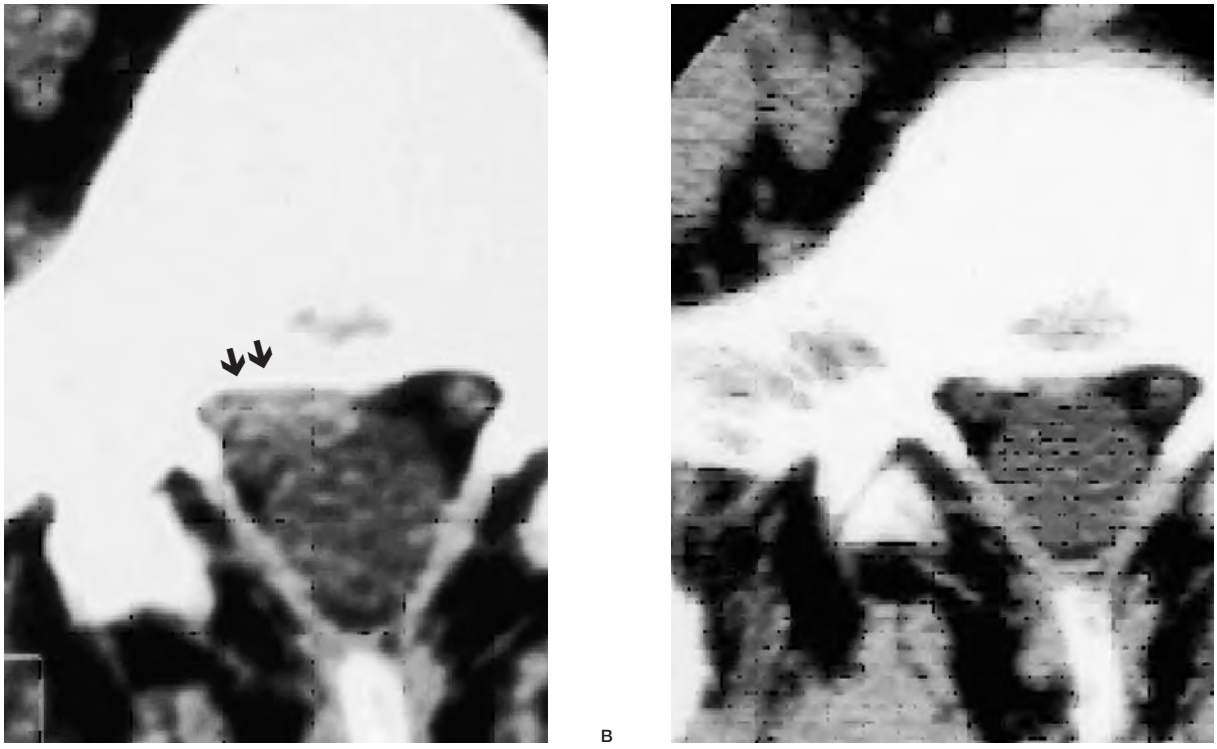
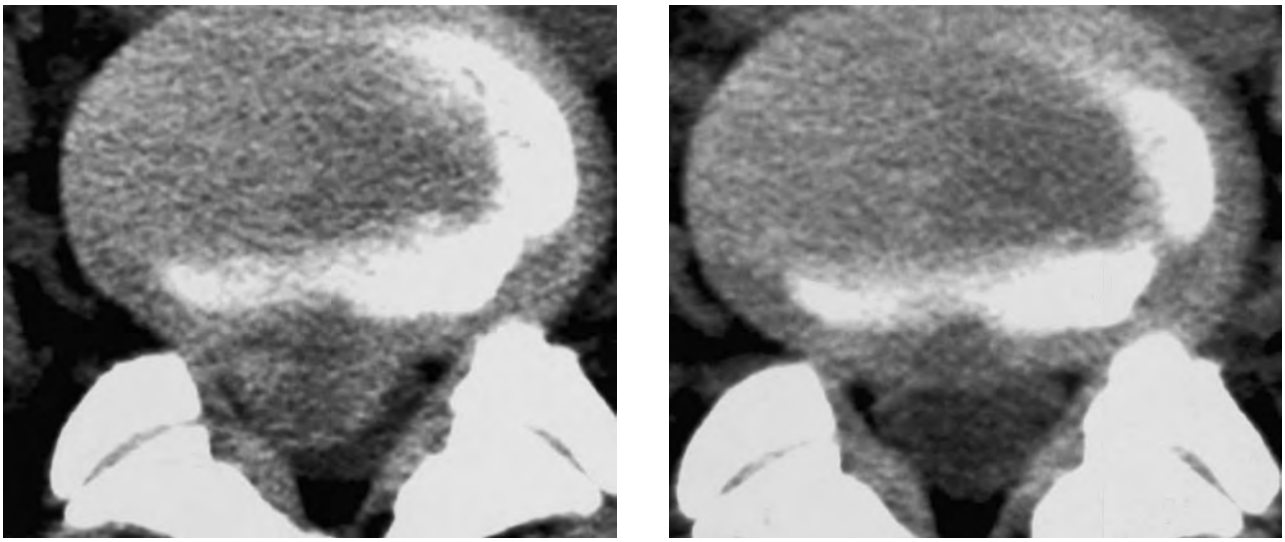



Figure 2 A) Right extruded L5-S1 herniation (arrows); B) CT follow-up after treatment demonstrating complete disappearance of the hernia.



A B

Figure 3 A-B) Large L4-L5 herniation bifore and after oxygen-ozone treatment.

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# Oxygen-Ozone Therapy in Sport.
## A Case Report

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**Key words:** sport pathology, oxygen-ozone treatment

**Summary** – The application of oxygen ozone therapy in muscle and joint injuries has been neglected in the past both for the presence of consolidated pharmacological principles like FANS, corticosteroids, and for the presence of instrumental and rehabilitative techniques endowed with a certain and safe effect. Our experience with ozone derives from different basic studies on the neuromuscular junction, the enormous clinical potential at medical level and the treatments performed with oxygen ozone in numerous cases of sport injuries such as distortions with or without swelling. The results obtained in several traumas of different degrees depending on diagnostic and prognostic severity have convinced us of the effectiveness of this therapeutic method. The observations of recovery, the speed of recovery being faster the earlier the treatment after the traumatic event, the disappearance of muscular lesions and the full *restitutio ad integrum* of the athletes have led us to report our findings.

### Introduction

Our interest in ozone's therapeutic potential was first aroused in 1993 after a discussion on the hypothesis of a positive conditioning induced by low ozone concentrations against oxidative stress.

The basic evidence of some biochemical effects induced by ozone was first proposed by Léon Fernández et al. in 1998. The theory is based on the fact that low non-toxic ozone doses could raise the efficacy of the endogenous antioxidant system by increasing the production or activity of some enzymatic isoforms.

Like ischemic preconditioning in which it is scientifically proven that repetitive brief ischemia plays an important role in the acquisition of late-phase cardioprotection against ischemia/reperfusion injury in rats (Yamashita 2000), we can speculate that repetitive brief oxidative stress induced with low ozone doses could enhance the cell defence mechanisms against ROS.

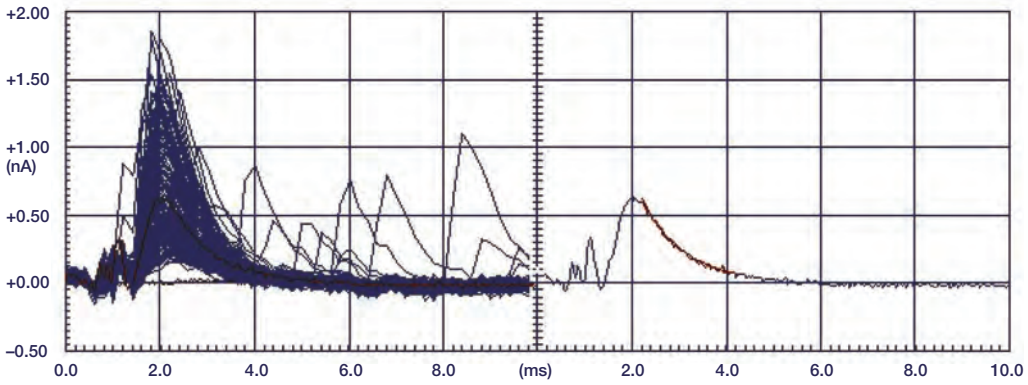
The hypothesis is supported by other data reported by Rao and Shaha in 2000 demonstrating the formation of multiple isoforms of glutathione S-transferase after exposure to $H_2O_2$.

### Molecular Hypotheses

Due to our pharmacological experience and previous research devoted mainly to the study of the molecular events underlying the pharmacological action of drugs, our group was initially attracted by a pure scientific curiosity. The main questions addressed were: Why do many epidemiological data report evidence of a benefit of this gas in different, apparently unrelated, pathologies? Is there a dose-effect relationship? Is this therapy completely safe? How could an agent known for its strong oxidative potential induce a benefit other than its intrinsic bactericidal action?

### What Is Ozone?

Ozone ($O_3$ - PM 48) is an allotropic form of oxygen. It represents an extremely unstable molecule characterized by three atoms of oxygen. At room temperature it is a colourless gas with sharp pungent odour. Ozone is an extremely important mixture for life on the earth and one of the fundamental components of the atmosphere.




Graph 1

**Ozone on Acetylcholine Release**

Following the idea of some colleagues, we tested low ozone doses on an in vitro preparation widely used in the pharmacological field: the neuromuscular junction. On this experimental model we proved the reduction of intracellular calcium at presynaptic levels after exposure to low ozone concentrations [4-5].

Cytosolic calcium could be considered the common final pathway of cellular damage, either physiologically or pathologically. A low calcium level represents a further element supporting the idea of oxidative cell damage protection either in chronic or acute ageing other than the reduction of some inflammation mediators.

**Mouse NeuroMuscular Junction.**
**Evoked End-Plate Currents.**
**Loose Patch Clamp Technique.**

- Control
- $O_2$-$O_3$ 20 mg/ml

**Further Basic Evidence**

With the aim of stimulating scientists in this field and trying to obtain direct proof of the reported data, we started an experiment at clinical level and boosted our efforts to add more scientific data on the possible action mechanisms exerted by ozone at the biological level.

Following the calcium theory and the multisystem action of ozone we performed a study on hepatic enzymes induction and the possible modulation of NOs [2-6]. More scientific data indicated that the therapeutic potential of ozone treatment could be ascribed to its effect induced at low doses on the cellular antioxidant system, the vascular system or the modulation of the inflammatory mediators.

Further studies are in progress to evaluate a possible modulation of ozone on the COX cascade, both isoforms 1 and 2.

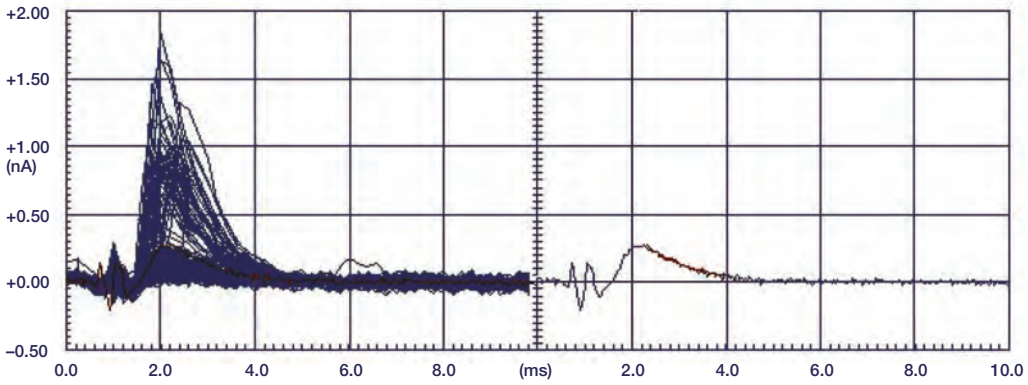
These biochemical pathways are shared by all the cells of the organism and represent, primitively or as a consequence, the target of either chronic (aging) or acute (illness) cellular damage. Apoptosis is the final result preceding cell death.

**Ozone in Sport**

The application of oxygen ozone therapy in muscle and joint injuries has been neglected in the past both for the presence of consolidated pharmacological principles like FANS, corticosteroids, etc., and for the presence of instrumental and rehabilitative techniques endowed with a certain and safe effect. Another reason oxygen-ozone has been underestimated is the still limited knowledge at scientific level and the erroneous conviction that its mechanism of action is extremely slow in relation to recovery of the athlete.

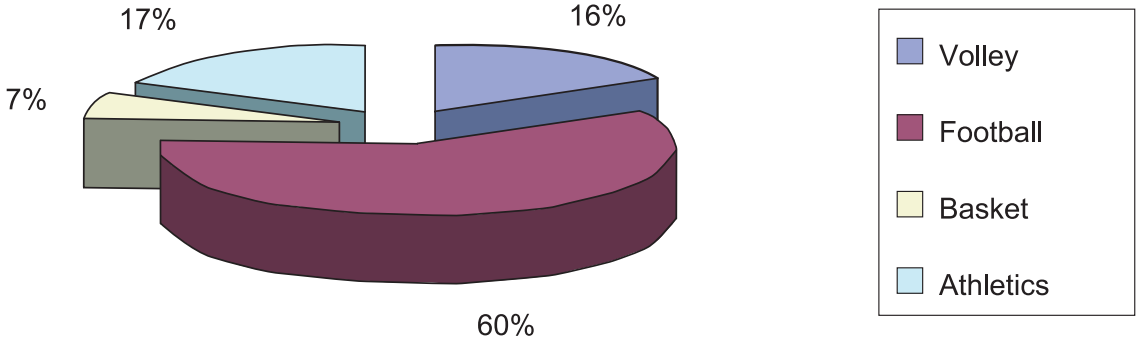
Our experience with ozone derives from different basic studies on the neuromuscular junction [4], the enormous clinical potential at medical level [3] and the treatments performed with oxygen ozone in numerous cases of sport injuries such as distortions with or without swelling.

The results obtained in several traumas of different degrees depending on diagnostic and prognostic severity have convinced us of the effectiveness of this therapeutic method. The observations of recovery, the speed of recovery being faster the earlier the treatment after the traumatic event, the disappearance of muscular lesions and the full restitutio ad integrum of the athletes have led us to report our findings.

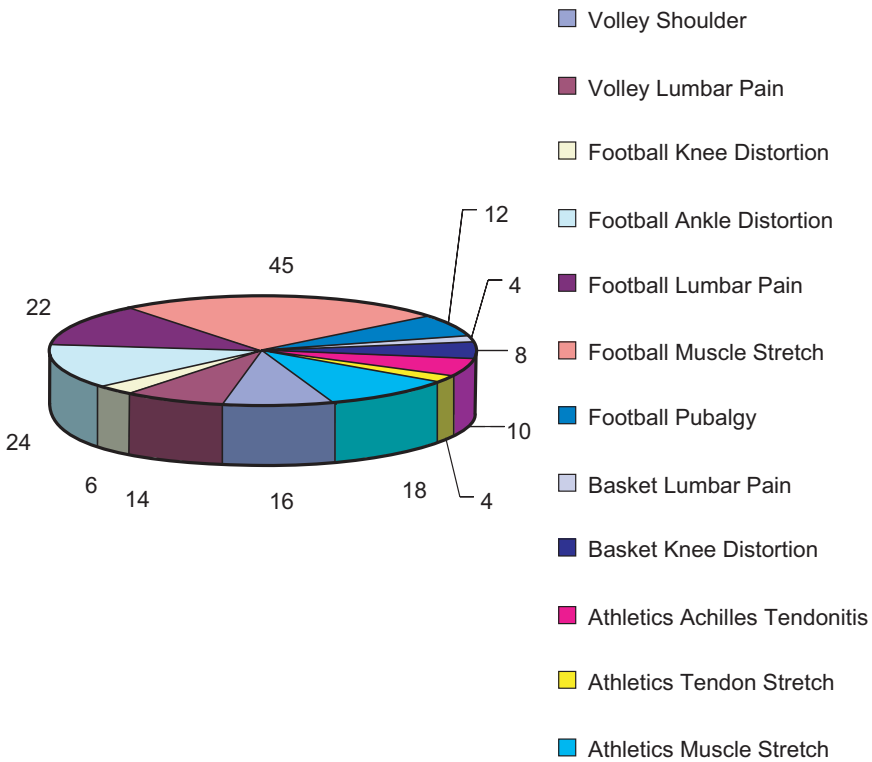



Graph 2

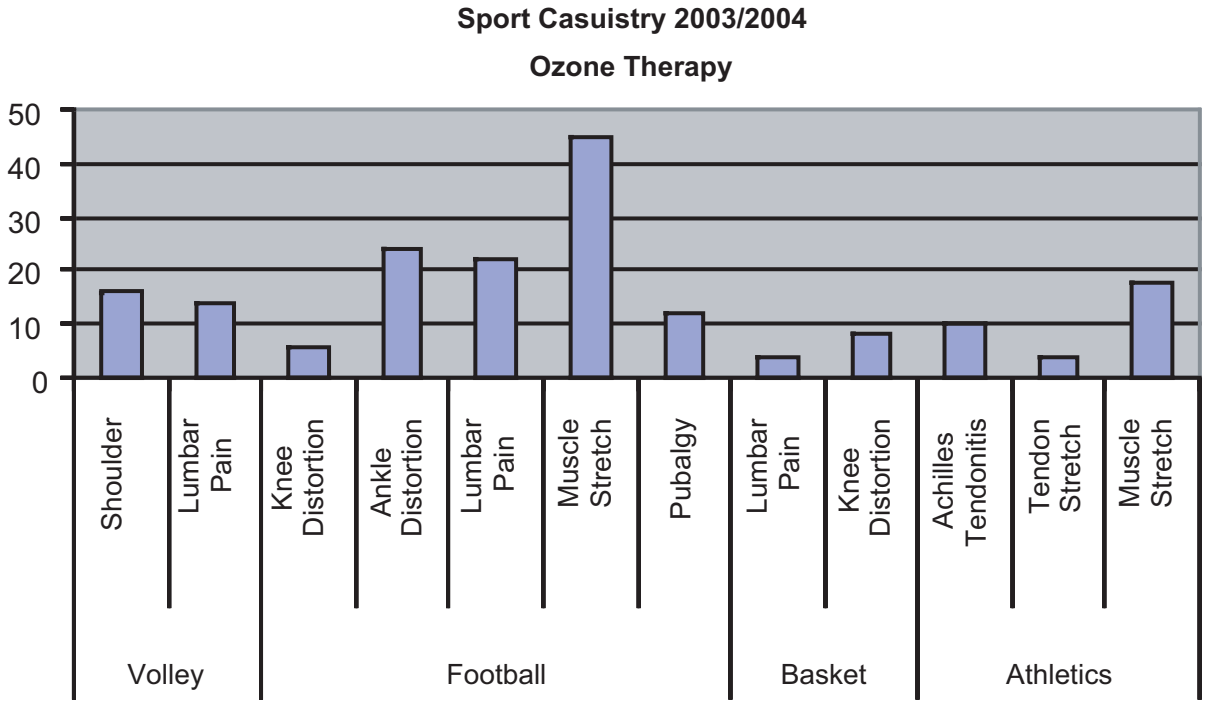
# Sport Casuistry 2003/2004
# Ozone Therapy




Graph 3




Graph 4




Graph 5

Our series in the years of reference comprises around 183 athletes divided for various disciplines as in graph [1].

In most treated cases, as in the case report described below, prognosis and clinical efficacy were assessed by medical examination and subjective evaluation of the symptoms relief.

The majority of athletes (85%) resumed competitive activity within the first week after treatment.

A reduction of the intake of medicines like FANS and corticosteroids, usually not lacking serious collateral effects when taken chronically, was also reported.

The cases described will be assessed statistically in a follow-up of 12 and 24 months to establish the stability of symptoms in the absence of other trauma and during maximum competitive training.

## Case Report

An 18-year-old male, belonging to the National Athletic Italian League for the specialties of 100 and 200 meters had a good sensory response and was cooperative and in excellent physical and mental state. His weight was 65 Kg, height 1,78 cm. He had an Asian phenotype with no evident structural or postural alterations. His arterial pressure and vital parameters were normal.

He was referred to us in May 2003 with a history of trauma to the right leg during a competition the preceding year with diagnosis of femoral two-headed stretching and an MR scan performed on 13th August 2002 stating the following:

"*Superficial lesion of the right semi-membranous muscle to the distal third medium, in proximity of the interface with the great abductor muscle and subcutaneous muscles in the back region of the thigh. The lesion is characterized by elevated signal intensity in T2-weighted sequences due to congestion and presence of fluid*".

*The examination was repeated in October 2002 after various rehabilitative cycles and showed:*

*... omissis ... reduced congestion and fluid swelling … omissis ... the reduction of such phenomena reveals a structure with "cluster" aspect of probable vascular origin ... omissis..*

A further ultrasound scan was performed on 23rd October 2002 with the following diagnostic conclusion:

"*A hyperechogenic structural alteration is evident in the middle portion of the semi-membranous muscle compatible with partial fibrous evolution. Underneath it lies a linear fibrous strip. Dynamic phase disclosed the camber of the superficial muscular profile, selectively painful. No calcifications or fluid collections were noted*."

Given the persistence of pain, the athlete underwent further medical visits following which exer-

cises were prescribed to be performed on isokinetic apparatus, both in a sitting position and in extension using passive mobilization.

Another ultrasound scan was performed on 30th April 2003 with the following report

"*Wide inhomogeneous hyperechogenic area (4×3×2) with some fluid gaps on loading of the semi-membranous muscle in its middle line. The finding appears to reflect a recent tear. The gaps were under one cm (degree 1). No calcifications were appreciated.*"

Due to the chronic persistence of the diagnostic elements and the pain symptoms which precluded normal athletic training, the athlete came to our observation on 24th May 2003 for an evaluation and possible oxygen-ozone therapy.

## Therapeutic Protocol

After careful history-taking, twice weekly sessions of intramuscular administration of oxygen-ozone were prescribed. Oxygen-ozone mixtures were used at a concentration of 8-12 μg/ml. The protocol of each session included dividing 60 cc of mixture at the above concentration and administration into the zone affected by the lesion and 30 cc in the same muscular area of the symmetric limb. At the end of each treatment a superficial massage was performed with ozonized cream to uniformly distribute the injected mixture.

The treatment was performed for four weeks. At the end of the cycle, given the improvement in symptoms as referred by the athlete, the applications were stopped.

## Results

The athlete had gradually resumed training before the end of the treatment cycle and continued to train without any painful or contractile symptoms. A complete absence of symptoms was also confirmed by the control MR scan performed in June 2003:

"*The images were obtained with T1 and T2 weighted sequences in the axial and coronal plans. No morphological or signal changes were noted on loading the examined muscular structures. In particular, no changes to the right semi-membranous muscle could be appreciated. After administration of contrast medium No areas of pathological contrast uptake or changes in vascular structures were evident*".

## Discussion

In the light of the present results, ozone therapy could be the topic of scientific discussion in relation to its potential use in sport injuries.

When correctly employed, the ozone molecule lacks any side effects and at low sensitizing doses can play a major role in vascular functionality [4] and in limiting inflammation thanks to the reduced release of inflammatory mediators [4,6].

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# Paravertebral $O_2$-$O_3$ Treatment in Mechanical Lumbar Pain in Riding Horses

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**Key words:** "back pain", $O_2$-$O_3$ therapy, paravertebral infiltration

**SUMMARY** – "Back pain" is common in horses, especially thoroughbreds and riding horses. Many soft tissue injuries and bone disorders are correlated with "back pain". Diagnosis is based on clinical examination possibly confirmed by x-ray and scintigraphy when available. Currently the most common treatments are local injection of steroids or systemic administration of steroids or NSAIDs. We studied 30 riding horses treated by local infiltration of $O_2$-$O_3$ administered in two sessions ten days apart. Despite our small cohort, the successful results show that $O_2$-$O_3$ therapy can be considered a valid alternative to current drug management protocols.

## Introduction

"Back pain" is a common problem among riding horses in all equestrian disciplines, especially thoroughbreds and riding horses which most often present problems in the thoracolumbar spine (Jeffcott 1980).

Disorders correlated to "back pain" can be divided into two groups affecting either the soft tissues or associated with vertebral problems. Soft tissue injuries include muscle and ligament dilaceration, contractures, intervertebral disc disease and skin lesions in the saddle area. Vertebral disorders include ossifying deforming spondylosis, superimposed spinous processes, and arthrosis of the joint processes, neural arches and vertebral bodies. In particular, lesions to the spinous processes are displayed radiographically as a narrowing of the intervertebral space, erosion of the cranial and caudal margins and areas of sclerosis alternating with cyst-like radiolucencies.

Diagnosis is initially based on clinical examination gauging pain when applying paravertebral and interspinous pressure, and history-taking: attempts to avoid being ridden, loss of propulsive power and gait impairment. Instrumentally, diagnosis is confirmed by laterolateral radiograms and scintigraphy when available.

In case of lesions to the joint processes, neural arches or vertebral bodies, diagnosis must be confirmed radiologically using higher strength non portable devices and scintigraphy.

Current treatment for "back pain" is local injection of steroids or systemic administration of steroidal or non-steroidal anti-inflammatory drugs which may have major side effects and fail to ensure good medium and long-term outcome.

## Materials and Methods

We undertook a two-year study on 30 horses (24 thoroughbreds, five trotting horses, one competition horse), in training and aged between three and 12 years (table 1).

The following parameters were chosen for assessment of back pain:
- thoracic pain and/or muscle contracture,
- pain between the spinous processes,
- lumbar pain and/or muscle contracture,
- change in spine curvature,
- asymmetric rump,
- pain in the sacro-iliac ligaments,
- gait impairment,
- loss of thrust/impulsion,
- "the horse lowers itself when the rider mounts".

**Table 1**

| Number | Sex | Age | Height | Time | Sympotoms | | | | | | | | | | Treatment | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Thoracic pain and contracture | Lumbar pain and contracture | Kyphosis | Rump asymmetry | Thoracic pain on interspinous pressure | Pain on pressure to the sacro-iliac ligaments | Gait impairment | Loss of thrust | Lowers when mounted | X-ray | Intraspinous infiltration | Paravertebral infiltration | Lombar infiltration |
| 1 | C | 3 | G | To | + | + | – | – | – | – | – | + | – | – | – | + | – |
| | | | | T1 | + | – | – | – | – | – | – | – | – | | | + | |
| | | | | T2 | + | – | – | – | – | – | – | – | – | | | – | |
| 2 | M | 4 | G | To | + | + | – | – | + | – | – | + | + | + | + | + | – |
| | | | | T1 | – | – | – | – | – | | | – | – | | – | + | |
| | | | | T2 | – | – | – | – | – | | | – | – | | – | – | |
| 3 | F | 3 | G | To | + | + | – | – | + | – | – | + | – | – | – | + | – |
| | | | | T1 | – | – | | | – | | | – | | | | + | |
| | | | | T2 | – | – | | | – | | | – | | | | – | |
| 4 | F | 4 | G | To | + | + | – | – | – | – | – | + | + | – | – | + | – |
| | | | | T1 | + | – | | | | | | – | – | | | + | |
| | | | | T2 | – | – | | | | | | – | – | | | – | |
| 5 | M | 3 | G | To | + | + | – | – | – | – | – | + | + | – | – | + | – |
| | | | | T1 | – | – | | | | | | – | – | | | – | |
| | | | | T2 | | | | | | | | | | | | | |
| 6 | F | 3 | G | To | + | + | – | – | – | + | + | + | + | – | – | + | – |
| | | | | T1 | + | + | | | | + | – | + | – | | | + | |
| | | | | T2 | – | + | | | – | + | – | – | – | | | – | |
| 7 | F | 3 | G | To | + | + | – | + | – | – | + | + | + | – | – | + | – |
| | | | | T1 | + | – | – | + | – | | – | – | – | | | + | |
| | | | | T2 | – | – | – | + | – | | | | | | | – | |
| 8 | C | 3 | G | To | + | + | – | – | – | – | – | + | + | – | – | + | – |
| | | | | T1 | + | – | – | | – | | – | – | – | – | – | + | |
| | | | | T2 | – | – | | | – | | | | | | | – | |
| 9 | C | 5 | T | To | – | – | – | – | – | + | + | + | – | – | – | + | + |
| | | | | T1 | – | – | | | | – | – | – | | | | + | – |
| | | | | T2 | – | – | | | | – | – | – | | | | – | – |
| 10 | F | 3 | G | To | + | + | – | – | + | – | + | + | + | + | + | + | – |
| | | | | T1 | + | – | | | – | | – | – | – | – | – | + | |
| | | | | T2 | + | | | | | | | | | | | – | |
| 11 | C | 6 | G | To | + | + | – | – | + | + | – | + | + | – | + | + | – |
| | | | | T1 | + | – | – | – | + | – | – | – | – | | – | + | |
| | | | | T2 | – | | | | – | | | | | | | – | |
| 12 | C | 3 | G | To | + | + | – | – | – | – | – | + | + | – | – | + | – |

*follows table* 1

**Table 1**

| Number | Sex | Age | Height | Time | Sympotoms | | | | | | | | | | Treatment | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Thoracic pain and contracture | Lumbar pain and contracture | Kyphosis | Rump asymmetry | Thoracic pain on interspinous pressure | Pain on pressure to the sacro-iliac ligaments | Gait impairment | Loss of thrust | Lowers when mounted | X-ray | Intraspinous infiltration | Paravertebral infiltration | Lombar infiltration |
| | | | | T1 | + | – | | | | | | – | – | | | + | |
| | | | | T2 | + | – | | | | | | – | – | | | – | |
| 13 | F | 3 | G | To | + | + | – | – | + | – | + | + | + | – | – | + | – |
| | | | | T1 | – | + | | | – | | – | – | – | | | + | |
| | | | | T2 | | + | | | | | | | | | | + | |
| 14 | M | 2 | G | To | + | – | – | – | – | – | + | + | – | + | – | + | + |
| | | | | T1 | – | | | | | | – | – | | – | | – | – |
| | | | | T2 | | | | | | | | | | | | | |
| 15 | F | 3 | G | To | + | + | – | – | – | – | – | + | – | – | – | + | – |
| | | | | T1 | + | – | | | | | | + | | | | + | |
| | | | | T2 | + | – | | | | | | + | | | | – | |
| 16 | F | 3 | G | To | – | + | – | – | – | – | – | + | + | – | – | + | – |
| | | | | T1 | | – | | | | | | – | – | | | + | |
| | | | | T2 | | | | | | | | | | | | – | |
| 17 | F | 3 | G | To | + | + | – | – | + | – | + | + | + | + | + | + | – |
| | | | | T1 | + | + | | | + | | + | + | + | | – | + | |
| | | | | T2 | + | + | | | + | | + | + | + | | – | – | |
| 18 | M | 3 | G | To | – | + | – | – | – | – | – | + | + | – | – | + | – |
| | | | | T1 | | + | | | | | | + | – | | | + | |
| | | | | T2 | | – | | | | | | – | | | | – | |
| 19 | C | 3 | G | To | + | – | – | – | – | – | – | + | + | – | – | + | – |
| | | | | T1 | + | | | | | | | – | – | | | + | |
| | | | | T2 | – | | | | | | | | | | | – | |
| 20 | C | 12 | G | To | + | + | – | – | – | – | + | + | – | – | – | + | – |
| | | | | T1 | + | – | | | | | – | – | | | | + | |
| | | | | T2 | + | | | | | | | | | | | – | |
| 21 | C | 12 | C | To | + | + | + | – | + | + | + | + | – | – | – | + | + |
| | | | | T1 | – | – | + | – | – | + | – | – | | | | + | – |
| | | | | T2 | | | + | | | + | | | | | | – | |
| 22 | F | 3 | G | To | + | + | + | – | – | – | – | + | – | – | – | + | – |
| | | | | T1 | – | + | + | | | | | + | | | | + | |
| | | | | T2 | | – | + | | | | | + | | | | – | |
| 23 | C | 3 | G | To | + | + | – | – | – | + | + | + | – | + | + | + | – |
| | | | | T1 | – | – | | | | + | – | – | | | – | + | |

*follows table* 1

**Table 1**

| Number | Sex | Age | Height | Time | Sympotoms | | | | | | | | | | Treatment | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Thoracic pain and contracture | Lumbar pain and contracture | Kyphosis | Rump asymmetry | Thoracic pain on interspinous pressure | Pain on pressure to the sacro-iliac ligaments | Gait impairment | Loss of thrust | Lowers when mounted | X-ray | Intraspinous infiltration | Paravertebral infiltration | Lombar infiltration |
| | | | | T2 | | | | | | – | | | | | | – | |
| 24 | M | 8 | T | To | + | + | – | – | – | – | – | + | – | – | – | + | – |
| | | | | T1 | – | – | | | | | | – | | | | + | |
| | | | | T2 | | | | | | | | | | | | – | |
| 25 | M | 8 | G | To | + | + | – | – | – | – | + | + | + | – | – | + | – |
| | | | | T1 | – | – | | | | | – | – | – | | | + | |
| | | | | T2 | | | | | | | | | | | | – | |
| 26 | M | 4 | G | To | + | + | – | – | + | – | – | + | + | + | + | + | – |
| | | | | T1 | + | – | | | – | | | – | – | | – | + | |
| | | | | T2 | – | | | | | | | | | | | – | |
| 27 | M | 4 | G | To | + | + | – | – | – | – | – | + | + | – | – | + | – |
| | | | | T1 | + | + | | | | | | – | – | | | + | |
| | | | | T2 | + | – | | | | | | | | | | – | |
| 28 | M | 3 | T | To | + | + | + | – | – | + | – | + | – | – | – | + | + |
| | | | | T1 | – | – | + | | | – | | – | | | | + | – |
| | | | | T2 | | | + | | | | | | | | | – | |
| 29 | F | 5 | T | To | – | + | + | – | – | – | – | + | – | – | – | + | + |
| | | | | T1 | | – | + | | | | | – | | | | + | – |
| | | | | T2 | | | + | | | | | | | | | – | |
| 30 | M | 9 | T | To | – | + | – | – | – | – | – | + | – | – | – | + | |
| | | | | T1 | | – | | | | | | – | | | | + | |
| | | | | T2 | | | | | | | | | | | | – | |

After clinical examination, in case of interspinous thoracic pain an x-ray was taken to disclose any changes along the edges of the spinous processes known as "kiss lesions", before proceeding to infiltration of the $O_2$-$O_3$ mixture in between the spinous processes. If pain was confined to the muscles we undertook paravertebral infiltration directly, whereas in case of suspicion or diagnosis of arthrosis in the lumbar facet joints, infiltration was carried out at a deeper periarticular paravertebral level.

An OZOLINE model E 80 device fitted with a differential digital photometer for real time display of $O_2$-$O_3$ concentrations was used for treatment.

Some of the horses were given mild sedation (10 mg detomidine) before treatment to make them easier to constrain and in most animals application of a twitch/barnacle was sufficient.

Two treatment sessions were held ten days apart followed by clinical follow-up ten days later. The time of clinical examination and the first infiltration was termed T0; the second infiltration was T1; clinical follow-up was T2.

Paravertebral treatment consisted in administration of 15 ml of $O_2$-$O_3$ gas mixture at a concentration of 30 μg/ml with a 20 G needle 40 mm long, injected bilaterally into the muscle and about 4cm from the spinous apophysis throughout the area of pain.

## Thoracic pain and contracture

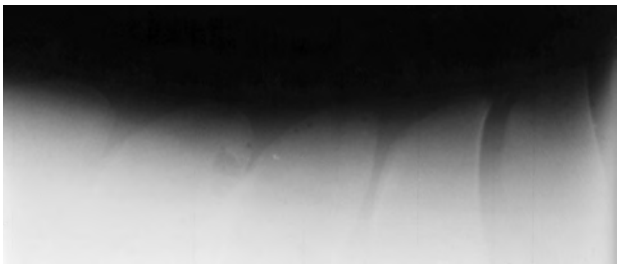
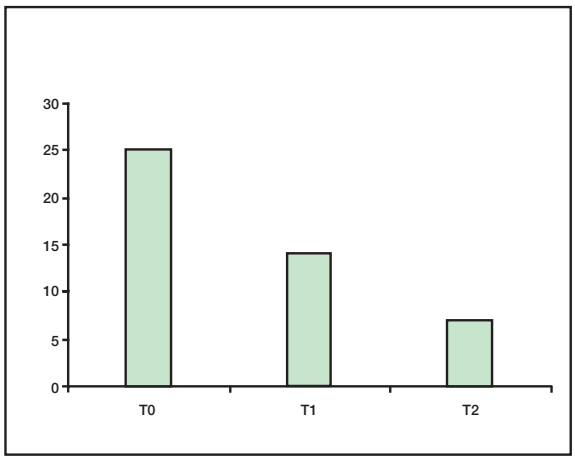


Figure 1 *Case* n° 17. Narrowing of the spaces between the spinous processes of the 13th and 14th thoracic vertebrae with cysts at the cranial margin of the 14 thoracic vertebra.

| | |
|---|---|
| T0 | 25 |
| T1 | 14 |
| T2 | 7 |




Graph 1

## Lumbar pain and contracture

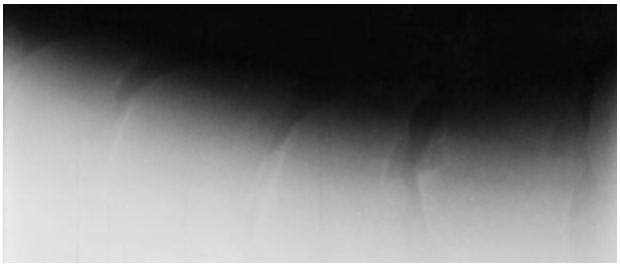
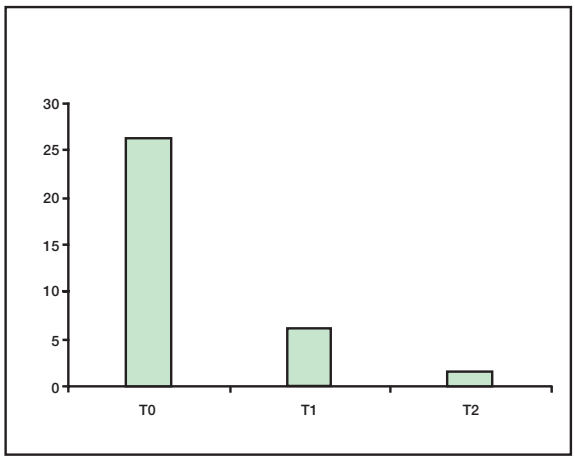


Figure 2 *Case* n° 26. Narrowing of the spaces between the spinous processes of the 13th and 14th thoracic vertebrae with cysts at the cranial and caudal margins of the 14th thoracic vertebra; sclerosis of the cranial margin of the 15th thoracic vertebra; narrowing of the space between the spinous processes of the 15th and 16th thoracic vertebrae.

| | |
|---|---|
| T0 | 27 |
| T1 | 6 |
| T2 | 2 |




Graph 2

For interspinous disease we administered 15 ml of $O_2$-$O_3$ gas mixture at a concentration of 30 μg/ml with a 20 G spinal needle 90 mm long injected in between the spinous processes. No anti-inflammatory drugs were given in the treatment period.

### Results

Of the 30 horses examined, 25 presented thoracic pain and contracture but after the first treatment session 11 animals had a remission of symptoms, whereas only seven horses still had pain after the second infiltration (graph 1)

Thoracic interspinous pain was less common (eight horses) and after one treatment session two animals had a remission of symptoms.

Almost all the horses (27) had pain and contracture in the lumbar region. After the first infiltration only six animals still had pain and after the second session only two horses proved refractory to treatment (graph 2).

Four out of 30 horses also had a change in curvature of the lumbar spine and were treated by deep paravertebral infiltration into the facet joints. All four animals had a remission of pain after the first treatment session even though the spine curvature remained unchanged.

One horse with an symmetric rump failed to benefit from treatment whereas six animals also had pain in the sacro-iliac ligaments which resolved in three horses at $T_1$, but persisted in two also at $T_2$. Of the 11 horses presenting gait impairment, only one failed to improve after two infiltrations.

All horses examined had a loss of thrust/impulsion, but only ten out of 25 animals (24 thoroughbred and one competition horse) lowered themselves when their riders mounted the saddle.

All 30 horses examined received paravertebral $O_2$-$O_3$ injection, six also had interspinous infiltration and five only periarticular infiltration.

## Conclusion

Although our cohort is small, the $O_2$-$O_3$ treatment at interspinous and paravertebral level was well tolerated in back disorders in riding horses. These encouraging results show $O_2$-$O_3$ therapy can be considered a valid alternative to current drug management protocols.

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# Oxygen-Ozone Therapy for Spinal Muscle Disorders in the Horse

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**Key words:** "Back pain", $O_2$-$O_3$ therapy, paravertebral infiltration

## Introduction

Changes in the thoracolumbar spine are a major cause of impaired performance in athletic horses and a high incidence of these disorders has been found in exhibition and competition jumping horses, dressage and trotting horses. The many pathologic changes affecting the thoracolumbar spine fall into three main categories: 1) congenital spinal deformities, 2) soft tissue lesions, 3) vertebral bone disorders.

Congenital deformities of the thoracolumbar spine include abnormal curvature (scoliosis or lordosis) and union of the vertebrae (synostosis).

Soft tissue lesions include muscle sprains, ligament tears, disc disease and skin injury caused by sores or parasite lesions.

Bone changes include ossifying spondylosis, deforming spondylosis, overriding of the dorsal spinous processes and fracture of the spinous processes, intervertebral joints, neural arch and vertebral bodies.

This study focuses on soft tissue spinal lesions (longissimus dorsi muscles, psoas muscles, gluteal muscles etc.). Following intense muscular stress, e.g. a race or other activity requiring a swift start, or other causes, these muscles may suffer varying degrees of inflammation.

Conservative management of thoracolumbar disorders includes anti-inflammatory treatments, acupuncture, physiotherapy techniques like short wave diathermy, thermography, ultrasound, and pulsating magnetic fields, and lastly manipulating techniques like chiropractic and osteopathy.

These traditional treatments have recently been flanked by oxygen-ozone therapy now well established in human medicine.

In view of the scant literature on the administration of oxygen-ozone to treat spine disorders in the horse, this study summarizes the case reports of four trotting horses treated by oxygen-ozone infiltration.

## Etiology

Soft tissue spinal lesions are caused by muscle fatigue/sprain. The muscles running along the spine to the dock of the tail are very important in maintaining balance and harmonious movement of the spine with the rest of the body. Together with the pelvic muscles, spinal muscles are involved in the thrust of the posterior muscle train and subject to varying degrees of injury when the horse is treated wrongly: incorrect training, prolonged excessive stress, falls, poor nutrition, inappropriate shoeing, cold, lesions to other joints resulting in irregular gait with negative effects on the spine, etc.

## Symptoms and Diagnosis

Palpating one or more muscles involved, the back of the horse feels tense, hard and contracted: the inflamed area may be confined to a single region of the spine (thoracic, lumbar, sacral) or involve several segments and different muscles. Spinal pain must be assessed by examination with the hand open and fingers outstretched. The hands should run delicately over the dorsal muscles from the withers to the dock of the tail increasing pressure as the movement is repeated. A positive sign of pain is evoked when the horse draws back and

Figure 1

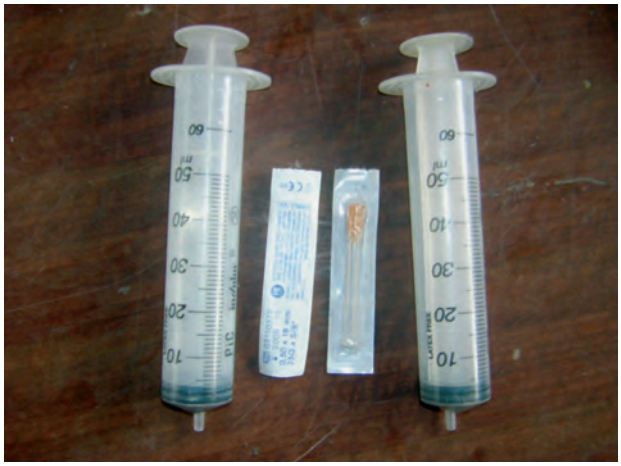

Figure 2

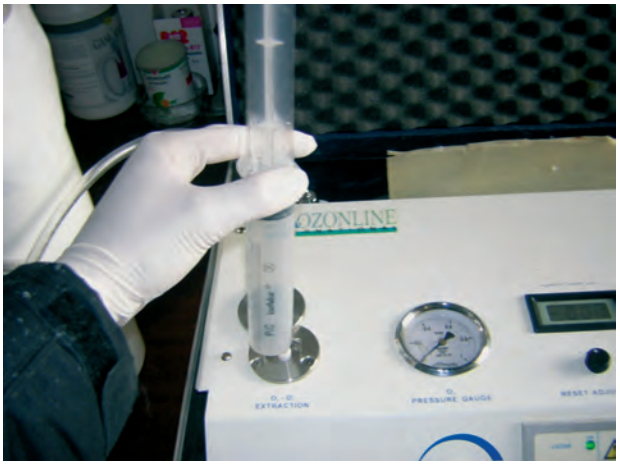


Figure 3

Figure 4

a muscle contraction (spasm) is noted over the lesion. The horse's muscular response is protection against moving the injured area: in some dramatic cases, this response is accompanied by whining, arching of the back to escape palpation/pressure, kicking, rearing, etc.

On moving the horse, its walking gait is stiff, insecure in the early stages of trotting and the animal is unable to lengthen its stride with short close-set movements of the anterior and posterior limbs producing trotting gait alternating with pacing, loss of flexion of hock and patella (differential diagnosis) and a tendency to drag its hooves. On warming up the horse's gait improves but as trotting speed increases the animal cannot perform normal propulsion movements with its posterior limbs and acceleration and speed are affected so that the horse's fatigue threshold is reached more quickly thereby diminishing its athletic performance both during training and in competition.

In the long-term, the horse shows a progressive loss of convexity of the pelvic muscles and mono or bilateral atrophy of the rump muscles caused by limited use of the posterior train.

Diagnosis can be confirmed in hyperacute forms by a two to fivefold increase in serum levels of the muscle enzymes AST and CK.

## Materials and Methods

We studied four trotting horses (three mares aged three and five years and a three-year-old stallion) in full competitive activity and all belonging to the same stables located in a training centre in the Bologna area, Northern Italy.

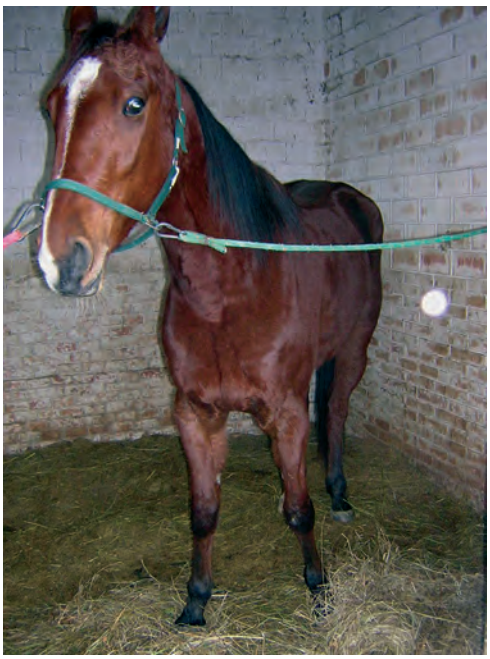

Figure 5

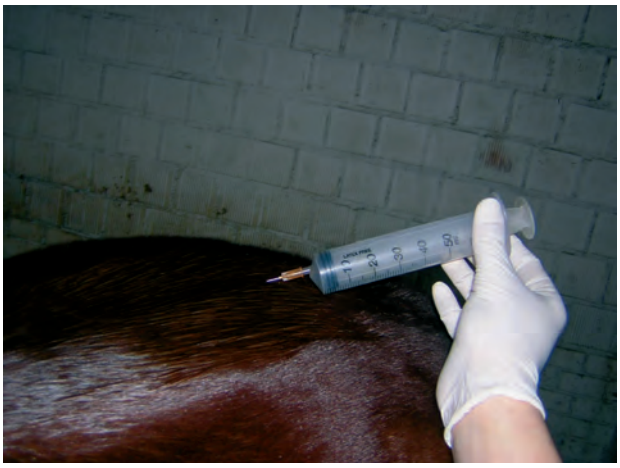

Figure 6

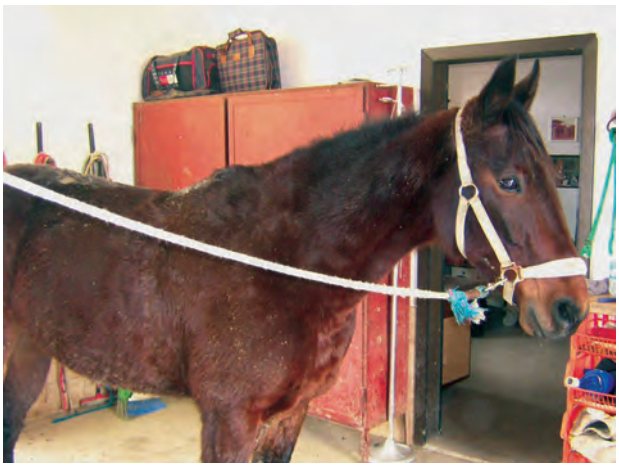

Figure 7

The four horses all presented the symptoms described above: pain on finger palpation/pressure over the affected muscles, arching of the back and rigid gait of the posterior muscle chain (gait is rigid as trotting starts then gradually disappears as the horse warms up before the race or in training to then return during or after physical stress, negatively affecting performance), confirmed by the trainer and stable staff.

We used a portable ISIS 2000 OZONLINE generator producing an ozone concentration of 75 mg/ml with an oxygen cylinder of 1 and/or 5 kg, 60 ml disposable syringes to collect the ozone and 25 G mesotherapy needles for infiltration of the gas mixture into the inflamed muscles.

Treatment consisted of weekly $O_2$-$O_3$ infiltration for three to four weeks depending on symptoms. A 25 G needle was inserted subcutaneously in an oblique direction followed by injection of 20-25cc ozone at a concentration of 30 mg/ml into each point. The treatment area depended on the extent of inflammation varying from one part of the back (thoracic, lumbar or sacral regions) to the whole stretch of the spine from the withers running along the thoracolumbar spine to the sacral dock of the tail. Treatment of the whole spine involved ten injection sites located at 7-8 cm intervals 4-5 cm away from the sides of the spine along the muscle fascia, see figures 1, 2, 3, 4, 5, 6, 7).

During infiltration the ozone expands subcuta-

neously leading to swelling which gradually subsides within 24 hours (corresponding to the time necessary for ozone absorption). Soon after injection the ozone has an analgesic effect in the infiltration site confirmed by lacking of arching of the spine on pressure/palpation of the injured part.

Before infiltration the injection site was disinfected with betadine then rubbed with ethyl alcohol followed by walking the horse for 15-20 minutes to accelerate the process of absorption. During the rest of the week the horse underwent regular trotting training, avoiding intense or prolonged stress. Throughout the treatment cycle the animals' diet was supplemented daily with 30-40 g vitamin C in powder form to balance the oxidants/antioxidants ratio changed by ozone injection.

## Results

The four horses had a positive response to treatment after the first and second injections of $O_2$-$O_3$ showing an improvement in both walking and trotting gait. The animals' movements were less stiff as trotting started and posterior muscle chain thrust was more vigorous as trotting speed increased. These improvements continued until full recovery at the end of treatment which was discontinued after the third infiltration in two of the horses.

In addition, rigidity and tension on palpating the muscles involved had disappeared and there was no response to pain on applying pressure to the treated area or the resulting contraction and arching of the spine. Lastly, there was a progressive filling and rounding of the back muscles.

The improvement was confirmed by the trainer and by the animals' training performance and during races. No allergic reactions were encountered either at the site of injection or generally.

## Discussion

We administered subcutaneous infiltration of an $O_2$-$O_3$ mixture but the gas can also given at the same doses and concentration by vertical injection into the deep muscles using 21 G needles or intravertebral infiltration with spinal needles.

During and just after injection the ozone produces a tingling/itchy sensation gradually replaced by an analgesic effect as subsequent palpation of the treated area failed to elicit pain or arching of the spine.

It is not possible to determine the duration of the beneficial effect of treatment or claim that the disorders will not recur since the ongoing muscle stress in trotting horses engaged in competitions throughout the year combined with one of the causes of spinal disorders could lead to further acute muscle inflammation.

I have had occasion to administer different treatment cycles to the same horse and have always noted a positive response without short or long-term side effects.

In conclusion, this study and the daily administration of $O_2$-$O_3$ to treat a variety of disorders show that the therapy is a reliable, safe and effective alternative to the many treatments currently administered in equine veterinary practice.

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# Letters to the Editor

Dr.Matteo Bonetti
Scientific Director
Rivista Italiana di Ossigeno-Ozonoterapia

Dear Matteo,

I am writing you about my first experiences with ozone-oxygen therapy for herniated disc.

I heard first time about ozone-oxygen therapy on 17th Annual Meeting of the International Intradiscal Therapy Society, which taked place in Munich, Germany on May 19-23, 2004.

I have attended this meeting with interesting in chemonucleolysis with chymopapain. I have been surprised, when I heard a lecture Dr G.Mazzo about his 9 years experiences with ozone-oxygen therapy for lumbar disc herniation. Dr Kumar's poster showed his first experie nces with ozone-oxygen therapy.

I wrote to prof.Leonardi after my return at home. I have payed all issues of Rivista Italiana di Ossigeno-Ozonoterapia, where I found many topics about ozonotherapy for herniated disc.

I came in contact with Dr G.Fabris by internet, and he was my first teacher for ozone therapy.

Later I have visited you. I thank both , you and Dr G. Fabris for very kind relations to me and for your help in first steps with the starting ozone therapy.

It is very interesting.that immediately my first patient with sciatica has excellent result with ozone-oxygen therapy.

He is 44-year-old man, who suffered from sciatica from August 2004. Two month he was treated with bed rest, analgetics, myorelaxants and physiotherapy. Clinically he had radiculopathy S1 on the left side. He was worsen last week of october. MRI was performed On Nov. 8, 2004 with result of large paramedial hernia L5/Sl left side (figures 1 A-B). His physiatrist and neurologist recommended surgery for his sciatica. One day before admitting to the neurosurgery department the patient asked me for ozone-oxygen therapy. We performed CT-guided foraminal ozone-oxygen therapy with

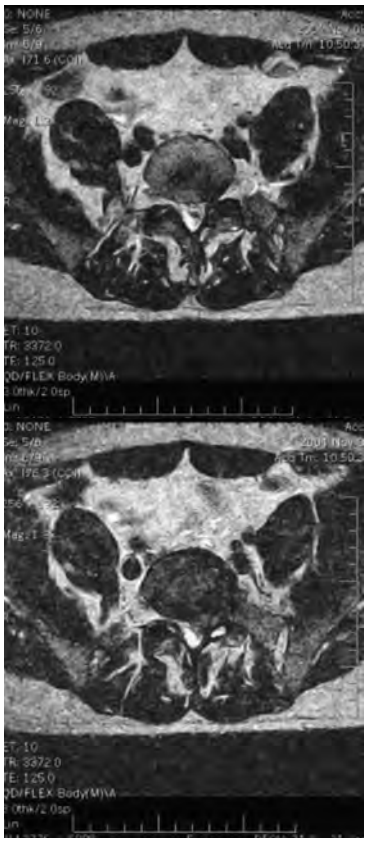



Figure 1 A
Left paramedial L5/S1 hernia.

Figure 1 B
Left paramedial L5/S1 hernia.

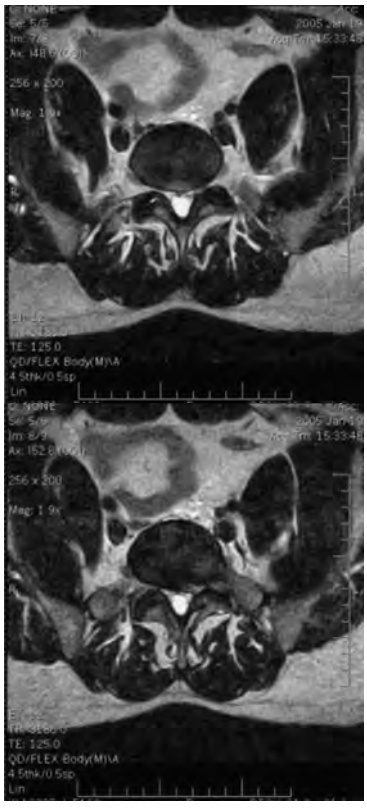



Figure 2 A
Almost complete recovery.

Figure 2 B
Almost complete recovery.

concentration of ozone 27 micrograms/ml, volume was 5 ml to foramen, 10 ml to facet region. Two weeks after ozone therapy patient started working without any problem with his back and left leg. Two months after therapy he had MRI with large decrease of hernia volume (figures 2 A-B).

That excellent first result is very high encouragement for the future. I have treated more than 100 patients with foraminal and paravertebral approach with good results.

I thank you and Dr.G.Fabris once more, and I wish you very successfull work on spreading ozone therapy in more countries.

S*incerely*,

MU Dr. Juraj Vyletelka
Head of Dept. Neurology
Regional Hospital
012 07 Žilina
SLOVAKIA
e-mail: vyletelka@nextra.sk

*Dear Juray*

*Thank you for letting me know so soon about your new found enthusiasm for oxygen-ozone therapy. Reading your letter reminded me of when I first approached oxygen-ozone therapy diffident about the true potential of this new treatment. Nearly fifteen years have gone by since then and my personal series of treated patients numbers some twenty thousand: an amazing number of people successfully treated and freed from the operating table with ensuing cuts in the cost of drug management. I hope you too will discover the passion and enthusiasm aroused by the success of oxygen-ozone therapy.*

*With kind regards*,

Matteo Bonetti

Dr.Matteo Bonetti
Scientific Director
Rivista Italiana di Ossigeno-Ozonoterapia

Dear friends,

Congratulations are in order for a magnificent issue of Ozonoterapia. The cover is most interesting, I may say.

I will like about twenty copies of the journal, it will be very helpful to display this issue to promote our cause in India. What ever is the cost, I will pay for it.

I have had very successful visits to Barcelona and Karachi. The name of Ozone injection for disc hernia is becoming well known. I have just sent in an abstract for next meeting of IITS that will be held in San Diego in may next year. I will also send papers for I-SIS meeting in NY as well as for World Congress on Pain in Sydney in August 2005. My paper for your journal should be ready in one month and I want to send in a paper for Pain Practice around the same time.

I had a nice visit with Dr. Gastaldi from Italian Embassy. We may get same support from their office. I will try to rope in the representative from the EC in New Delhi and our Science and Technology Minister to inaugurate our function. This years program will be extending to two days and I pan top make it a bit more elaborate, if that is possible.

First announcement for the April meeting has been sent. I am expecting a response from some overseas doctors this year. This is a good time for me to have a list of your topics so we can insert them in the second announcement that should be sent in by first week of December.

Vijay Kumar

*Dear Vijay,*

*I was delighted to hear that you appreciated the issue of the journal dedicated to the Indian meeting. For us this was an important occasion and a constructive experience reflecting positively on what the Italian school has achieved in the field of oxygen-ozone therapy. We are proud that thanks to your contribution our journal will now be included in Elsevier's Embase Index.*

*Thank you again and here's to the next course in Delhi.*

Matteo Bonetti

*Imola, 02/04/05*

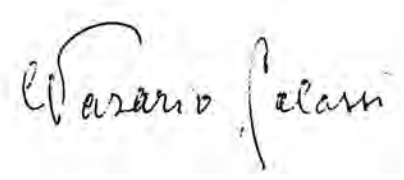
*Ch.mo Prof. Leonardi,*

*riparando a una mia imperdonabile dimenticanza, desidero comunicarLe che il trattamento di infiltrazioni di ozono, praticatomi su una doppia ernia del disco lombo-sacrale il 19-2 e il 21-4-2004 ha avuto esito mirabilmente positivo, per non dire miracoloso.*

*Mentre prima quasi non riuscivo a muovermi per i dolori lancinanti anche da fermo, ora cammino, corro, salto senza il minimo dolore nonostante la mia rispettabile età di 82 anni.*

*Tenga conto che venivo da una vicenda tormentata. Operato di ernia discale al Traumatologico di Bologna senza risultati, poi con diagnosi di morbo di Pot ricoverato sei anni solo con qualche breve interruzione presso il Codivilla-Putti di Cortina con tre di immobilità pressoché assoluta ne fui dimesso con molti dubbi e dolori superati con trattamenti di Voltaren. Può quindi immaginare la gratitudine che provo per Lei e per il Dr Simonetti che mi praticò il trattamento e al quale*
*La prego di trasmettere questi miei versi.*

*Ancora con riconoscenza indelebile*



# *Tipical species from Puerto Rico's Rain Forest*

Photos by Matteo Bonetti

*Rivista Italiana di Ossigeno-Ozonoterapia* 4: 79-93, 2005

# THE AMERICAN SOCIETY OF SPINE RADIOLOGY

2005 Annual Symposium

San Juan Puerto Rico

23–27 february, 2005

## Ozone Therapy: Intradiscal and Periradicular Therapy

**Mario Muto - Matteo Bonetti**

Mario Muto, John Mathis, Matteo Bonetti

# Federazione Italiana di Ossigeno-Ozonoterapia

# Italian Federation of Oxygen-Ozonetherapy

Cari amici, cari soci della FIO

Si è recentemente tenuto a Nuova Delhi, il 9 e 10 aprile, il 2° Symposium on Spine Intervention organizzato dal Dr V.S. Kumar.

Il Dr Kumar ha introdotto per primo in India l'uso della miscela di ossigeno-ozono nel trattamento percutaneo dell'ernia del disco lombare, appreso in Italia nei nostri centri. I risultati della sua attività, sviluppatasi negli ultimi due anni, sono stati molto positivi e lo hanno portato all'organizzazione di questo appuntamento scientifico annuale, nuova tradizione per noi. Quest'anno la partecipazione è stata particolarmente alta, con partecipanti arrivati dal Canada, dalla Cina, dalla Corea, dal Pakistan, dalla Spagna, da Taiwan, dalla Russia, dagli USA, oltre naturalmente alla nostra delegazione Italiana (Andreula, Bonetti, Muto e Leonardi) e alla folta presenza di medici indiani.

Questo incontro si prefigura come una delle prime realizzazioni concrete di cooperazione Italo-Indiana nel settore medico, anticipatrice di un importante accordo in corso di studio fra i relativi Ministeri della Salute dei due paesi. Notevole e particolarmente affettuoso il supporto dell'Ambasciata Italiana in India e dei suoi rappresentanti.

In questa occasione, come potete vedere anche dal verbale redatto da Bonetti, abbiamo ipotizzato l'allargamento della nostra Associazione per raccogliere in modo adeguato i colleghi stranieri, nella prospettiva di uno scambio scientifico, professionale ed umano sempre più ricco.

Vi faremo avere più avanti le idee e le proposte in merito che il Consiglio Direttivo cercherà di mettere a punto. Ne parleremo più compiutamente in occasione dell'Assemblea di ottobre.

Desidero sinceramente ringraziare il Dr Kumar, con i suoi collaboratori e i suoi familiari, per il suo impegno e per il suo entusiasmo.

Un particolare ringraziamento al nostro Ambasciatore Armellini e ai suoi collaboratori Dr Starace e Dr Gastaldi.

Dear friends and FIO members,

The 2nd Symposium on Spine Intervention organized by Dr V.S. Kumar was held in New Delhi on 9th and 10th April last.

Dr V.S. Kumar learnt the technique of oxygen-ozone therapy at our centres in Italy and was the first to use the gas mixture in the percutaneous treatment of herniated lumbar disc in India. The positive outcome of his activity over the past two years led to the organization of this new annual scientific event.

This year's meeting was attended by participants from the Canada, China, Pakistan, Spain, Taiwan, USA. Korea and Russia in addition to the Italian delegation (Cosma Andreula, Matteo Bonetti, Mario Muto and Marco Leonardi) and numerous Indian doctors.

This Symposium was one of the first tangible signs of Italo-Indian cooperation in the medical field, heralding a major agreement currently being negotiated by the Ministers of Health from both countries. The initiative was warmly supported by the Italian Embassy in India and its representatives.

As you will also see from the Minutes drafted by Matteo Bonetti, the meeting offered us the opportunity to broaden our Association to welcome foreign colleagues with a view to increasingly important scientific, professional and human exchange in the future.

The ideas and proposals to be developed by our Executive Committee will be made available in due course and we shall have an opportunity to discuss such topics at the October meeting.

I offer my sincere thanks to Dr Kumar, his colleagues and his family for their commitment and lively enthusiasm.

Special thanks are extended to our Ambassador Mr. Armellini and his staff Mr. Starace and Mr. Gastaldi.

*Marco Leonardi*
FIO President

# WFOT - World Federation of Ozone Therapy

## Founding Meeting
## New Delhi 10.04.2005

Sono presenti le delegazioni Italiana (Leonardi, Andreula, Bonetti, Muto), Indiana (Vijay and Vikram Kumar), Spagnola (Baeza Noci, Algara), China (Mok), Taiwan (Teng), Russia (Vetrile St. and Ma), Pakistan (Chaudhry) e Canada (Bergeron)

Apre la seduta il Prof. Vijay Kumar, che la ha proposta e motivata con il bisogno di avere una Federazione Internazionale con protocolli e linee guida internazionali.

Il Prof. Marco Leonardi specifica come in Italia siano stati fatti importanti passi in avanti dapprima con la creazione della Rivista Italiana di Ossigeno-Ozonoterapia giunta al suo quarto anno, pubblicata per i primi tre anni in italiano e da quest'anno totalmente in lingua inglese, visto il grande interesse non solo nazionale ma internazionale. Il Prof. Leonardi specifica come in Italia sia stata fondata la Federazione delle Società Scientifiche di Ozonoterapia e come si possa studiare il progetto di una Federazione Internazionale. Il dottor Andreula che spiega come oggi non solo in Italia ma nel mondo ogni medico tenda ad essere autodidatta e come non vi siano ancora delle linee guida precise per tutti, ritiene pertanto questo un importante e fondamentale passo. Il Dr Mok, di Guangzhou China, sostiene che la via dettata dal professor Leonardi sia quella giusta. Viene anche proposta l'idea di Sezioni Nazionali con Corsi Internazionali sotto l'egida della WFOT.

Il Dr Mu Huo Teng, radiologo intervetista di Taiwan, propone la possibilità di certificare le persone che esercitano l'ozonoterapia e ovviamente anche le apparecchiature. Il Dr Baeza Noci, spagnolo, sostiene che sia fondamentale partire da una base comune e di protocolli, il Dr Mu Huo Teng risottolinea l'importanza di proporre una certificazione delle persone e delle apparecchiature, Vikram Kumar sostiene che le cose andranno più veloci in Asia che in Europa. Il Dr Andreula ritiene molto utile quanto fatto in Italia con tanti corsi residenziali che avvicinano in maniera corretta tanti medici alla terapia, ma l'obiettivo più importante e l'analisi scientifica da parte dei medici di tutto il mondo. Leonardi propone di modificare la struttura redazionale della Rivista per aprirla ai contributi scientifici delle varie nazionalità. Andreula interviene proponendo un website della WFOT gestito in Italia. Andreula riassume i cinque punti fondamentali da sviluppare nell'immediato futuro a conclusione della riunione:

i) società internazionale di $O_2O_3$;
ii) rivista internazionale; iii) protocolli internazionali;
iv) sito web;
v) certificazione delle tecnologiche e degli operatori.

Si conviene di lavorare alla proposta di uno statuto adeguato, rinviando le decisioni formali e conclusive alla prossima riunione, in occasione del WFITN Congress, Venezia 18-22 ottobre.

# WFOT - World Federation of Ozone Therapy

## Founding Meeting
## New Delhi 10.04.2005

Delegations from the following countries were present: Canada (Bergeron), China (Mok), India (Vijay and Vikram Kumar), Italy (Leonardi, Andreula, Bonetti, Muto), Pakistan (Chaudhry), Spain (Baeza Noci, Algara), Taiwan (Teng), Russia (Vetrile St. and Ma).

The session was opened by Prof. Vijay Kumar who first proposed the need for a World Federation with international protocols and guidelines.

Prof. Marco Leonardi outlined the advances made in the field with the new journal Rivista Italiana di Ossigeno-Ozonoterapia published for the first three years in Italian and now entirely in English to meet the growing international interest in this new field. Prof. Leonardi also described the foundation in Italy of the Federation of Ozone Therapy Scientific Societies and plans to set up a World Federation.

Dr Andreula welcomed this important step forward in the light of the current trend in Italy and elsewhere for individual doctors to be self-taught lacking standard universally recognized guidelines in the field. Dr Mok from Guangzhou, China supported Prof. Leonardi's efforts to establish a Federation. The idea was also voiced to set up National Sections with International Courses under the aegis of the WFOT.

Dr Mu Huo Teng, an interventional neuroradiologist from Taiwan, proposed certification for oxygen-ozone practitioners and equipment. Dr Baeza Noci from Spain claimed that it was essential to establish a common starting-point and protocols, while Dr Mu Huo Teng again emphasized the importance of certification for medical staff and equipment. Dr Vikram Kumar claimed that things will move more quickly in Asia than in Europe. Dr Andreula deemed the many residential courses held in Italy a useful means of offering accurate training for doctors, but the most important target will be scientific analysis by doctors from all over the world. Prof. Leonardi suggested changing the editorial format of the Rivista to open it to scientific contributions from different countries. Dr Andreula proposed setting up a WFOT website to be run in Italy, and closed the meeting summarizing five key issues to be developed in the near future:

i) an international $O_2O_3$ society;
ii) an international journal;
iii) international protocols;
iv) a website;
v) certification of technology and practitioners.

It was agreed to work on an appropriate set of by-laws, deferring all formal resolutions to the forthcoming meeting to be held during the WFITN Congress in Venice from 18th to 22nd October.

*Dr Matteo Bonetti*
Reporting Secretary


**9th & 10th April 2005, New Delhi, India**

# Programme

**April 9th, 2005**

*Inaugural Function*

Session 1

*Chairpersons*: Dr L Gastaldi, Dr Byung Jeon, Dr Harsh Mahajan

*Ozone: what, why and how. A brief overview of Ozonucleolysis*
Prof. Vijay Sheel Kumar • New Delhi

*Technique of discal puncture with fluoroscopic guidance*
Prof. Marco Leonardi • Italy

*The intradiscal technique using CT control*
Dr Cosma Andreula • Italy

Session 2

*Chairpersons*: Chairpersons: Dr Cosma Andreula, Dr Arjun D. Sehgal, Dr Manpreet Gambhir

*Intraforaminal $O_2$-$O_3$ versus Periradicular Steroidal Infiltrations in Lower Back Pain: A Randomized Controlled Study*
Dr Matteo Bonetti • Italy

*Results of the treatments of cervical discal hernias by direct intradiscal injection and of cervicalgia by intramuscular injections*
Prof. Marco Leonardi • Italy

*A multi-center, retrospective, three-year follow-up study of lumbar disc herniation treated with EUNI (European Neurosurgical Institute) modified protocol of ozone-therapy*
Dr Jose Baeza Noci • Spain

Session 3

*Chairpersons*: Dr Mario Muto, Prof. V. S Mehta, Dr. Parveen Gulati

*Intradiscal Ozonotherapy. An experimental study on lambs*
Dr Carlos Algara, Dr Oscar Casas Garcia • Spain

*Thermo-graphic Assessment of Ozone Chemonucleolysis*
Prof. Byung Chan Jeon • Korea

*CT-Guided Oxygen-Ozone Treatment for First Degree Spondylolisthesis and Spondylolysis*
Dr Matteo Bonetti • Italy

Session 4

*Chairpersons*: Prof. Marco Leonardi, Dr Matteo Bonetti, Dr Amitabh Goel

*The inflammatory cascades of pain: potential sites of ozone action?*
Dr Vikram Sheel Kumar • USA

*Ozone generators and materials*
Ing. Alberto Fiameni • Italy

*Ozone Injection Therapy, The Pakistan Experience*
Dr Umair Chaudhry • Lahore- PAK

*Ozonucleolysis, The Delhi Experience using Kumar Protocol; What, Why and How*
Dr Vijay Sheel Kumar • New Delhi

*Ozone for OA knee joint pain, bagging the limb for diabetic foot and non- healing ulcers and Ozonated oil*
Dr Parul Saheba

Session 5

*Chairpersons*: Col. P. K. Sahoo, Dr Rana Patir, Dr Oscar Casas Garcia

*Evidence based review of role of surgery for lumbar disc prolapse*
Dr H S Chhabra • New Delhi

*Minimally Invasive Surgical Treatment of Nonspecific Spondylodiscitis*
Dr Stephen Vetrile • Moscow, Russia

*Minimally invasive spinal instrumentation and fusion*
Dr Arvind Jayswal • New Delhi

*Cervical Disc Replacement, rationale and techniques*
Dr A. K. Singh • New Delhi

Session 6

*Chairpersons*: Prof Atul Goel, Prof Karamchand, Dr. Ramesh Goyal, Dr. G. S. Garewal

**April 10th, 2005**

*How to prevent complication of percutaneous vertebroplasty*
Michael Mu Huo Teng • Taiwan

Session 7

*Chairpersons*: Dr Jose Baeza Noci, Dr S. K. Sogani, Dr S Chakrabarty

*Modern trends in treatment of Caries Spine*
Dr Yash Gulati • New Delhi

*Spine fusion*
Dr. Harsh Bhargava • New Delhi

*Microscopic laminotomy without laminectomy for lumbar canal stenosis*
Dr. Rajinder Prasad • New Delhi

*Endoscopic Lumbar Disc Surgery*
Dr Satnam Chhabra • New Delhi

Session 9

*Chairpersons*: Prof. Ravi Bhatia, Prof. A. Sharma, Prof. Byung Chan Jeon

*Key Hole Concept in Spinal Intra Dural Surgery*
Prof. Basant Kumar Misra • Mumbai

*Basilar invagination, syringomyelia, fixed atlantoaxial dislocation, torticollis: Treatment by atlantoaxial joint distraction and direct lateral mass fixation*
Prof. Atul Goel • Mumbai

Session 8

*Chairpersons*: Dr Cosma Andreula, Dr V.S.Madan, Dr Rajesh Kapoor

*Vertebroplasty Guided by CT Scan. Cost Effectiveness and efficacy*
Dr. Carlos Algara, Dr. Oscar Casas Garcia • Spain

*Vertebroplasty and kyphoplasty*
Dr Mario Muto • Italy

*Kyphoplasty. Indications and technique*
Dr. Carlos Algara, Dr. Garcia Casas Oscar • Spain

Session 10

*Chairpersons*: Dr Arjun Sehgal, Prof. AK Banerji, Prof. R. Gaulatia

*Clinical research, its relevance in current medical scenario*
Prof. P N Tandon • New Delhi

*Introduction of Prof Yash Pal*
Prof Madhu Kishwar • New Delhi

*Tomorrows education - inclusive and diverse*
Prof Yash Pal • New Delhi

## Session 11

*Chairpersons*: Dr V.P.Singh, Dr Raju Vaishya, Dr Satnam Chhabra

*Lumbar Facet Joint Denervation By Laser Thermocoagulation*
Dr. Sri Kantha • USA

*Laser Discectomy*
Dr. Manoj Sharma • New Delhi

*Cervical Nucleoplasty using arthrocare coblation technique*
Dr Sri Kantha • USA

## Session 12

*Chairpersons*: Dr Carlos Algara, Dr Vijay Sheel Kumar, Dr Pradeep Jain

*Failed Back Syndrome a patho-surgical perspective*
Dr Arvind Jayswal • New Delhi

*Interventional Management of Failed Back Surgical Syndrome*
Dr G P Dureja • New Delhi

## Session 13

*Chairpersons*: Prof G.P.Dureja, Dr Ajay Jha, Dr Sunil K Singh

*Percutaneous lumbar Sympathectomy, using Laser Thermocoagulation of the Sympathetic Chain*
Dr Sri Kantha • USA

*Radio frequency in clinical Practice in sympathetic mediated pain*
Dr Pradeep Jain • New Delhi

## Session 14

*Chairpersons*: Dr Daljeet Singh, Dr Jawahar Dhar, Dr Prateek Gupta, Dr K. K. Kohli

*Vote of Thanks*
Dr Vijay Sheel Kumar • New Delhi

THIS PROGRAMME HAS BEEN ACCREDITED FOR 14 CME CREDIT HOURS BY DELHI MEDICAL COUNCIL.

KUMAR PAIN MANAGEMENT & SPECIALITY CENTRE

M L KUMAR MEMORIAL MEDICAL TRUST

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# Reportage from 2nd Symposium on Spine Intervention

## New Delhi 9th and 10th April 2005


Vijay Kumar

Leonardo Gastaldi

Mino and Antonella Andreula, Marco Leonardi, Sudarshan and Pramila Aggarwal, Mario Muto, Matteo Bonetti

## MESSAGE FROM PRIME MINISTER'S OFFICE

**Dr. Sanjaya Baru**
Media Adviser to PM
**Tel : 2301 6920**

प्रधान मंत्री कार्यालय
नई दिल्ली - 110011
**PRIME MINISTER'S OFFICE**
New Delhi - 110011

The Prime Minister is happy to know that the 2nd International "Spine Intervention : Full Spectrum" is being organized by ML Kumar Memorial Medical Trust and the Embassy of Italy at the India Habitat Centre of 9th – 10th April, 2005.

The Prime Minister hopes that a large number of people from India and around the world will benefit from this academic exchange.

The PM wishes the organizers success in their endeavour of providing knowledge of safe, effective and affordable technology for the masses.

**(Sanjaya Baru)**

New Delhi
March 23, 2005.

## MESSAGE FROM CHIEF MINISTER, DELHI

**SHEILA DIKSHIT**
CHIEF MINISTER

GOVT. OF NATIONAL CAPITAL TERRITORY OF DELHI
DELHI SECRETARIAT, I.P. ESTATE, NEW DELHI-110002

D.O. NO. : CM/VS/19
Dated : 28.03.05

I am happy to know that **Kumar Pain Management & Specialty Centre** is organizing a seminar entitled 'Spine Intervention, Full Spectrum' on April 9 and 10, 2005 in the Capital.

I hope this seminar that focuses on spine intervention and ozonucleolysis as an alternative to surgery in many cases, will help lessen suffering and bring cost effective treatment to residents of Delhi, NCR and other parts of the country.

This topic is very relevant in today's scenario and I am sure that a large number of people will benefit from deliberations at the seminar.

I congratulate the organizers for their efforts and wish the programme a great success.

Sheila Dikshit

**(SHEILA DIKSHIT)**

PHONE : OFF. 23392020, 23392030 • FAX : 23392111

## MESSAGE FROM AMBASSADOR OF ITALY

*The Ambassador of Italy*
*New Delhi*

I am pleased to know that the 2nd International Symposium "Spine Intervention: Full Spectrum" is being organized by ML Kumar Memorial Medical Trust and the Embassy of Italy at the India Habitat Centre on 9th –10th April 2005.

Italian doctors have developed and popularized the technique of Ozone Discectomy for patients who suffer from pain from disc prolapse.

I am pleased to note that Kumar Pain Management and Speciality Centre has introduced this procedure in India, fostering scientific co-operation between Italy and India.

I am optimistic that a large number of people from India and around the world will benefit from this academic exchange.

I wish the organizers success in their endeavor and I congratulate them for their efforts.

**H E. Antonio Armellini**
Ambassador of Italy
New Delhi, India

## MESSAGE FROM MINISTER OF HEALTH & SOCIAL WELFARE

डा. योगानंद शास्त्री
**Dr. YOGANAND SHASTRI**

स्वास्थ्य एवं समाज कल्याण मंत्री
राष्ट्रीय राजधानी क्षेत्र दिल्ली सरकार
**MINISTER OF HEALTH & SOCIAL WELFARE**
**GOVT. OF NCT OF DELHI**

**D. O. No.**
**Date**_____

PA®/MHSW/2005/481
March 22, 2005

I am glad to know that Kumar Pain Management & Speciality Centre is organising its 2nd International Symposium 'Spine Intervention: Full Spectrum' on April 9 – 10, 2005 at New Delhi.

I sincerely hope that this symposium, which focuses on the use of Ozone injection as a major breakthrough as an alternative to other surgical procedures for disc disorders, will help immensely to popularise the medical use of Ozone in the form of Ozone Discectomy, which is a safe, least invasive alternative to surgery in individuals suffering from the dreaded disorder of back pain stemming from prolapsed disc.

I extend my warm greetings and felicitations to all those associated with this International Symposium and send my best wishes for the success of the event.

**(DR YOGANAND SHASTRI)**

**DR VIJAY SHEEL KUMAR**
**Kumar Pain Management &**
**Speciality Centre**
**D1/28, Vasant Vihar**
**New Delhi – 110 057.**

दिल्ली सचिवालय, आई. पी. एस्टेट, नई दिल्ली-110002 दूरभाष : 23392067, 23392123
DELHI SECRETARIAT, I.P. ESTATE, NEW DELHI - 110002 TEL.: 23392067, 23392123

## MESSAGE FROM HONOURED GUEST

Dr. S. P. AGARWAL
M,S. (Surg.) M. Ch. (Neuro)
DIRECTOR GENERAL

भारत सरकार
स्वास्थ्य सेवा महानिदेशालय
निर्माण भवन, नई दिल्ली-110011
GOVERNMENT OF INDIA
DIRECTORATE GENERAL OF HEALTH SERVICES
NIRMAN BHAVAN, NEW DELHI-110011
TEL. NO. 23018438, 23019063
FAX NO. 91-11-23017924

Dated..... 30th March, 2005

I congratulate the Kumar Pain Management & Speciality Centre for organizing the 2nd Annual International Symposium, entitled 'Spine interventions: full spectrum from least invasive Ozonucleolysis to Full Disc Replacement' at New Delhi on 9th April, 2005.

Orthopaedic Surgery has made rapid strides in the past few decades. The emergence of newer sub-specialties such as Orthopaedic Oncology and Paediatric Orthopaedics clearly reflect the diversity of clinical problems in Orthopaedics and Traumatology. Improvements in bio-materials, implants and prosthetic design, better understanding of biomechanics and improved imaging methods and surgical techniques have contributed greatly to this progress. The focus in now on minimally invasive techniques.

The management of fractures has also seen a sea change over last few years. The aim now is not only to get the broken bones united, but also to get bone-union with excellent motion in the adjoining joints. "Life is motion, motion is life" is the motto. Total joint replacement of the hip and knees are among the most successful group of surgical procedures in any specialty. The present day total hip or knee replacements can restore near normal function to patients with severe pain or markedly limited function.

There is no doubt that trauma care of a high standard is available in major centres, but the number of patients requiring care after road traffic accidents, industrial and domestic injuries is enormous. Dedicated trauma centres are the need of the hour in the private as well as Government sectors. Let us also not forget the needs of the more than one third of our population living below the poverty line. Their interests must be kept in mind and we should aim at provision of services through optimal utilization of the meager resources. The time has come for concerted action, with public- private partnership, for developing the required infrastructure in our country.

I wish the conference all the success.

(S. P. Agarwal)

## MESSAGE FROM SCIENTIFIC ATTACHE, EMBASSY OF ITALY

EMBASSY OF ITALY
NEW DELHI

I wish to congratulate the organizers for 2nd International Symposium "Spine Intervention: Full Spectrum" that is being held at the India Habitat Centre, New Delhi on April 9 and 10, 2005.

This is a great example of friendship and scientific exchange between Italy and India that will benefit the mankind around the world.

I wish Dr. Vijay Sheel Kumar and his team success in their endeavor and appreciate his pioneering vision and enthusiasm.

**Dr Leonardo Gastaldi**
Scientific Attaché
Embassy of Italy
New Delhi, India

## WELCOME FROM ORGANISING SECRETARY

My Dear Colleagues,

Last year at the 1st International Symposium *Spine Intervention : Full Spectrum* held in New Delhi, the use of ozone in the treatment of disc disease was introduced in India for the first time and met with an overwhelming positive response from the medical communities in India and abroad.

We rejoin at the 2nd International Symposium in New Delhi to discuss further, the concept of ozonucleolysis, a term I coined to describe the technique of injecting ozone into the intervertebral disc. This year the symposium will be held over a 2 day intense scientific programme with leading experts from Italy, Spain, Korea, Pakistan, Russia, Taiwan, United States and India, covering topics ranging from ozone discectomy to full disc replacement.

Your participation in this event is proof that learning continues to be paramount in the delivery of exceptional medical care and that new techniques deserve the time to be introduced, understood, debated and appreciated.

The creation of this meeting proves to be a big step forward for the medical community in the receipt of a therapeutic procedure that is safe, effective, minimally invasive and successful. I look to you all to make this collaboration of international medical minds a memorable event with exciting and productive discourse.

On behalf of the MLK Memorial Trust and Kumar Pain Management and Specialty Centre, I welcome you!

Best wishes,

Dr. Vijay Sheel Kumar, MBBS, MD, FACS, FIPP, DABNS
Organising Secretary
Chairman, Kumar Pain Management and Specialty Centre

ELSEVIER

Bibliography Databases

Prof. Marco Leonardi
Edizioni del Centauro
c/o Via del Pratello 8
Bologna 40122
Italy

Amsterdam, 17th December 2004

Re: Rivista Italiana di Ossigeno-Ozonoterapia

Dear Prof. Marco Leonardi,

As you may know, Elsevier's Bibliography Databases is a leading indexing service, which scans the world's STM serials literature materials suitable for the inclusion in its comprehensive bibliographic databases. These databases include EMBASE, Compendex, Geobase amd Scopus, a re-launch of the ScienceDirect Navigator, as well as several more specialized subject databases and other derivative products such as Mosby Yearbooks. Please take a few minutes to visit our websites as given below for more information.

As we are in the process of broadening the scope of our databases we would very much like to add the above title(s) to the collection of journal covered by Elsevier's Bibiographic Databases, starting with publication year 2005. The information we would like to index concerns the standard A&I information, such as title, abstract and references, allowing for the full use of linking and citation functionality. Please note that we will not make any full text available, or provide this to a third party. An index or classification is added to a record depending on the database.

Coverage by our Databases is our recognition of the journal's quality and importance and attracts traffic to articles published by you. Therefore, I would like to ask to consider grating us a complimentary subscription for that purpose.

If you decide to grant us a complimentary subscription to the above journal(s) we would need to receive a single copy of each issue, as soon after publication as possible, at the address listed on the next page.

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We look forward to your response.

Your sincerely,

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www.elsevier.com - www.ei.org - www.scopus.com

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Sostituisce l'originale
Ai sensi dell'art. 6, comma 2, della L. 412/1991

**RegioneLombardia**

**Giunta Regionale**
**Direzione Generale Sanità**

*Data*

*Protocollo*

Ai Direttori Generali
- Aziende Sanitarie Locali
- Aziende Ospedaliere

Ai Commissari Straordinari
I.R.C.C.S. di Diritto Pubblico

Ai Legali Rappresentanti
- I.R.C.C.S di Diritto Privato
- Ospedali Classificati
- Case di Cura Accreditate

Al Comando Generale
dei Nas Lombardia

LORO SEDI

Regione Lombardia - Giunta
Sanità
P 11/03/2003 17.20

H1.2003.0014707

Oggetto: Nota integrativa al protocollo n° H1.2003.008793 del 17/02/2003 inerente l'applicazione della Circolare Ministeriale sull'ossigeno-ozono terapia.

In riferimento alla Circolare Ministeriale del 31 dicembre 2002 inerente l'ossigeno-ozono terapia si precisa quanto segue:

- si ritiene che la Circolare in oggetto, come già affermato dall'ordinanza del TAR Lazio del 26 settembre 1996, a seguito di ricorso contro una Circolare di contenuto simile emessa dal Ministero della Sanità il 14 marzo 1996, non inibisca e comunque non interferisca nell'attività di pratica terapeutica con l'utilizzo di ossigeno-ozono terapia svolta dagli ambulatori medici privati;
- per quanto riguarda gli impieghi dell'ossigeno-ozono terapia in strutture accreditate e a contratto con il Sistema Sanitario Regionale, si precisa che l'indicazione terapeutica della iniezione intradiscale, citata dalla Circolare Ministeriale, vada interpretata in senso più estensivo e cioè non come esclusiva iniezione intradiscale, ma includendo il corredo operativo previsto nelle Linee Guida già individuate dalla Società Scientifica Italiana di Ossigeno Ozono Terapia. Si intendono pertanto incluse le modalità operative dell'ozonoterapia riferite alle iniezioni intramuscolo paravertebrali, intraforaminali, periganglionari ed episacrali.

Si ritiene inoltre:
- che per la pratica ambulatoriale sia acquisito il consenso informato del paziente che si sottopone alla procedura di ossigeno-ozono terapia;
- che tutte le apparecchiature impiegate per il trattamento abbiano ottenuto la certificazione CE, ai sensi del D.L.vo 46/97;
- che le prestazioni di ossigeno-ozono terapia non debbano essere effettuate in centri di estetica o di fitness o simili.

Si raccomanda inoltre l'organizzazione di adeguati corsi formativi per i medici che praticano l'ossigeno ozono terapia.

Il Direttore Generale
Carlo Lucchina

Referente: Luca Merlino tel 02/6765.3061

Qualità e appropriatezza dei servizi sanitari
Via Pola, 9 e 11 – 20124 Milano - http://www.regione.lombardia.it
Tel. 02/67653061 – Fax 02/67653938

**ORDINE DEI MEDICI CHIRURGHI E DEGLI ODONTOIATRI DELLA PROVINCIA DI CATANIA**

---

**Protocollo N.**.948
**Risposta al foglio N. ...**
**del .....**

**95127 Catania,01/03/2005**
Lungomare Ruggero di Lauria,81
Tel . 095/4035511 Fax 095/ 498.424
**e– mail: consiglio@ordinemedct.org**

**OGGETTO**
*Concessione patrocinio dell'Ordine.*

DOTT. MATTEO BONETTI

Riscontro la cortese richiesta e sono lieto di comunicarLe che il Consiglio Direttivo, nella seduta del 24 febbraio 2005, si è espresso favorevolmente alla concessione del patrocinio per il "Corso Itinerante in Ossigeno-ozono terapia" che avrà luogo a Catania il 30 aprile p.v.

Colgo l'occasione per esprimere auguri all'evento ed invio a Lei collegiali saluti.

IL PRESIDENTE
(Prof. Ercole Cirino)

FEDERAZIONE ITALIANA DI (C081)
OSSIGENO-OZONOTERAPIA
VIA L. DA VINCI 20
25122 BRESCIA

---

PROT. 1731/2005 UFF. GAB.
SINDACO DI CATANIA ON. PROF. UMBERTO SCAPAGNINI E' LIETO PATROCINARE CORSO ITINERANTE IN OSSIGENO-OZONOTERAPIA ORGANIZZATO DA CODESTA FEDERAZIONE. PORGE AUGURI DI PROFICUO LAVORO.
LUIGI MANIA CERIMONIERE

MITTENTE:
UFFICIO DEL GABINETTO SINDACO
PIAZZA DUOMO
95124 CATANIA

AZIENDA
UNITA'
SANITARIA
LOCALE N. 9
TRAPANI

SERVIZIO SANITARIO
NAZIONALE
REGIONE SICILIANA

Via Mazzini, 1 – 91100 Trapani
Tel. 0923805111 – Fax (0923) 873745 –26580
P.Iva 01760610814

Prot. N: 104
Direzione Generale

Trapani, li: 13 GEN. 2005

Oggetto: Corso itinerante in ossigeno ozono terapia - Concessione patrocinio.

\

Dott. Matteo Bonetti
Segretario Federazione
Ossigeno Ozono Terapia
Via Leonardo da Vinci
25122 Brescia

Nell'esprimere il più vivo apprezzamento per l'iniziativa scientifica che codesta Federazione sta organizzando, si concede il patrocinio a titolo gratuito da parte di questa Amministrazione.

Si porgono distinti saluti.

AZIENDA UNITA' SANITARIA LOCALE N. 9 TRAPANI

IL DIRETTORE GENERALE
(Avv. Fulvio Manno)

*Il Presidente*
*della Provincia Regionale di Catania*

Catania, 02 MAR 2005

prot. n. 526/Gab

Egregio Signore
dott. MATTEO BONETTI
Responsabile "F.I.O."
via Leonardo da Vinci, 20
25122 BRESCIA

**fax 030/3197171**

Con riferimento alla Sua dell'1/02/2005, sono lieto di informarLa che questa Provincia Regionale intende concedere il patrocinio gratuito al "Corso Itinerante in ossigeno-ozono terapia", che si svolgerà a Catania il 30 aprile p.v.
Nel formularLe i migliori auguri di ogni successo per l'interessante evento scientifico, l'occasione mi è gradita per porgerLe i più cordiali saluti.

on. dott. Raffaele Lombardo

# III° CORSO TEORICO-PRATICO IN OSSIGENO-OZONOTERAPIA


**Relatori**

| | |
|---|---|
| Luigi Simonetti | Bologna |
| Giuliano Fabris | Udine |
| Antonio Gjonovich | Monselice (PD) |
| Gabriele Tabaracci | Montichiari (BS) |
| Matteo Bonetti | Brescia |
| Giovanni Roveglia | Rovato (BS) |
| Maurizio Puppis | Udine |
| Mario Sirito | Genova |
| Alessio Zambello | Varese |
| Marco Leonardi | Bologna |
| Francesco Ceccherelli | Padova |
| Roberto Dall'Aglio | Parma |
| Alberto Alexandre | Treviso |

Sig.ra Vittoria, Segretaria FIO

Dr Giuliano Fabris

Dr Mario Sirito

# CORSO ITINERANTE IN OSSIGENO-OZONOTERAPIA

## 12 marzo 2005


**Relatori**

| | |
|---|---|
| Cosma Andreula | Bari |
| Matteo Bonetti | Brescia |
| Philippe Cardonnet | Montpellier |
| Roberto Dall'aglio | Parma |
| Marco Leonardi | Bologna |
| Benedetto Morana | Marsala (TP) |
| Luigi Simonetti | Bologna |
| Gabriele Tabaracci | Montichiari (BS) |
| Francesco Paolo Sieli | Trapani |
| Giuseppe Venza | Trapani |
| Alessio Zambello | Varese |

Il Corso si è tenuto a Marsala presso la sala congressi ARMONY S.r.l., ed era riservato ad un numero chiuso di 60 partecipanti.

Il corso di aggiornamento si è svolto nell'arco di una giornata della durata di 8 ore, al termine della quale sono state effettuate prove pratiche e successivamente è seguito un test di valutazione.

Il corso si è concluso con la relazione del Dr G. Venza "L'ozonoterapia oggi in Sicilia".

Al termine è stato consegnato un attestato di partecipazione.

La Commissione Nazionale per l'Educazione Continua in Medicina del Ministero della Salute ha assegnato all'evento n. 5 crediti formativi.

Dr Giuseppe Venza, Dr Riccardo Morara, Dr Cosma Andreula

Dr Cosma Andreula, Dr Matteo Bonetti


# CORSO ITINERANTE IN OSSIGENO-OZONOTERAPIA

## 30 Aprile 2005

Con il patrocinio di:

ORDINE DEI MEDICI CHIRURGHI E DEGLI ODONTOIATRI DELLA PROVINCIA DI CATANIA

Comune di Catania

Provincia Regionale di Catania

*Direttore del Corso* **Dott. Maurizio Arena**

Il Corso si terrà a Catania presso l'Hotel Parco degli Aragonesi - Viale Kennedy, Loc. La Playa
Il corso di aggiornamento si svolge in una giornata della durata di 8 ore, al termine della quale verranno effettuate prove pratiche cui successivamente farà seguito test di valutazione.
Al termine verrà consegnato un attestato di partecipazione.
L'iscrizione è aperta fino a 2 settimane prima del corso e prevede una quota di 50,00 Euro per i soci FIO, 75,00 Euro per i non soci, comprensiva di materiale didattico e colazione di lavoro.
Il Corso è accreditato nell'ambito della formazione continua in Medicina (ECM). N. 4 crediti assegnati.

**PROGRAMMA**

08.30 - Registrazione partecipanti
09.00 - Apertura corso e benvenuto - Dr. C. Cristaudo
09.15 - Il razionale dell'ossigeno-ozonoterapia nel trattamento della patologia muscolo-scheletrica
Prof. M. Leonardi - Dr. L. Simonetti
09.45 - Ozonoterapia oggi - Dr. M. Bonetti
10.15 - Trattamenti integrati nella terapia dei conflitti disco-radicolari - Dr. M. Arena
10.45 - Coffee Break
11.15 - Etoricoxib e $O_2$-$O_3$ terapia vs $O_2$-$O_3$ terapia nel trattamento della spondiloartrosi - Dr. G. Savoca
11.45 - I trattamenti mininvasivi del rachide lombosacrale Dr. L. Manfre'
12.30 - Basi biochimiche e farmacologiche dell'azione della mi scela ossigeno-ozono - Prof. R. Dall'Aglio
13.00 - Colazione di Lavoro
14.30 - Ozono terapia Vs tecniche mininvasive di trattamento del rachide lombosacrale - Dr. A. Alexandre
15.00 - La patologia intrarticolare dell'articolazione temporo-mandibolare: ozonoterapia - Dr. M. Bonetti
15.30 - Ossigeno-ozono terapia nel trattamento della patologia dolorosa del piede e della mano - G. Tabaracci
16.00 - Pausa
16.30 - Prove pratiche
17.00 - Il parere dell'Anestesista - Dr. A. Zambello
17.30 - Test di valutazione
18.00 - CHIUSURA DEL CORSO

**Relatori**

| | | | |
|---|---|---|---|
| Alberto Alexandre | Treviso | Luigi Manfrè | Catania |
| Maurizio Arena | Catania | Luigi Simonetti | Bologna |
| Matteo Bonetti | Brescia | Gabriele Tabaracci | Montichiari (BS) |
| Concetto Cristaudo | Catania | Giovanni Savoca | Catania |
| Roberto Dall'Aglio | Parma | Alessio Zambello | Varese |
| Marco Leonardi | Bologna | | |

Segreteria Organizzativa:
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Tehran-5,6 May 2005

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**Tel:** (+98) 21 881 23 91 - 830 79 83
**Fax:** (+98) 21 882 89 95
**E-mail:** info@irpaincenter.org
**Web site:** www.irpaincenter.org
برگزارکننده: جهاددانشگاهی علوم پزشکی ایران (ACECR)


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USE OF OZONE IN
PREVENTION AND THERAPY

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89 Roehampton Ave, Toronto, Ontario M4P 1P9

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Sunday, May 22, 2005 9:30 am – 6:00 pm lectures and workshops
Monday, May 23, 2005 9:30 am – 12:30 pm Training

Speakers:

Dr. Mary Danylak, Dr. Hartmut Dorstewitz,

Dr. Renate Viebahn

Place:

Clinic Dr. Mary Danylak

89 Roehampton Ave, Toronto, Ontario M4P 1P9

Congress fee: 200.00 US $

Responsible: Ärztliche Gesellschaft für Ozon - Anwendung in Prävention und Therapie
1. Vorsitzender: Prof. Dr. med. Dr.hc H.G. Knoch, D-03238 Lindthal-Rehain

Sekretariat: Nordring 8, D-76473 Iffezheim e-mail: renateviebahn@t-online.de

See also: www.ozongesellschaft.de and www.ozone-association.com

# UTILIZZO DEI MEZZI DI CONTRASTO IN RM NELLO STUDIO DELLA PATOLOGIA DEL RACHIDE

*Con il patrocinio del*
*Comune di Carzago di Calvagese*

**Palazzo Arzaga**
**Carzago di Calvagese (BS)**

## 28 MAGGIO 2005

Il Corso si terrà presso il Palazzo Arzaga Hotel Saturnia Spa & Golf Resort, a Carzago di Calvagese della Riviera, Brescia
Il Corso è riservato a 100 partecipanti, le iscrizioni devono pervenire alla segreteria organizzativa entro e non oltre il 24 Maggio 2005.
Il Corso di aggiornamento si svolge in una giornata della durata di 7 ore, ed è riservato a medici neuroradiologi e radiologi.
La quota d'iscrizione è pari ad € 120, comprensiva di materiale didattico e colazione di lavoro.
Al termine dell'evento verrà rilasciato un attestato di partecipazione. È in corso la richiesta di accreditamento al Ministero della Sanità nell'ambito del Programma Nazionale d'Educazione Continua in Medicina ECM.

DIRETTORE DEL CORSO: **Dr. Matteo Bonetti**
Servizio di Neuroradiologia, Istituto Clinico Città di Brescia • Tel. +39.030.3197173 • Fax +39.030.3197171
cell.: 335.8344139 • e-mail: info@matteobonetti.com

DOCENTI

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Responsabile Servizio di Neuroradiologia • Istituto Clinico Città di Brescia

Graziella Bragaglio
Resp. Tecn. dei Servizi di Radiologia • Gruppo Ospedaliero San Donato

Paola D'Aprile
U.O.S. di Neuroradiologia • Ospedale San Paolo • Bari

Massimo Gallucci
Dip. Medicina Sperimentale • Università dell'Aquila

Attilio Gastaldi
Presidente Istituto Clinico Città di Brescia

Marco Leonardi
Direttore Servizio di Neuroradiologia • Ospedale Bellaria • Bologna

Mario Muto
Servizio di Neuroradiologia • Ospedale Cardarelli • Napoli

Gianni Pellicanò
Dipartimento di Radiologia • Università di Firenze

Luigi Simonetti
Servizio di Neuroradiologia • Ospedale Bellaria • Bologna

Alfredo Tarantino
U.O.S. di Neuroradiologia • Ospedale San Paolo • Bari

PROGRAMMA

Ore 08.30 Registrazione Partecipanti

Ore 09.00 Apertura corso • Prof. A. Gastaldi

Moderatori: M. Leonardi, M. Gallucci

Ore 9.20 Un volto nuovo alla lombalgia. "Nonsolo ernia" • P. D'Aprile

Ore 10.00 Potenziale del mezzo di contrasto nel rachide "Reumatico" P. D'Aprile • A. Tarantino

Ore 10.20 Il mezzo di contrasto nella patologia degenerativa del rachide • L. Simonetti

Ore 11.00 Coffee Break

Ore 11.30 Il mezzo di contrasto nella patologia infettivo-infiammatoria del rachide C. Andreula

Ore 12.00 Il mezzo di contrasto nello studio della patologia intradurale • G. Pellicanò

Ore 13.15 Colazione Di Lavoro

Moderatori: M. Muto, C. Andreula

Ore 14.30 Vantaggi dell'utilizzo del mezzo di contrasto nello studio della patologia del rachide operato • M. Gallucci

Ore 15.00 Utilità della somministrazione del mezzo di contrasto in RM nel planning e nel follow up delle procedure di interventistica spinale M. Bonetti

Ore 15.30 Test Di Valutazione

Ore 16:00 Chiusura Corso

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ASSOCIAZIONE ITALIANA DI NEURORADIOLOGIA

# III CORSO NAZIONALE
# Neuroradiologia Interventiva Spinale

I ANNUNCIO

Dr. C. Cristaudo
Dir. U.O. Neuroradiologia
A.O. "Cannizzaro"

Dr. L. Manfrè
Consigliere
Ass. Italiana di Neuroradiologia

Giovedì 30 Giugno 2005
sede: A.O. Cannizzaro - Catania
Manifestazioni in corso di accreditamento per ECM Italia e Europa

## GIOVEDÌ 30 GIUGNO

**LETTURE MAGISTRALI:**

- Biomeccanica della colonna vertebrale - *A. Perciavalle*
- La Neuroradiologia Interventiva Spinale in Italia - *M. Leonardi*
- Spinal Interventional Neuroradiology in the USA - *G.H. Zoarski*

**NEURORADIOLOGIA INTERVENTIVA SPINALE PARTE I: IL DISCO E IL DOLORE RADICOLARE**

- Lombalgie e lombosciatalgie: cenni di clinica - *E. Costanzo*
- Nuove terapie chirurgiche dell'ernia discale - *S. Blanco*
- Stabilizzazione vertebrale chirurgica - *M. Giuffrida*
- Studio della colonna sotto carico in TC ed RM - *F. Cartolari, G. Trasimeni*
- Basi biochimiche e farmacologiche dell'ozono e trattamento percutaneo paravertebrale sotto guida TC - *M. Bonetti*
- Infiltrazione percutanea nelle sindromi radicolari - *C. Andreula*
- Ozono intradiscale: esperienze cliniche e strumentali - *M. Muto*
- Disco-nucleolisi percutanea - *G. Bonaldi*

**NEURORADIOLOGIA INTERVENTIVA SPINALE PARTE II: IL RACHIDE**

- Osteoporosi: cenni clinici e terapia medica - *D. Maugeri*
- Tumori del rachide: Chemioterapia - *F. Di Raimondo*
- Tumori del rachide: Radioterapia - *F. Marletta*
- Tumori del rachide: Termoablazione - *G. C. Anselmetti*
- Biomateriali e sistemi di iniezione nella vertebroplastica - *G. Pellicanò*
- Nuove applicazioni della cementoplastica vertebrale - *L. Manfrè*
- Malpractice e Problematiche Medico-Legali nelle pratiche di Interventiva Spinale - *C. Fiorenza*

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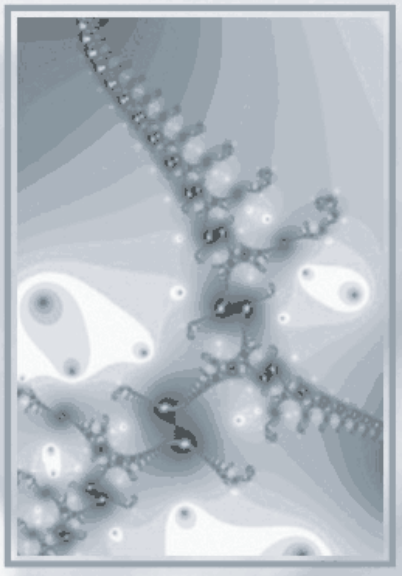

**PANEL SESSION**

- Il punto di vista del Neurochirurgo *F. Ventura*
- Il punto di vista del Medico di Base *G. Giardina*
- Il punto di vista dell' Oncologo *F. Ferraù*
- Il punto di vista dell'Ortopedico *G. Longo*
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# IV CORSO NAZIONALE DI NEURORADIOLOGIA

I ANNUNCIO

Dr. C. Cristaudo
Dir. U.O. Neuroradiologia
A.O. "Cannizzaro"

Dr. L. Manfrè
Consigliere
Ass. Italiana di Neuroradiologia

Venerdì 01 - Sabato 02 Luglio 2005
Manifestazioni in corso di accreditamento per ECM Italia e Europa

## VENERDÌ 01 LUGLIO

**PATOLOGIA CEREBRALE 1**
**Test di inizio**
- Anatomia, Tecniche e Semeiotica - *A.Banco, G. Sparacia*
- Le principali malformazioni del SNC - *A. Rossi*
- I Traumi Cranici - *G. Pellicanò*
- La Patologia Ischemica - *C. Cristaudo*
- La Patologia Emorragica - *S. Cirillo*

*ESERCITAZIONI INTERATTIVE CON CORREZIONE DEI TEST

**PATOLOGIA CEREBRALE 2**
**Test di inizio**
- La Patologia della sostanza bianca - *M. Gallucci*
- La Patologia infettiva - *M. Andreula*
- La Patologia neoplastica - *M. Longo*
- Nuove Metodiche in RM - *U. Salvolini*
- Il Gamma-Knife - *F. Ventura, C. D'Arrigo*

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## SABATO 02 LUGLIO

**PATOLOGIA CRANIO - FACCIALE**
**Test di inizio**
- L' orbita - *L. Manfrè*
- L'orecchio - *G. C. Ettorre*
- Il massiccio facciale - *M. Mandalà*
- L'ipofisi - *L. Manfrè*

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**PATOLOGIA DEL RACHIDE E MIDOLLO**
**Test di inizio**
- La Patologia degenerativa - *M. Bonetti*
- La Patologia traumatica - *G. Sirabella*
- La Patologia espansiva e infiammatoria - *R. Izzo, M. Muto*

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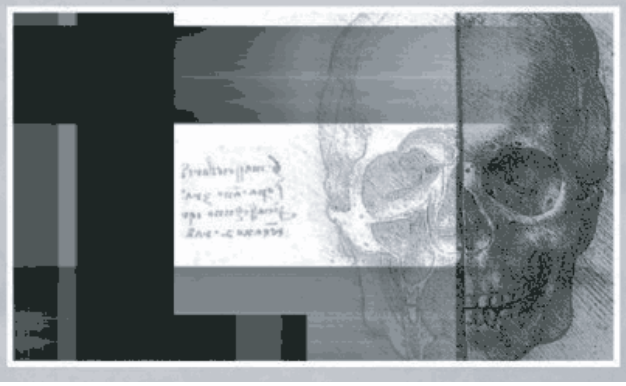

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## June 27 - 30, 2005

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Thanks a lot, We´ll meet in Havana
Organizing Commitee

FIRST ANNOUNCE-

# CORSO ITINERANTE IN OSSIGENO-OZONOTERAPIA

# CRETA

## 1 OTTOBRE 2005

**Direttore del Corso**

## Prof. Emmanuel Iliakis (Atene)

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Date…….

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Re: association membership fee

Dear Colleague,
This is a reminder that the Association *membership* fee for *2005 is € 125,00,*
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Thank you in advance for your prompt payment.

Yours sincerely,

Dr Matteo Bonetti
FIO Secretary

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Te agradezco desde ahora por el pago de la cuota.

Cordialmente

Dr Matteo Bonetti
Segreteria FIO

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Oggetto: quota associativa

Caro Collega,
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Ti ringrazio fin da ora per il pagamento,

Cordialmente

Dr Matteo Bonetti
Segreteria FIO

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**10 SEQUENCES:** In a Sequence it is possible to jump from a memorized concentration to another with a touch, to avoid dead times.

**$H_2O+O_3$:** Five Programs to ozonize the water, with a timer. It calculates the concentration of ozone in the water after the bubbling.

**OZONE-PROOF MATERIALS:** To avoid contamination of the output gas.

Medical Device CE marked.

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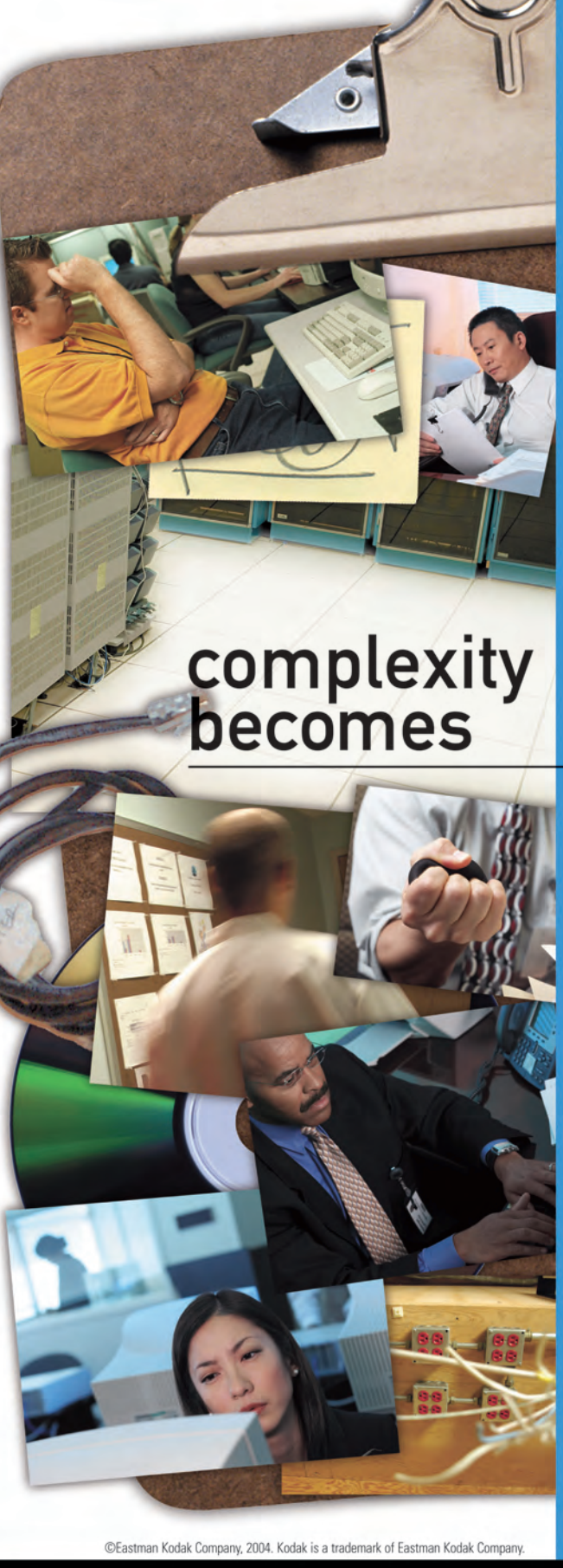

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