DEFENSIE
LA DÉFENSE

VOORRANG AAN VREDE
PRIORITÉ À LA PAIX

Clinical Indications for HBO in 2011

Part 2 – Non-emergency indications

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Principles of HBO Therapy

- Supplemental oxygen – cell survival
- Tissue hyperoxygenation – infection control
- Alternating hyperoxia / hypoxia – stimulation of tissue repair

HBO Therapy has a long history of not being taken seriously

- Hyperbaric Air
  - Henshaw 1667
  - Cunningham 1928
- Hyperbaric Oxygen
  - Chest 1987: 132 “indications” listed
  - Various internet sources

Essential questions

1. Is there a (local or generalised) lack of oxygen ?
2. Does this hypoxia cause or aggravate the disease ?
3. Can HBO improve tissue oxygenation ?
4. Is there evidence that improving tissue oxygenation improves the disease ?
5. Is there a good “risk-benefit” ratio for this particular patient ?

Oxygen as a drug

- Indications
- Dose
- Timing and duration of treatment
- Side effects
  - Claustrophobia
  - Barotrauma (> middle ear, sinus)
  - Oxygen toxicity (convulsions, myopia)
- Patient selection !

HBO as a primary therapy ?

- Decompression Sickness
- (Arterial) Gas Embolism
- BUT: no “valid” scientific evidence !
  - KCE Report 2008
  - Cochrane Reviews

HBO as an adjunctive therapy

- Level I Scientific Evidence = missing

- Reasons: multiple
  - Low number of comparable cases in variable diseases, some of (very) low prevalence
  - Low number of HBO centres, no/little financing
  - Sense of "un-ethics" to conduct RCTs

HBO as adjunctive therapy

- Treatment failure is not necessarily proof of "failure of HBO"

Accepted indications for HBO

- Based on Consensus of Evidence
- UHMS Indications Committee
  - HBOT Experts Panel
- ECHM Consensus Conference
  - Consensus between HBO Experts and Experts from non-HBO field
  - Acknowledgement of Level of Evidence

CONDITION	ACCEPTED		
	Level of Evidence		
	A	B	C
Type I			
CO intoxication		X	
Crush Syndrome		X	
Prevention of Osteoradionecrosis (dental extraction)		X	
Osteoradionecrosis (mandible)		X	
Soft Tissue Radionecrosis (cystitis)		X	
Decompression Accident			X
Gas Embolism			X
Anaerobic or Mixed Bacterial Anaerobic Infections			X
Type II			
Diabetic Foot Lesion		X	
Compromised Skin Graft and Musculocutaneous Flap			X
Osteoradionecrosis (other bones)			X
Radio-induced Proctitis / Enteritis			X
Radio-induced Lesions of Soft Tissues			X
Surgery and Implant in Irradiated Tissue (preventive action)			X
Sudden Deafness			X
Ischemic Ulcer			X
Refractory Chronic Osteomyelitis			X
Neuroblastoma Stage IV			X
Type III			
Post-anoxic Encephalopathy			X
Larynx Radionecrosis			X
Radio-induced C			
Post-vascular Pr			
Limb Re-implant			
Burns >20 % of			
Acute Ischemic			
Selected Non-he			
Pneumatosis Cystoides Intestinalis			X

Conditions where the use of HBO2 was supported by level A, B or C evidence were considered as accepted indications.

- Level A : At least 2 concordant, large, double-blind, controlled randomized studies with no or little methodological bias.
- Level B : Double-blind controlled, randomized studies but with methodological flaws; studies with only small samples, or only a single study.
- Level C : Consensus opinion of experts.

European Committee for Hyperbaric Medicine

www.echm.org
www.oxynet.org
www.achobel.be

Consensus Guidelines: are they "bad evidence" ?

- AHRQ Diabetes Guidelines 2005: 85% Consensus based !
- Consensus - based on best available evidence (if not Level I, go to next best level)
- Practical guidelines, not "proof" or "truth"
- Review periodically, according to strict methodology (systematic review)

(Anaerobic) infections

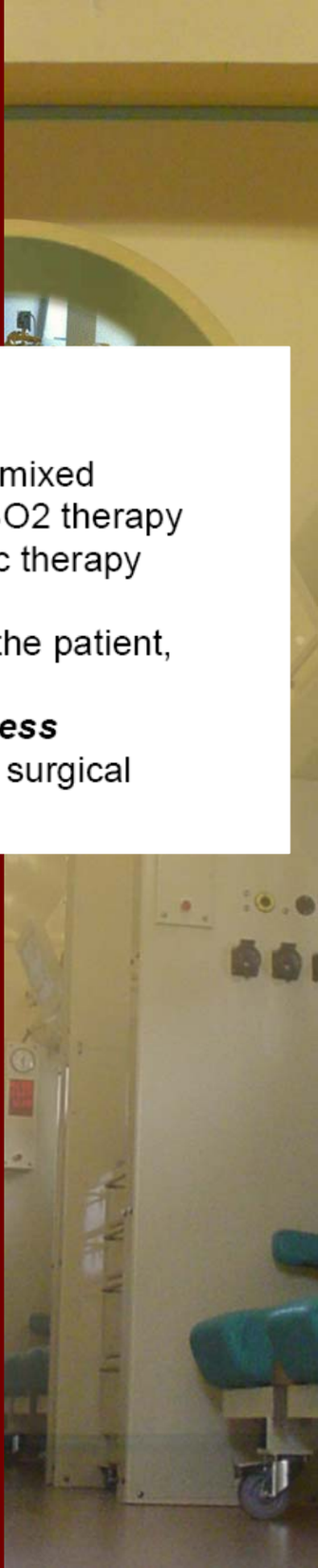
- Wide range of possible diseases
  - Clostridial Myonecrosis
  - Mixed (an)aerobic necrotising soft tissue infections
  - Deep abcesses (brain abces)
  - Mixed infections in compromised hosts (diabetic, aged, immunodepressed patients)

(An)aerobic infections

IV - Anaerobic or Mixed Anaerobic-aerobic Bacterial Infections

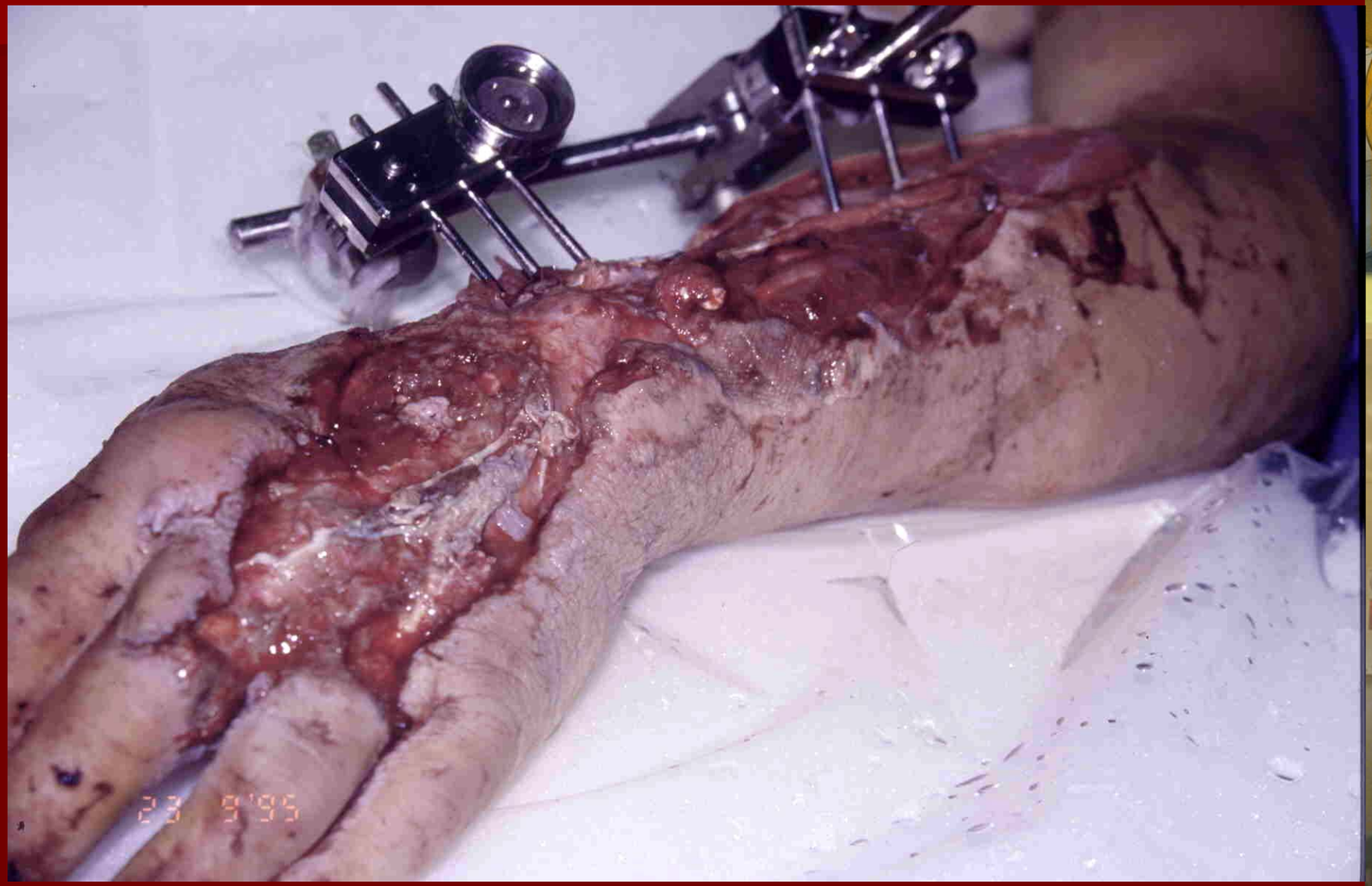
1- ***Necrotizing soft tissue infections***
   - Hyperbaric Oxygen Therapy is strongly recommended in the treatment of anaerobic or mixed bacterial necrotizing soft tissue infections (myonecrosis, necrotizing fasciitis, etc…). HBO2 therapy should be integrated in a treatment protocol comprising adequate surgical and antibiotic therapy (Type 1 recommendation).
   - The sequential order for HBO2, antibiotics and surgery is a function of the condition of the patient, the surgical possibilities and hyperbaric oxygen availability. (Type 1 recommendation)

2- ***Selected cases of organ abscess including intracranial, pleuro-pulmonary, and liver abscess***
   - Selection criteria may include failure of an appropriate conventional initial therapy, high surgical risk, compromised general condition of the patient. (Type 1 recommendation)



- Level of Evidence C : Consensus opinion of experts
- RCTs: none
- Adjunctive treatment – not compromising other optimised care

Anaerobic infections



Anaerobic infections

Wound healing

- Diabetic wounds
- Arterial insufficiency wounds
- Venous insufficiency wounds
- Radionecrosis lesions

- **Chronic hypoxia is a key factor** in the failure of wound detersion and granulation

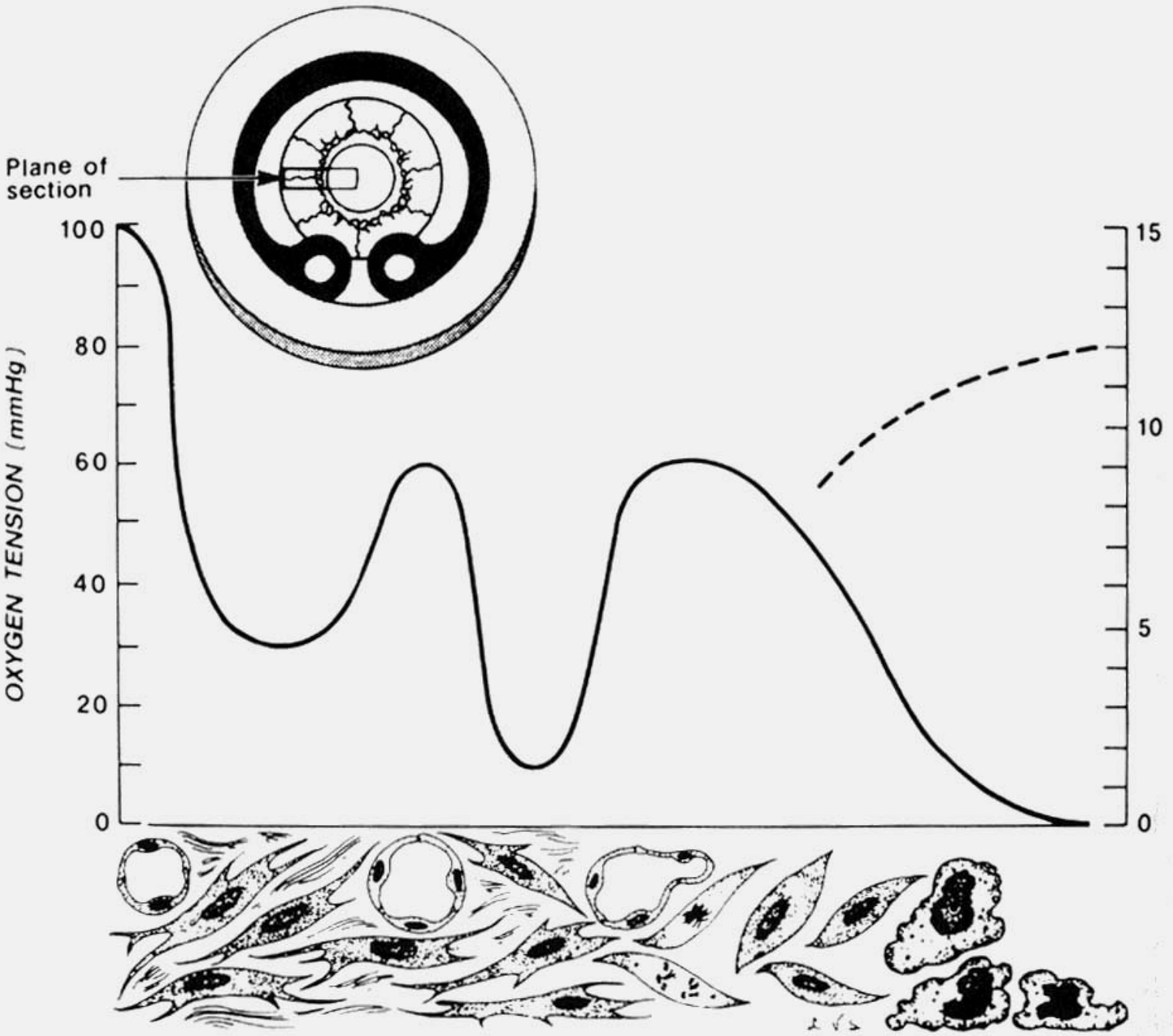


Fig. 1. Side view of the wound edge in a rabbit-ear chamber. The pO_2 profile is shown above the tissue. Note the peaks over the vessels and the long gradient down to almost zero at the wound edge. Note the lactate gradient, high in the dead space and lower toward the vasculature. This demonstrates how the central wound remains hypoxic and acidotic despite the advancing vasculature (From [24])

Chronic wounds

VII – Delayed wound healing

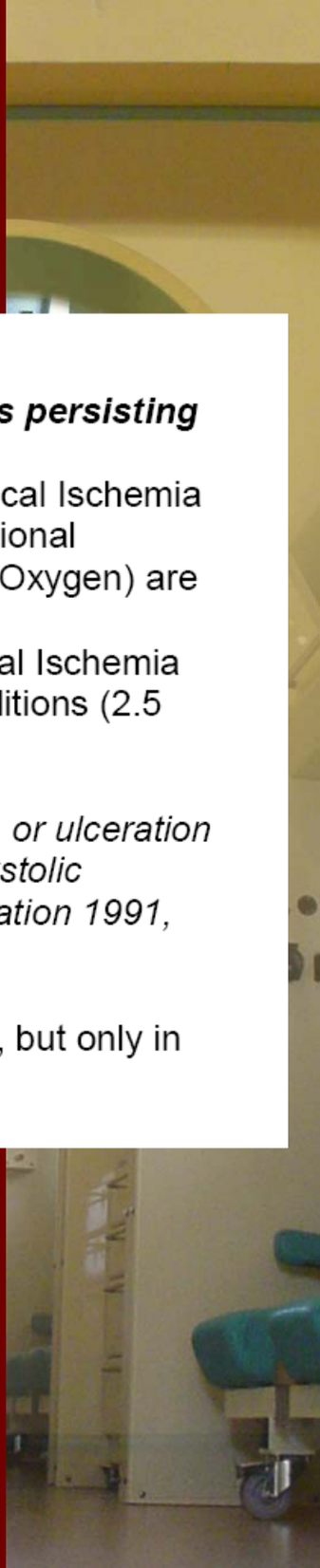
1- Ischemic lesions (ulcer or gangrene) without the possibility of revascularization, or lesions persisting after optimal revascularization:

- In the diabetic patient, the use of HBO2 is recommended in the presence of a Chronic Critical Ischemia as defined by the European Consensus Conference on Critical Ischemia *(note* 1), if perilesional transcutaneous oxygen pressures measured under hyperbaric conditions (2.5 ATA, 100% Oxygen) are higher than 100 mmHg (Type 2 recommendation)
- In the arteriosclerotic patient, the use of HBO2 is recommended in case of a Chronic Critical Ischemia *(note* 1), if perilesional transcutaneous oxygen pressures measured under hyperbaric conditions (2.5 ATA, 100% Oxygen) are higher than 50 mmHg (Type 2 recommendation)

Note 1 : Chronic Critical Ischemia:
periodical pain, persistent at rest, needing regular analgesic treatment for more than twoweeks, or ulceration or gangrene of foot or toes with ankle systolic pressure <50 mmHg in the non-diabetic or toe systolic pressure <30 mmHg in the diabetic (Second European Consensus on Critical Ischemia: Circulation 1991, 84, IV, 1-26)

2- Selected non-healing wounds secondary to inflammatory processes

- HBO2 may be used in selected non-healing wounds secondary to inflammatory processes, but only in association with optimized conventional treatment (Type 3 recommendation)



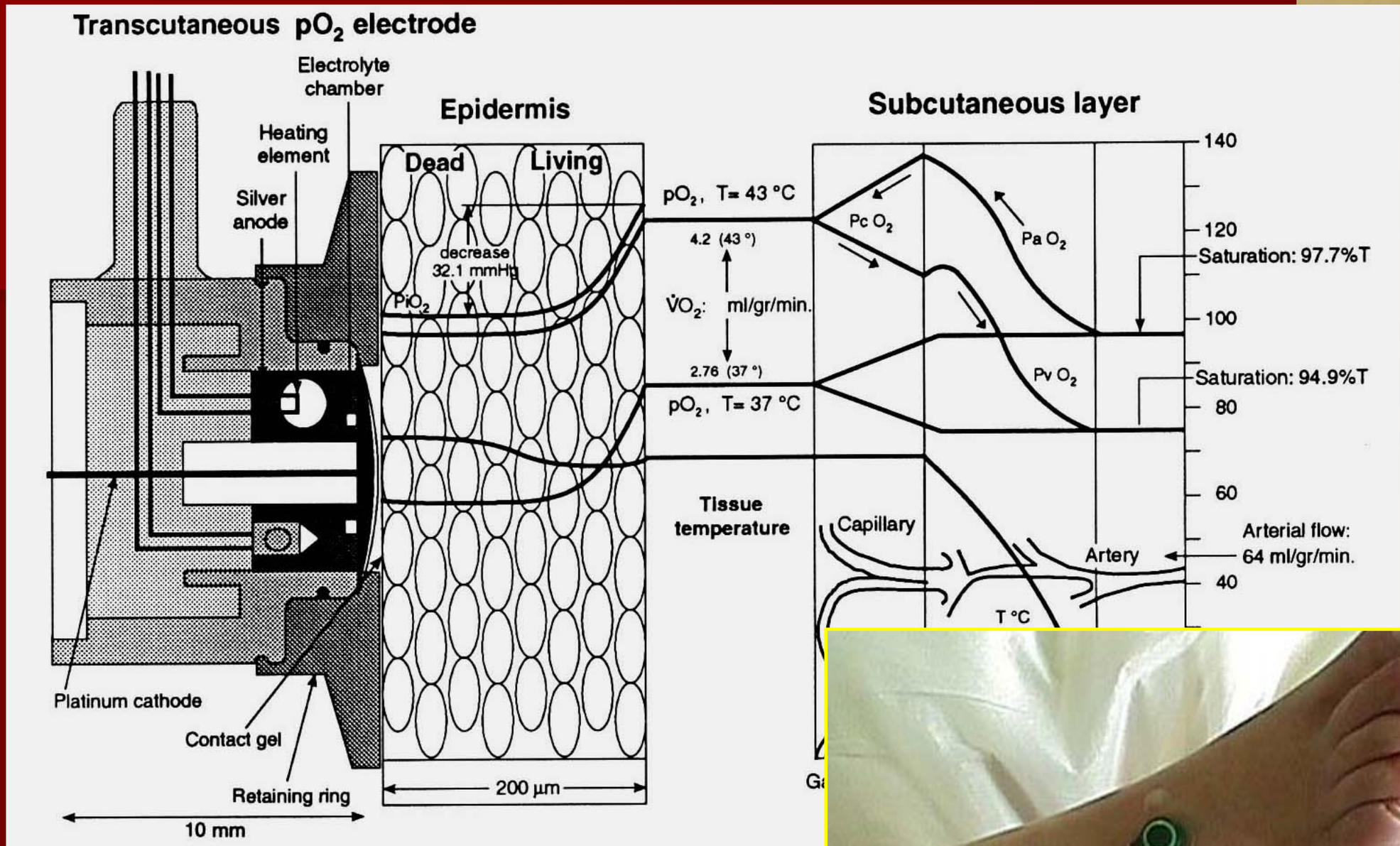
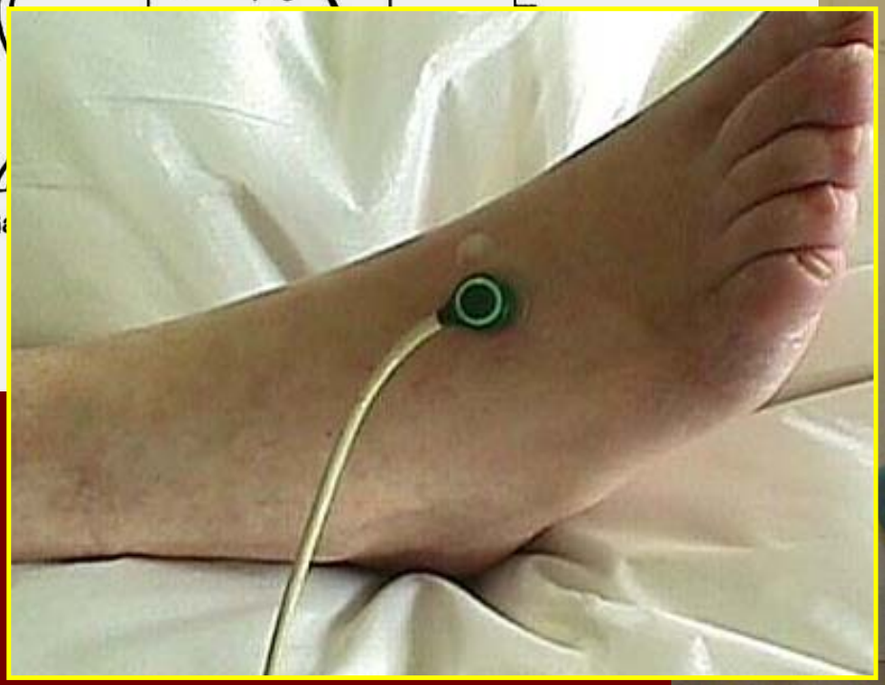
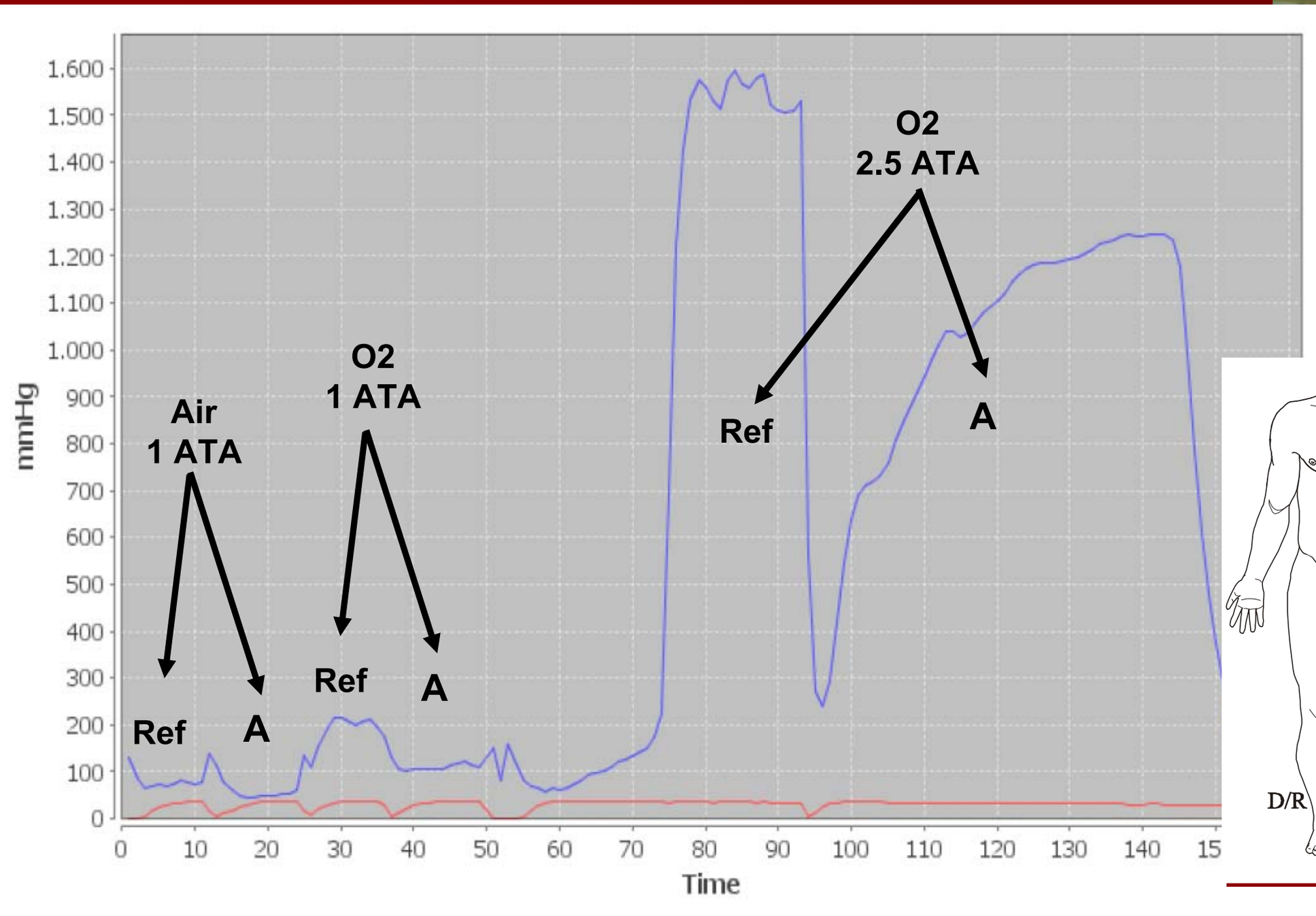
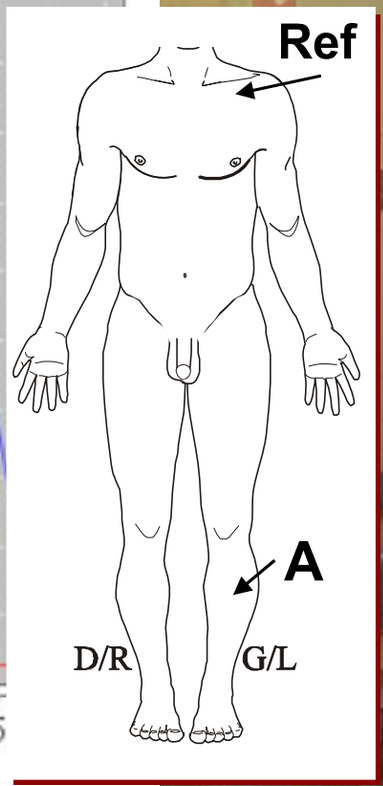


Fig. 4. Spatial distribution of pO_2 beneath the transcutanous pO_2 electrode



Transcutaneous pO_2 measurement





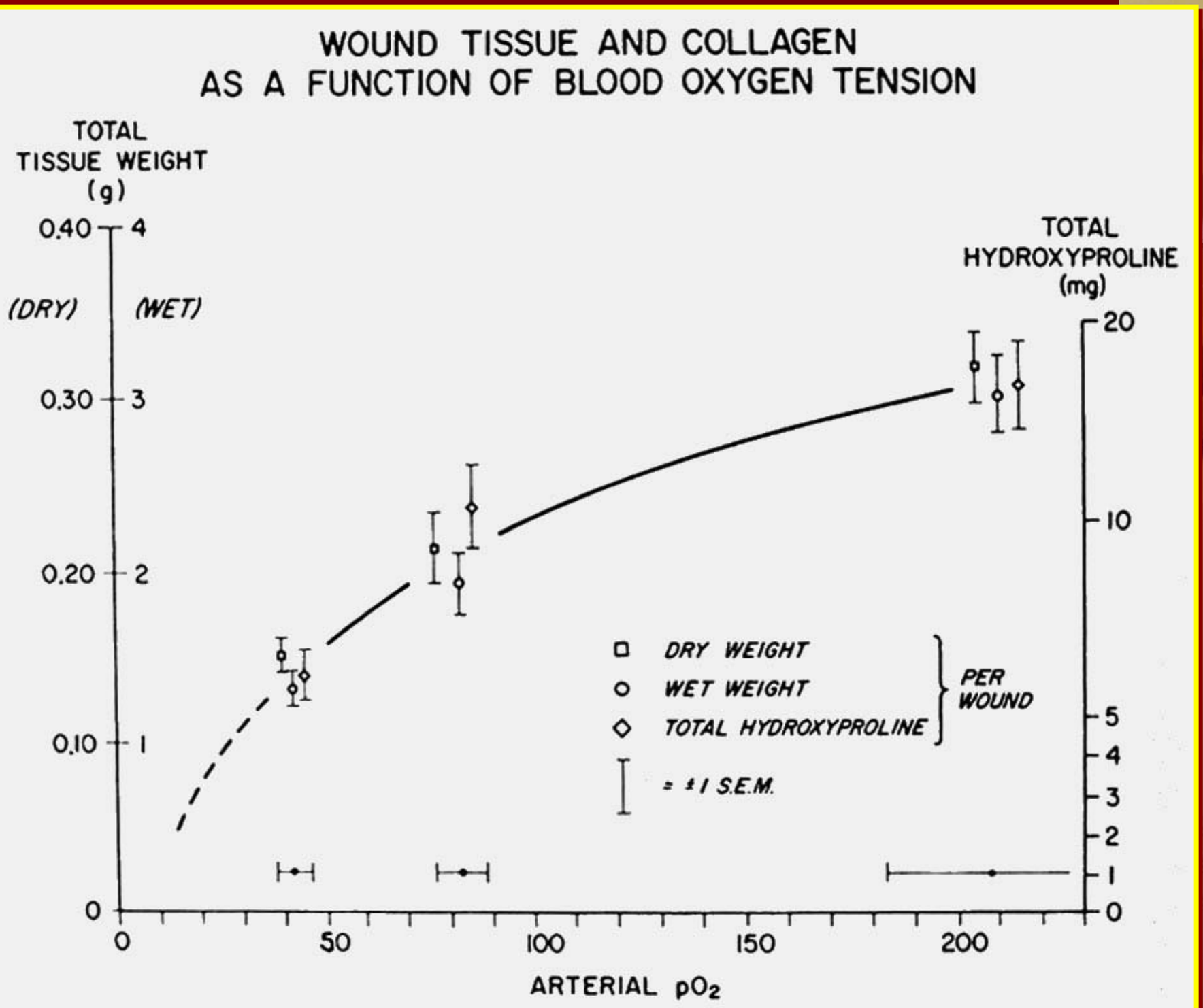
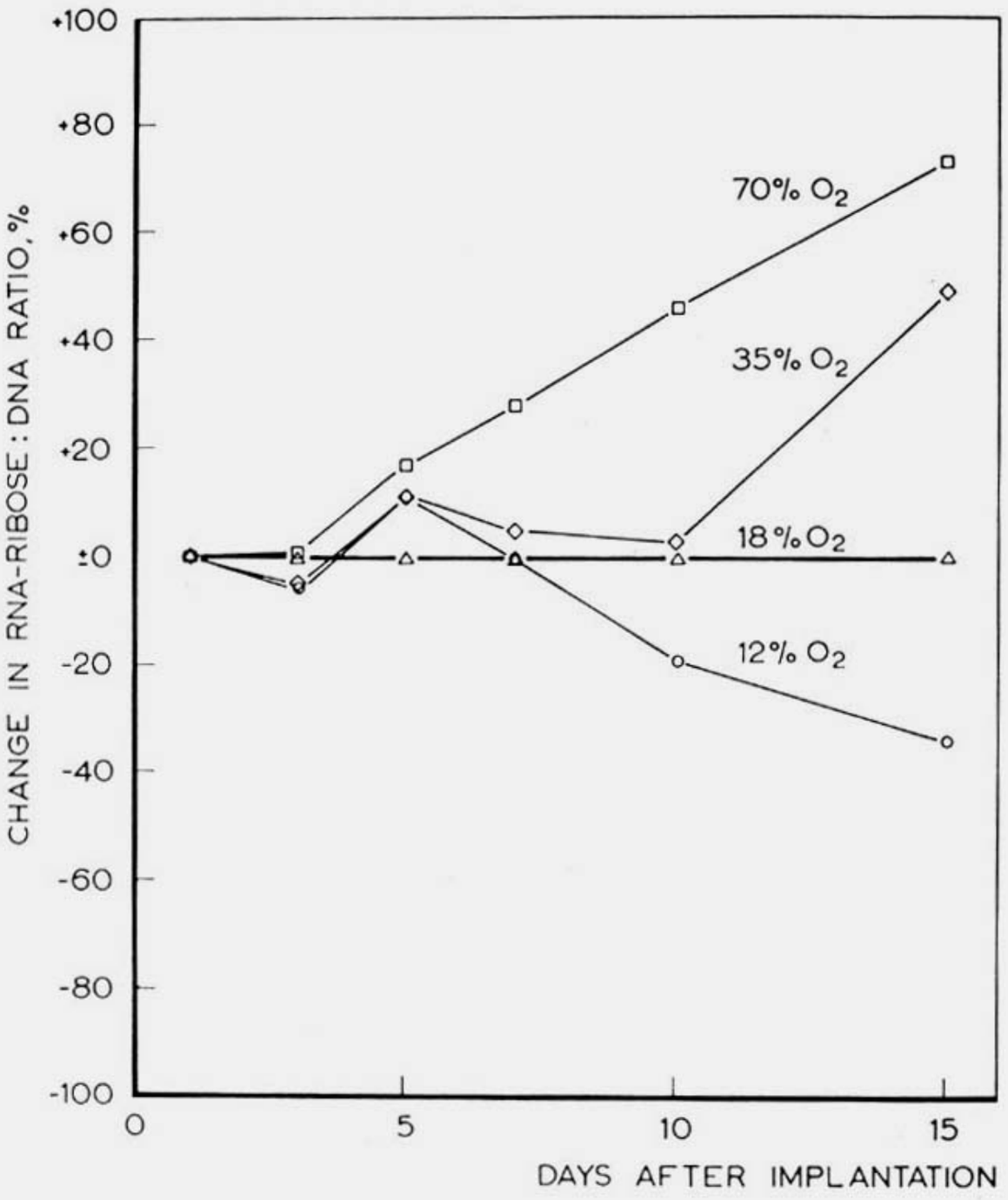


Fig. 3. Wound tissue and collagen as a function of arterial blood oxygen tension (From [22])

(Hunt et al. 1972)



Effect of changes in ambient oxygen tension on RNA/DNA ratio in experimental wounds in rats (from: Niinikoski, 1961)

Stimulation of tissue healing

- High P_aO_2 = High $P_{capill}\ O_2$
- High $P_{capill}\ O_2$ = High $P_{tissue}\ O_2$
- Alternating hyperoxia - normoxia

  - Fibroblast proliferation
  - Stimulation of granulation

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Wound healing

- HBO therapy will not change the macrovascular situation !
- Arterial insufficiency wounds : probably not a good indication if no long-term vascular improvement possible
- Diabetic, venous, radionecrotic lesions :
  - Comprehensive evaluation before HBO
  - Evaluation after 15-20 days




DD, Male 52yrs

NIDDM since 21yrs

Wound : 3yrs

Total HBO sessions: 37 (27 + 10 postop)

A: 15 days HBO

B: 30 days / graft 5d

C: 60 days

Clinical Evidence

Löndahl M. et al. : Hyperbaric Oxygenation Facilitates the Healing Rate of Chronic Foot Ulcers in Patients with Diabetes.
Diabetes Care 2010, 33: 998–1003

94 patients (Wagner 2, 3, or 4, present for >3 mths)
Randomised HBO 2.5 ATA 90min vs. placebo air.

ITT analysis - complete healing at 1-yr follow-up :
HBO : 25/48 (52%) vs Placebo Air : 12/42 (29%) (P<0.03)

Sub-analysis - patients with >35 HBO sessions :
HBO : 23/38 (61%) vs Placebo Air : 10/37 (27%) (P<0.009)

Conclusion: HBO facilitates the healing of chronic foot ulcers in selected diabetic patients
NNT: 4.2 patients for 1 non-healing ulcer (ITT analysis)

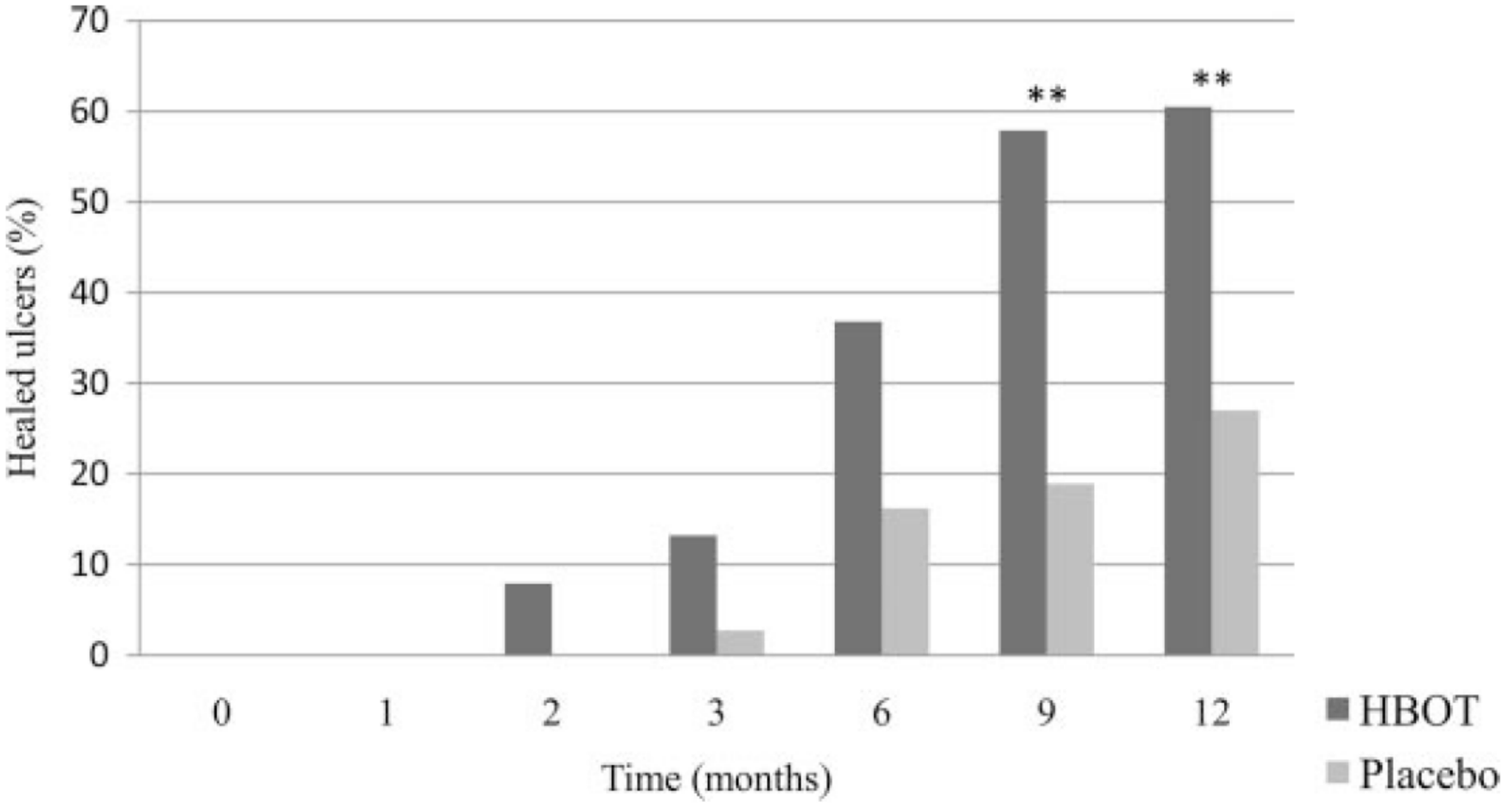


Figure 2—Healing rates in patients given treatment with hyperbaric oxygen therapy (HBOT) as compared with hyperbaric air (placebo). *P • 0.05; **P • 0.01.

Löhndal M. et al. Diabetes Care 2010

Pharmaco-economics, anyone ?

Roeckl-Wiedmann I, Bennett M, et al. : Systematic review of hyperbaric oxygen in the management of chronic wounds. *Br J Surg.* 2005 Jan;92(1):24-32

…pooled analyses of predetermined clinical outcomes of randomized controlled trials involving the use of HBOT for chronic wounds were performed.

…five trials on diabetic ulcers (118 patients) **suggested a significant reduction** in the risk of major amputation with HBOT (RR: 0.31; CI 0.13 to 0.71) with a NNT of 4 (CI 3 to 11).

More pharmaco-economics

Guo S, Counte MA, et al. : Cost-effectiveness of adjunctive hyperbaric oxygen in the treatment of diabetic ulcers. *Int J Technol Assess Health Care* 2003;19(4):731-7.

…that the incremental cost per additional quality-adjusted life year (QALY) gained at years 1, 5, and 12, was USD 27.310, USD 5.166, and USD 2.255, respectively.

…that HBO2 therapy in the treatment of diabetic ulcers is cost-effective, particularly based on a long-term perspective.

More pharmaco-economics ?

Health Technology Report 2007 - Adjunctive Hyperbaric Oxygen Therapy for Diabetic Foot Ulcer: An Economic Analysis (*Canadian Agency for Drugs and Technology in Healthcare (CADTH – www.cadth.ca*)

…lower proportion of major LEAs reported in patients who received adjunctive HBOT (11% versus 32%).
Wound healing occurred in 83% patients who had HBOT, compared with 43% of the controls.
The proportion of patients with wounds remaining unhealed, but who did not require amputation was 6% (HBOT) and 24% (controls).

…adjunctive HBOT for DFU is more effective than standard care alone. Based on available data, adjunctive HBOT for DFU is cost effective compared with standard care.

Final Pharmaco-economics

Rychlik R - Inst. of Empirical Health Economics (GE)

Basis	**Faglia et al. 1996 : 68 patients (35 HBO, 33 ctl)**	
Effectiveness (avoiding major amputations)	**HBO**	**0.91**
	Ctl	**0.66**
Cost (endpoint = "retirement")	**HBO**	**22500 EUR/ success**
	Ctl	**26000 EUR/success**
Reverse calculation	**HBO cost-efficient > 0.82**	

Importance of patient selection !!

Rychlik R. : HBO Therapie - Kosten/Effektivitäts Analyse. Expertenforum: HBO im Gesundheitsweisen. Germany 14 May 1997: 37-41

Sudden deafness

- 20-30/100.000 cases/yrs
- Rapid (3 days) > unilateral hearing loss
- Viral Upper Respiratory Tract infection
- Vertigo, nausea
- Tinnitus

Sudden deafness

- Vascular ? thrombosis, emboli, bleeding, vasospasm, rheological
- Viral infection ? echovirus, adenovirus, mumps, coxsackie virus
- (Baro)Trauma ?
- Auto-immune disease ?
- Retrocochlear tumor ?

Sudden deafness

- Spontaneous recovery : up to 65%
  Weinaug, 1984
- Corticosteroids : up to 78% recovery
  Wilson et al., 1980

- Haemodilution if Hb>14g/dl or Hct>44%
  Desloovere, 1988
- Antiviral medication, magnesium, Gingko Biloba, intratympanic corticosteroids, Ggl Stellatum Block… ns

Sudden Deafness

XI - Sudden Deafness

- Multiple treatment modalities have been proposed for sudden deafness with no high level evidence for any of those. HBO2 remains recommended in sudden deafness (Type 2 recommendation) until the results of the on-going European randomized controlled study are published.

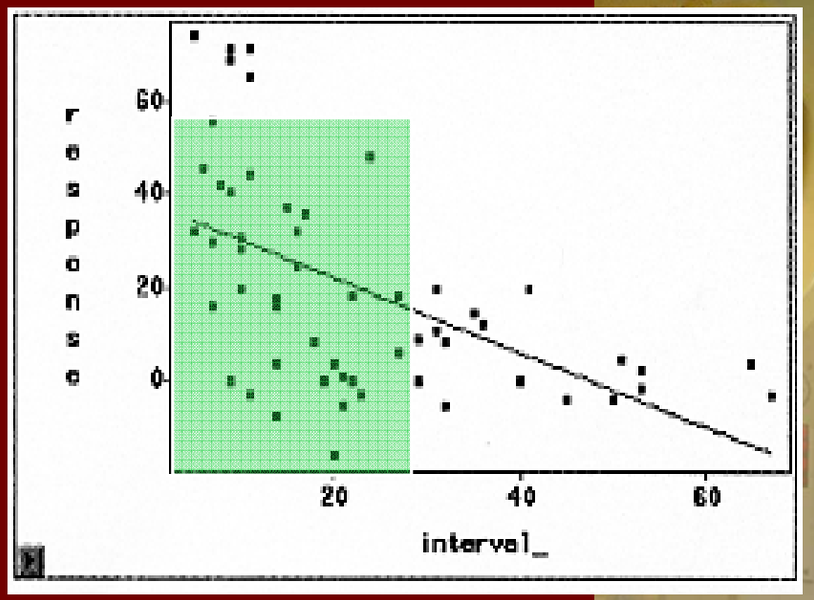
- Level of Evidence C
  - Retrospective studies
  - Comparative studies
- Spontaneous recovery rate = high
- Prospective randomised trial ongoing (COST B14) www.oxynet.org

Sudden deafness

- Treatment as soon as possible
  - Intuitively better
  - « shotgun therapy »
  - Impossible to « prove » in EBM
- Treatment after failure of medical therapy
  - Spontaneous recovery after 10 days of corticosteroids = (quasi) nihil
  - Loss of viable cells due to excessive delay ?

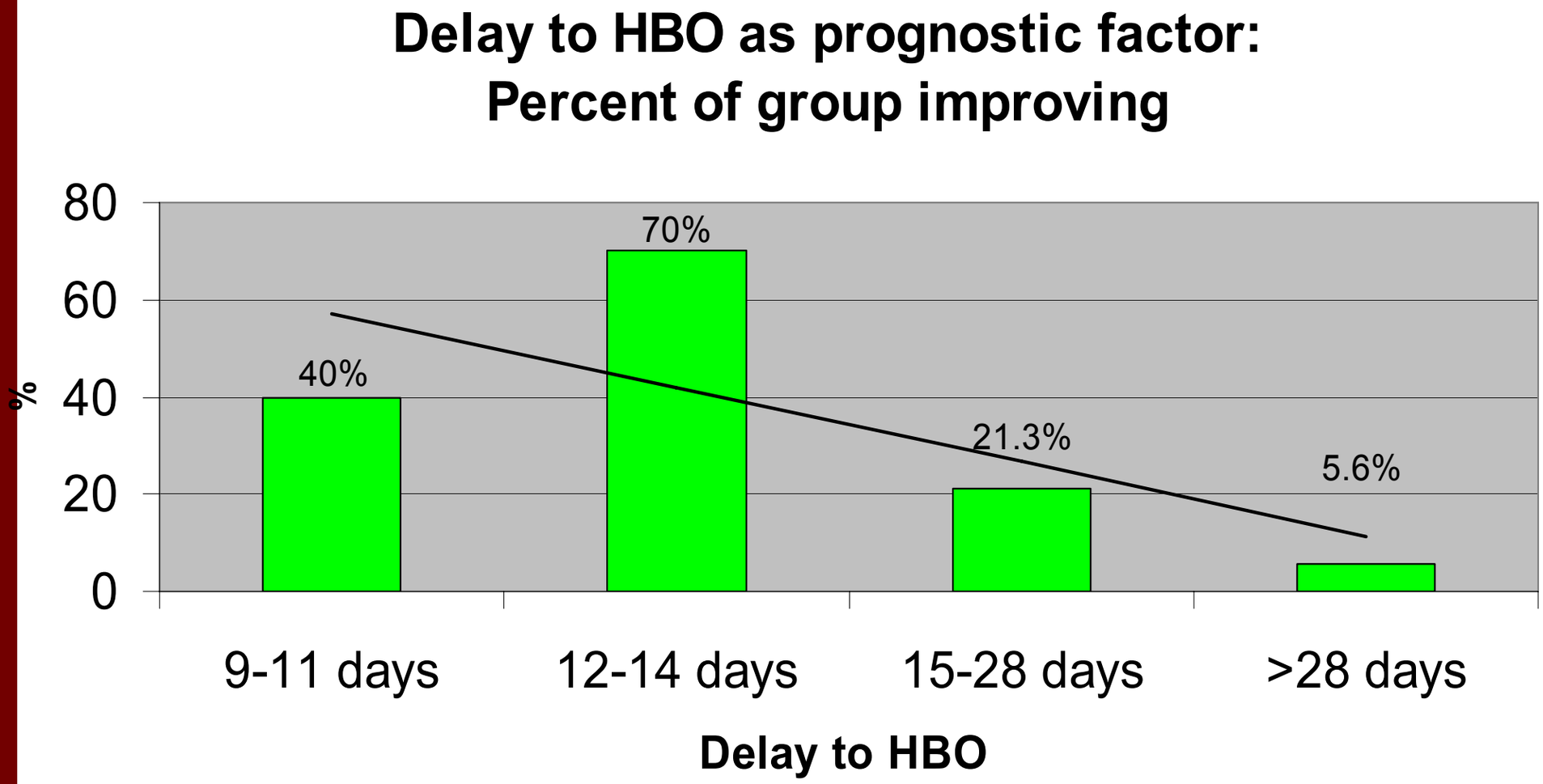
Sudden deafness

- Patient selection
  - maximum delay before HBO :
    - 14 days ?
    - 4 weeks ?



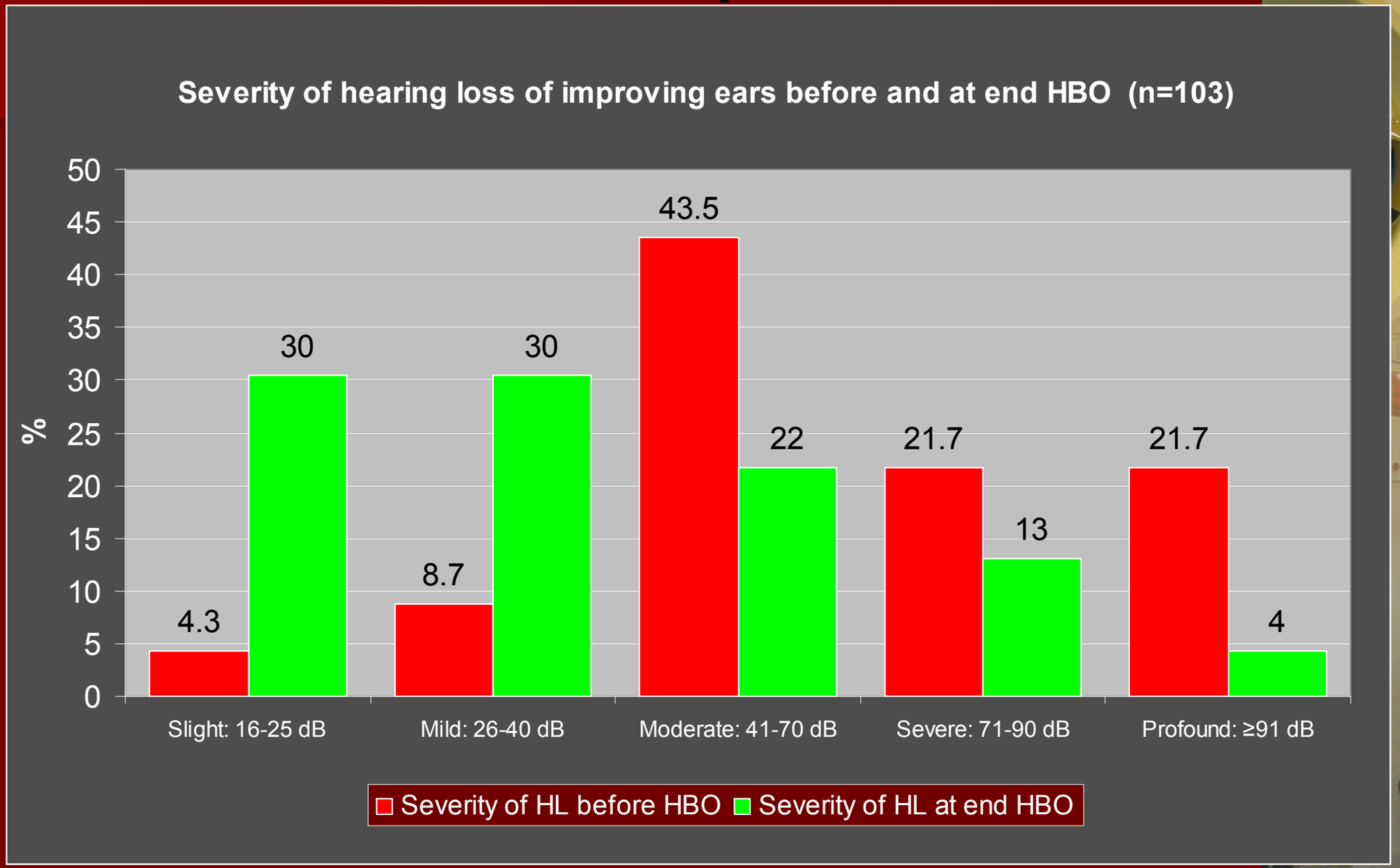
  - Trial of « less invasive therapy » warranted
- HBO: 10 sessions (10 days ?)

Analysis 2010



Caers et al, 2011

Clinical improvement



Caers et al, 2011