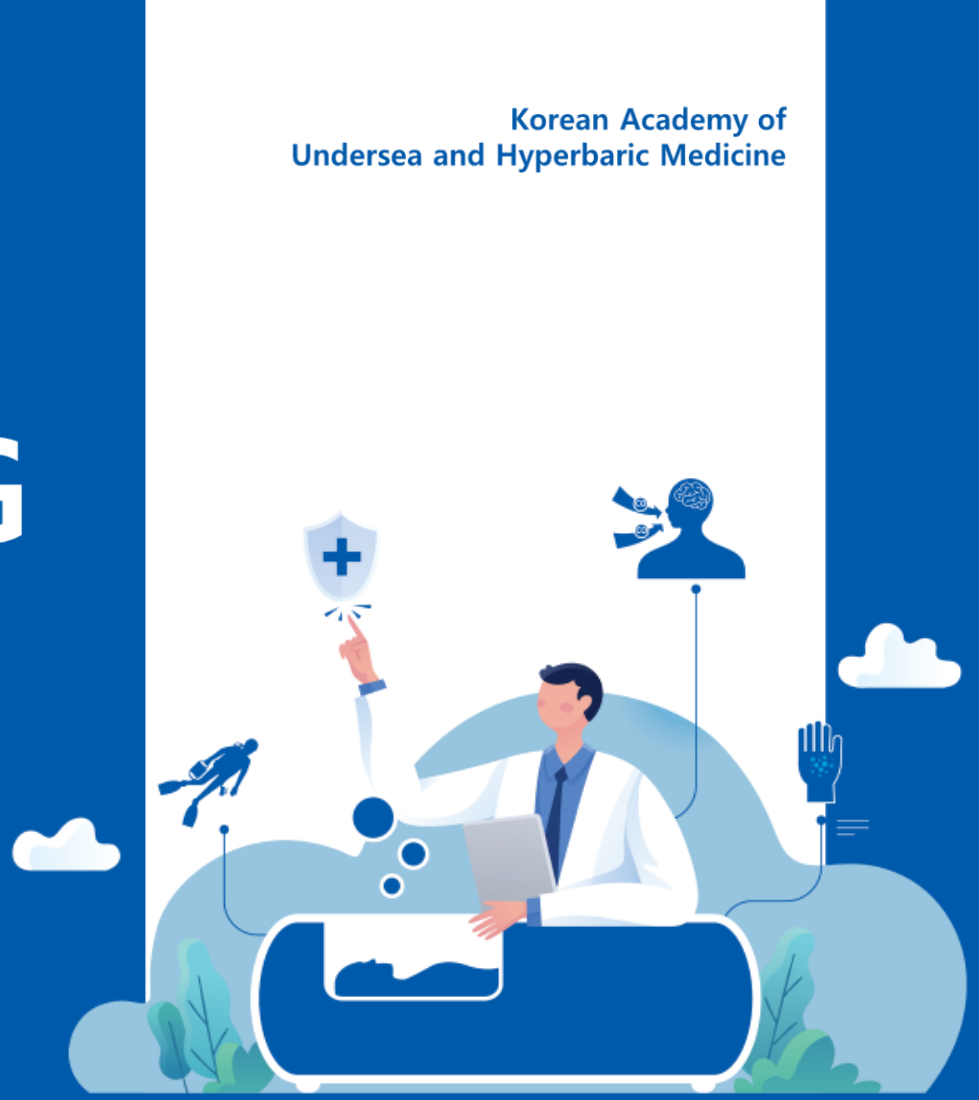
HBOT
WOUNG HEALING

2021.9.10



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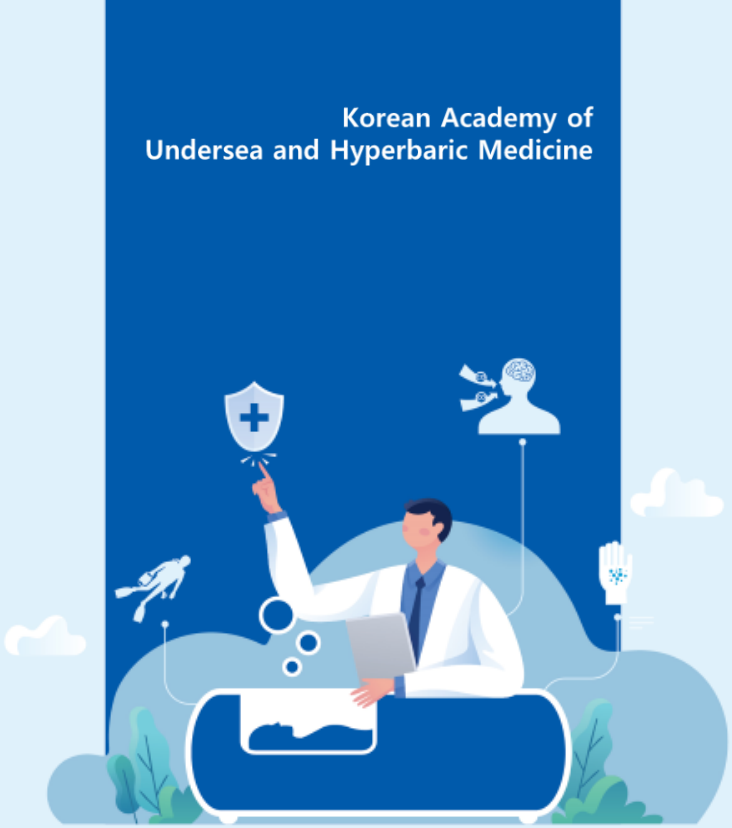
HBOT 기전



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Hyperbaric Oxygen Therapy (HBOT)란?

- UHMS 정의 – 1.4ATA 이상의 **압력**이 가해진 챔버 안에서, **100% 산소**로 호흡하는 치료
- **Hyperoxygenation** : Hemoglobin이 아닌 **Plasma와 Tissue fluid**에 녹아 있는 산소양이 증가

  A-V O2 difference 5vol% 까지 상승 -> 혈액이 공급되지 않는 상태에서 조직을 유지

Vol%, Blood 100ml에 녹아 있는 Oxygen의 양 (ml)

	Hemoglobin carried O2	Plasma carried O2	Total O2 content
1 ATA (Air)	19.5	0.5	20.0
2 ATA	19.5	**5.0** X 10	**24.5**
3 ATA	19.5	**7.5** X 15	**27.0**

Mechanisms of HBOT

Primary mechanism	Secondary mechanism
Hyperoxygenation Pressurization (Bubble reduction)	Vasoconstriction Host response Microbiological Effect Impede Reperfusion Injury Gas Washout

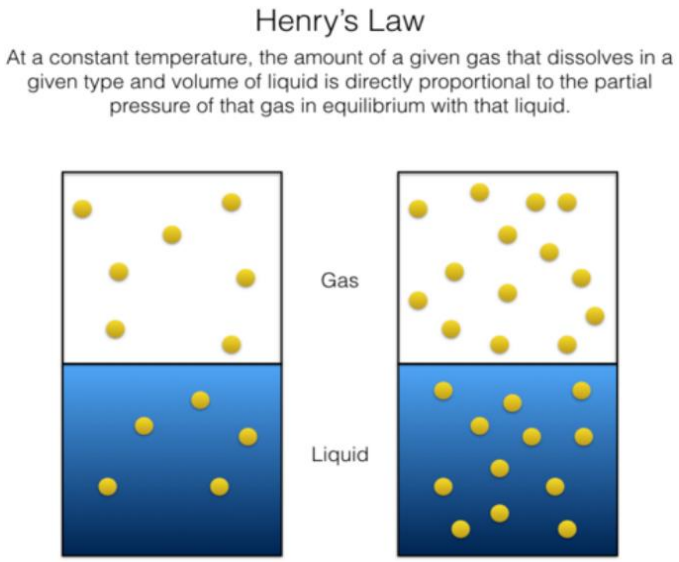
즉각적 효과

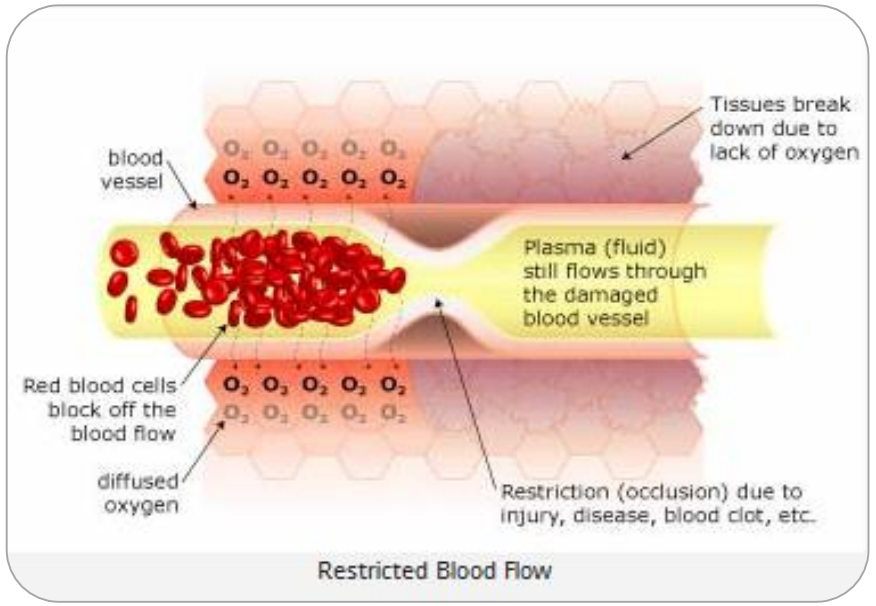
고농도 산소 효과의 누적

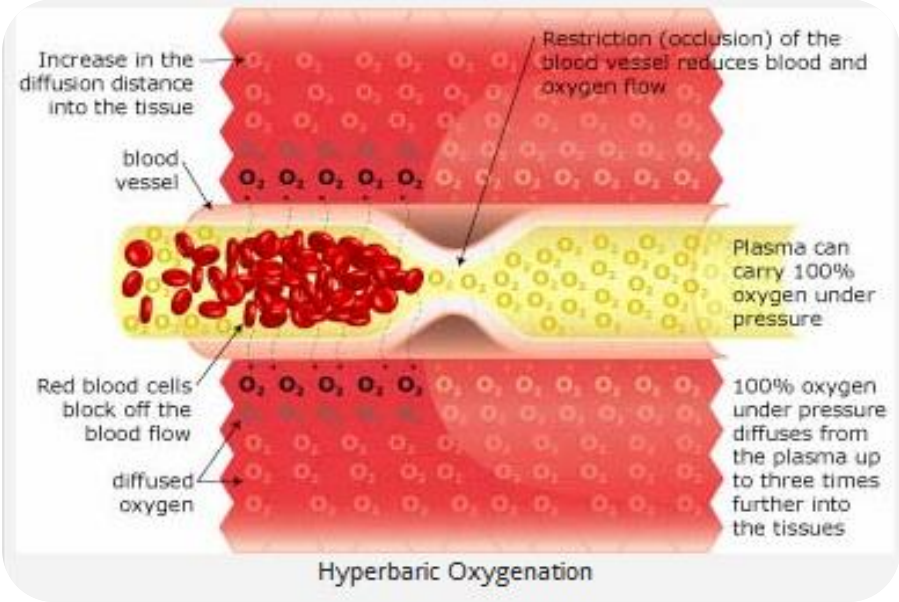
Wound care를 설명

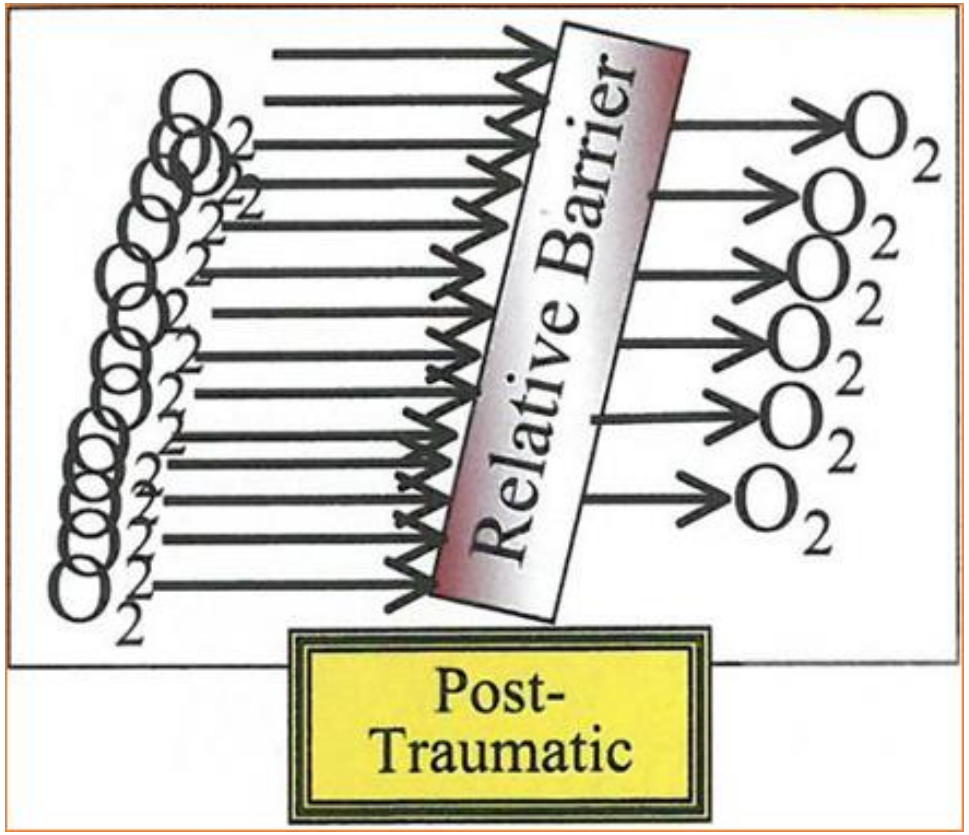
Hyperoxygenation (Primary mechanism)

- 고압환경에서 100% 산소를 공급, Plasma와 Tissue fluid의 산소양을 증가
- 모세혈관에서의 산소 확산률 증가 -> 다양한 barrier를 쉽게 통과 – 2ATA 환경, 기존 대비 3배 확산률





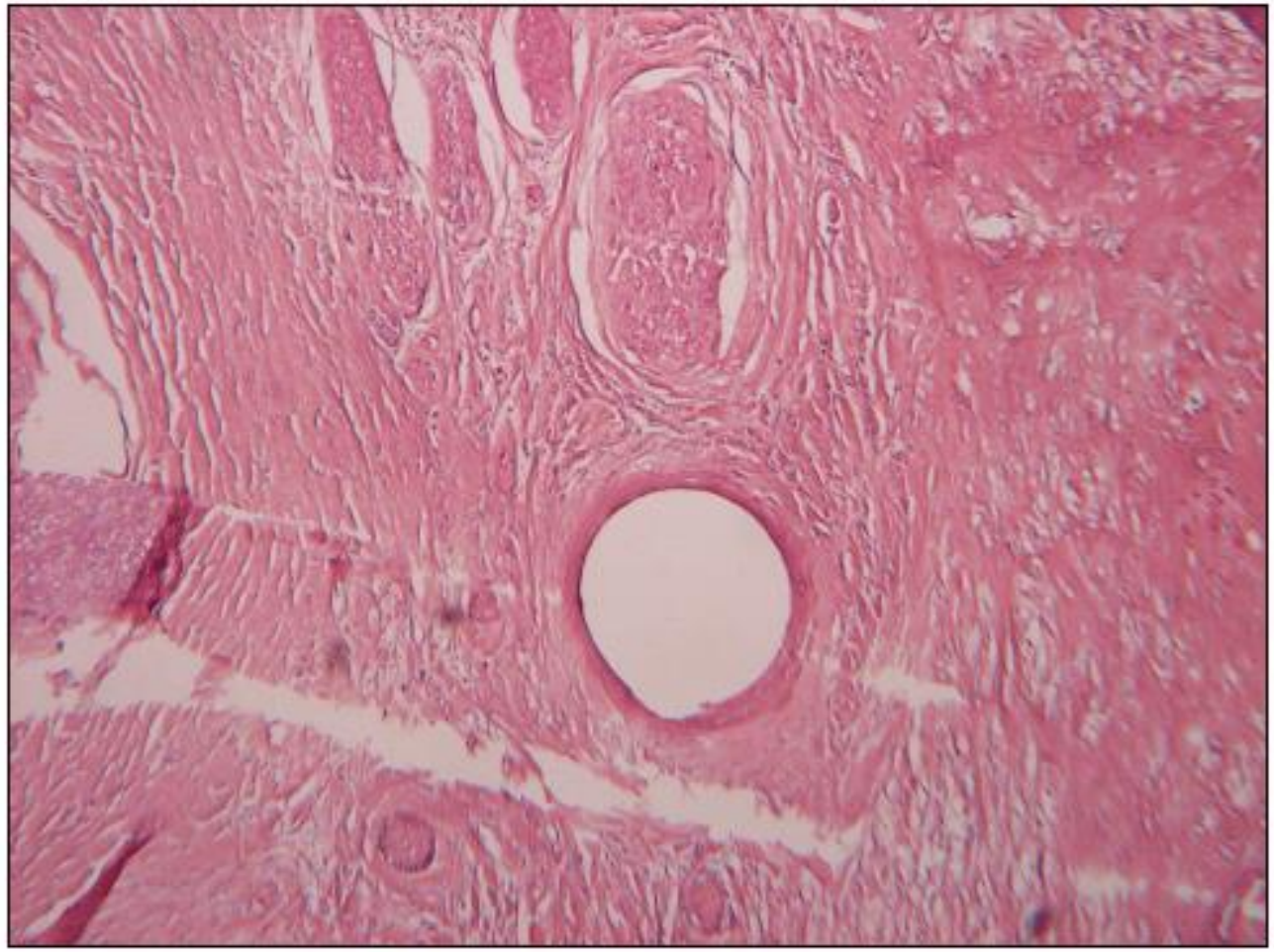




1/2

3H Tissue

- Hypovascular
- Hypocelluar
- Hypoxic



Hyperbaric medicine practice 4th edition

Wound Healing

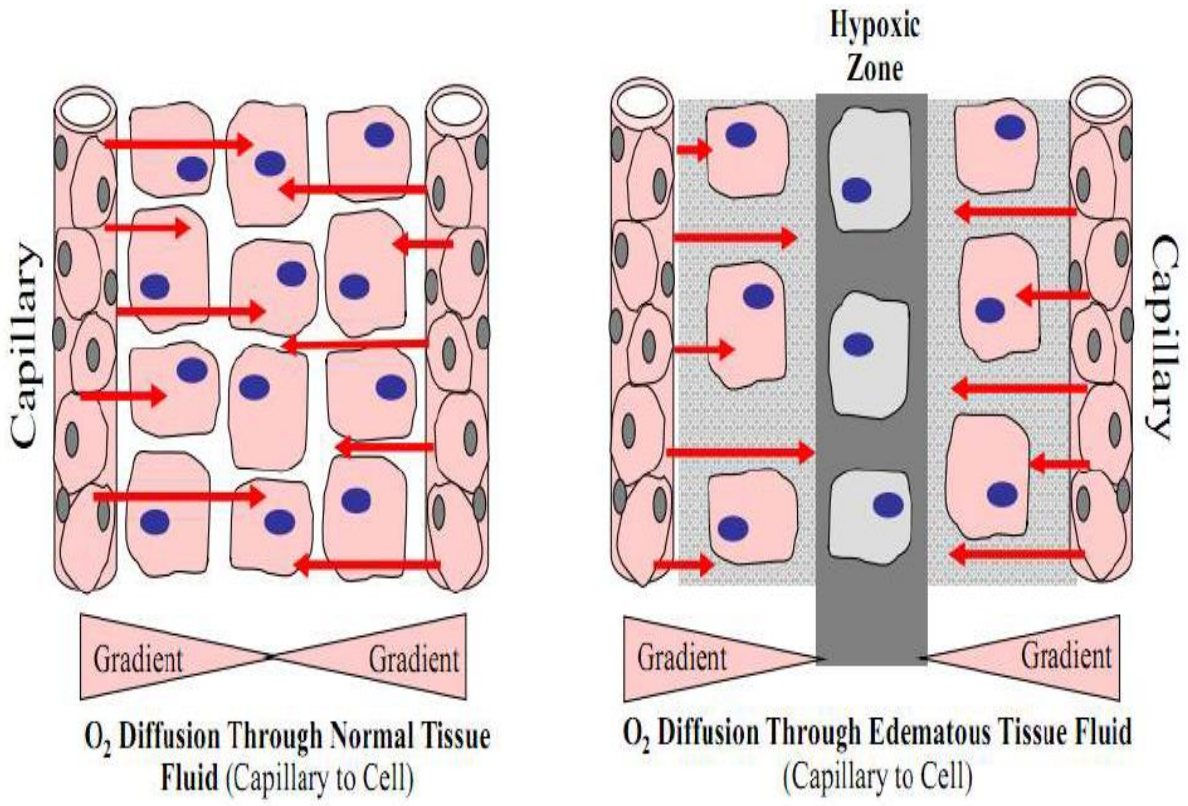
- Control contamination/infection
- Resolution of inflammation
- Regeneration of connective tissue
- Neovascularization
- Wd contration
- Resurfacing

Depend on

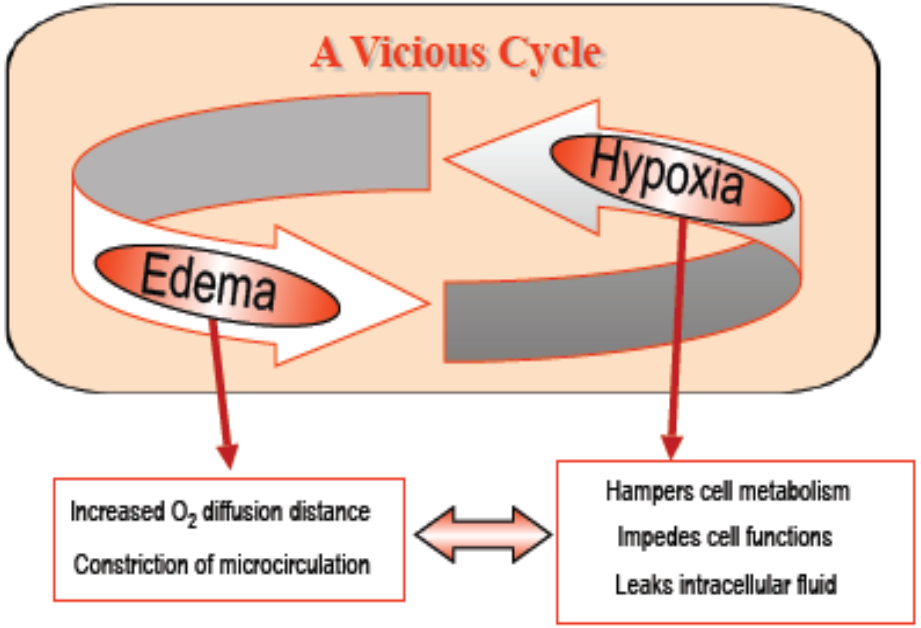
* **perfusion**
* **oxygen availability**

Vasoconstriction (Secondary mechanism)

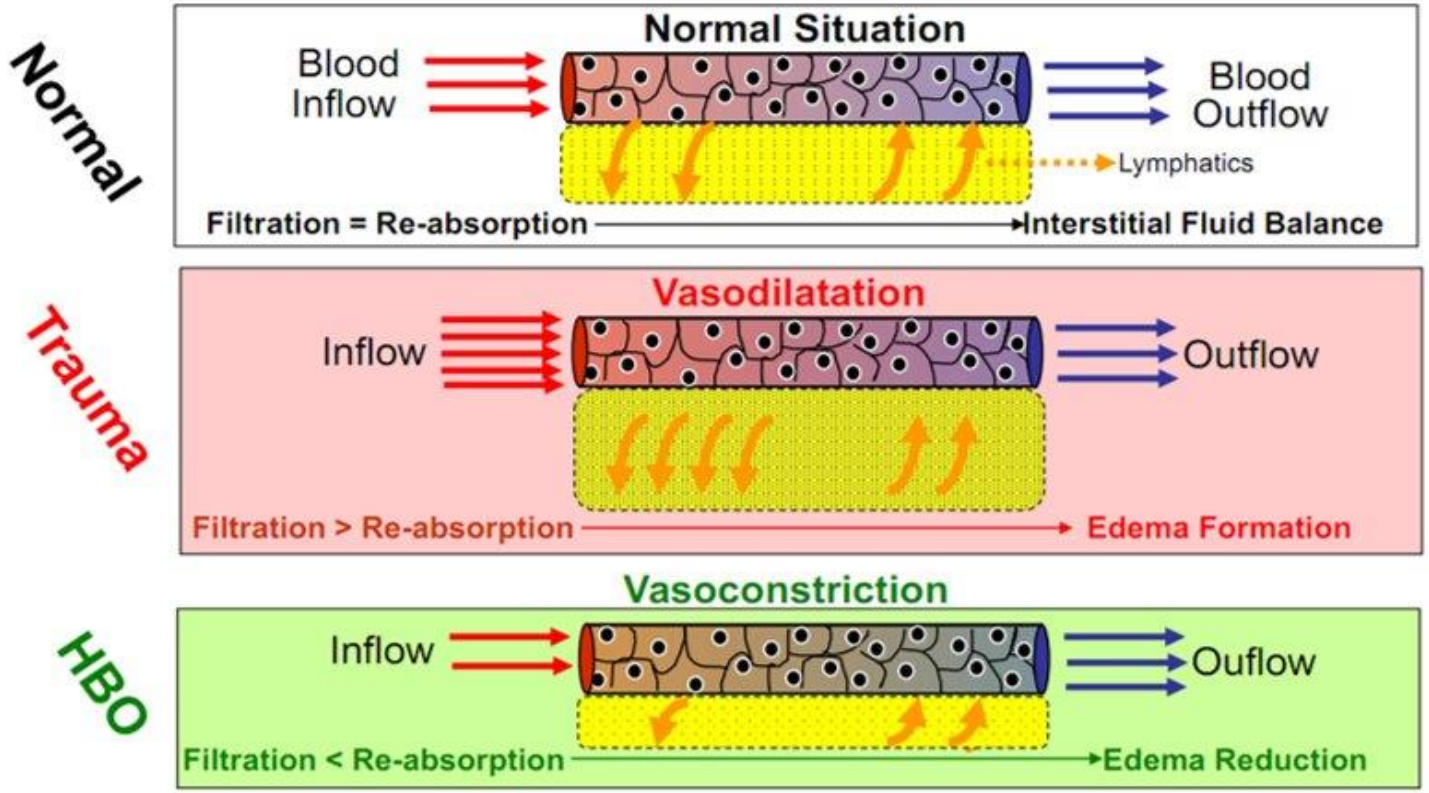
- 혈관 수축 -> Edema reduction
- 혈류량이 감소하더라도 Plasma, tissue내의 O2 농도는 높게 유지 -> Hypoxiczone의 O2 diffusion



Acute wound


A Vicious Cycle
Hypoxia
Edema
Increased O_2 diffusion distance
Constriction of microcirculation
Hampers cell metabolism
Impedes cell functions
Leaks intracellular fluid

Vasoconstriction



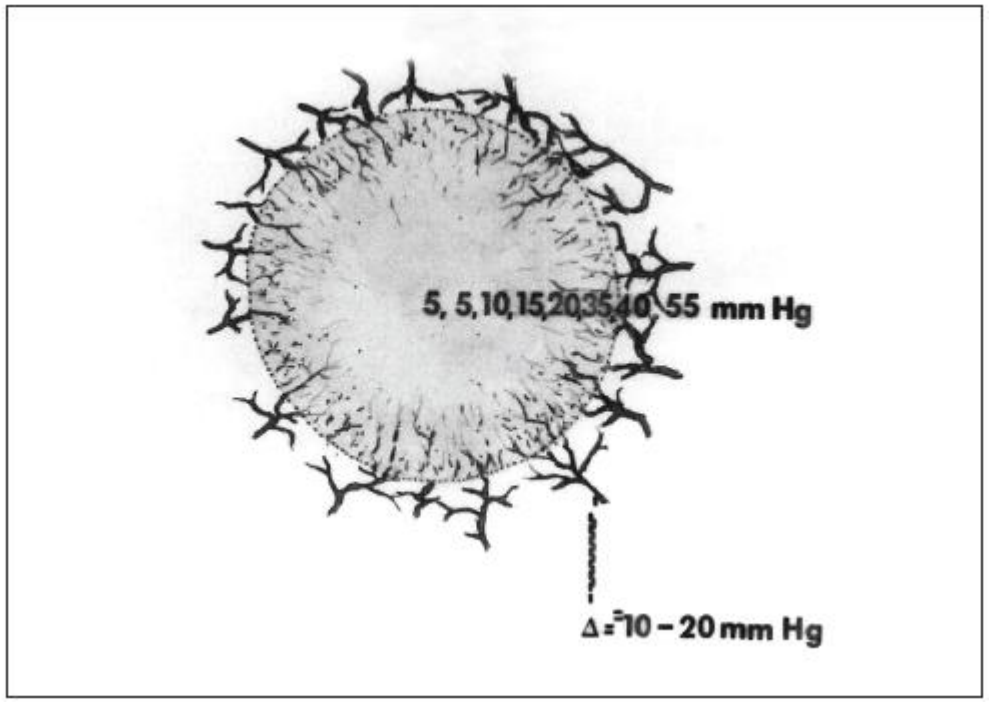
20%

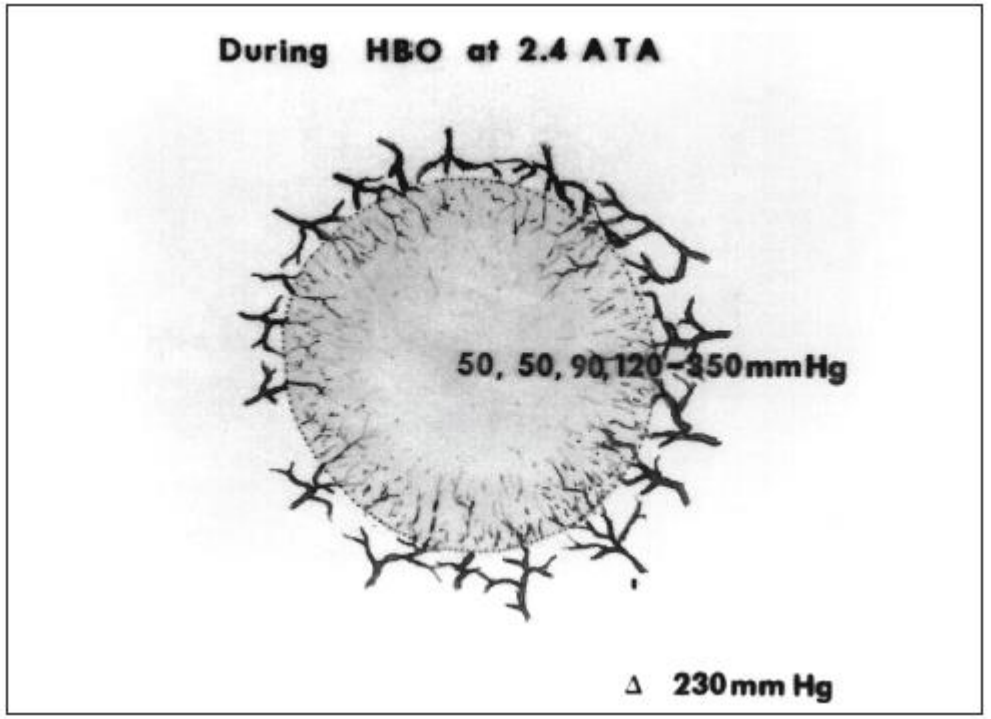
Compartment syndromes

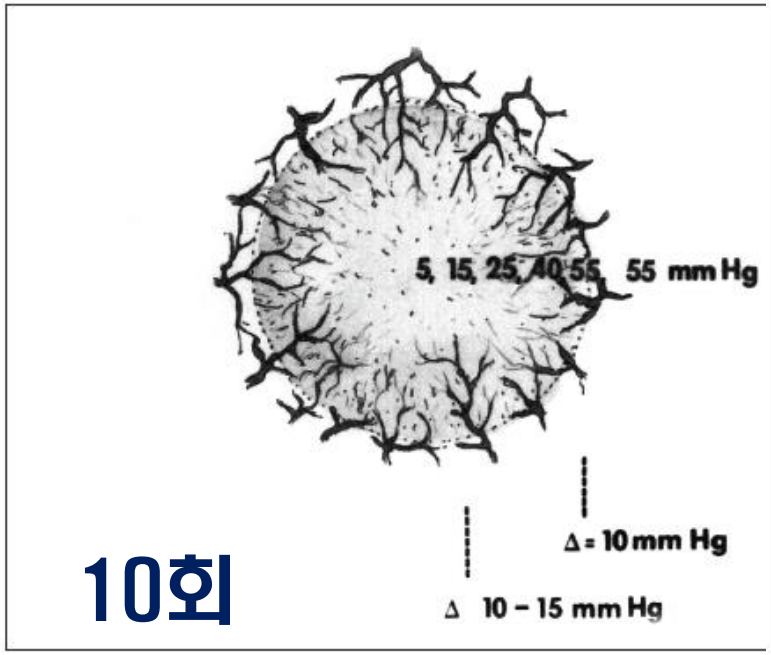
Host response (Secondary mechanism)

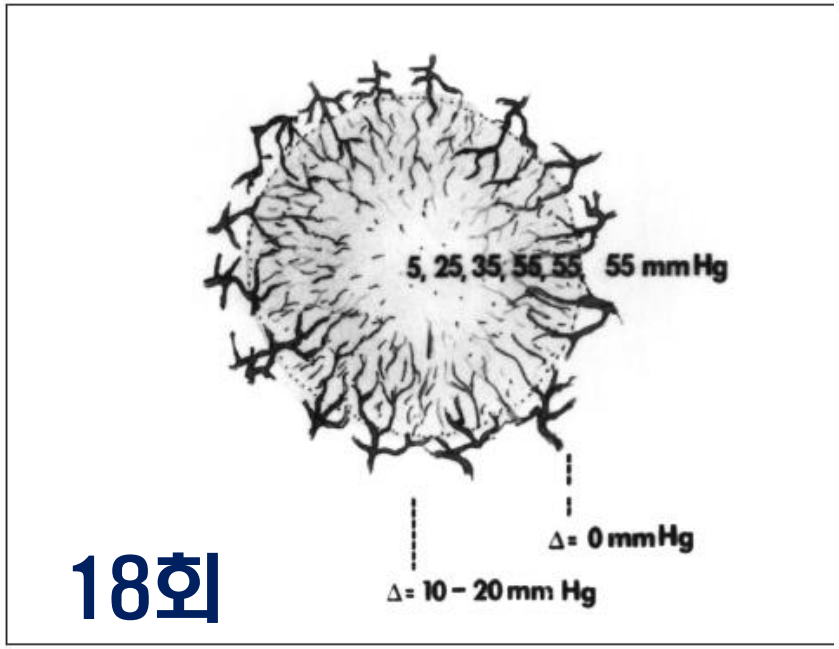
3 oxygen dependent host cells related to wound healing and infection control

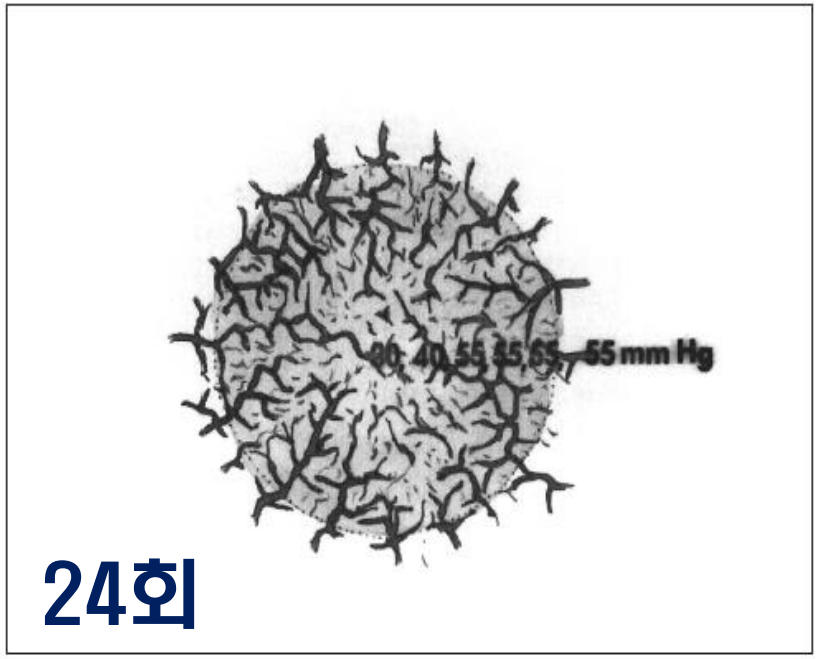
- **Fibroblast (associated with angiogenesis)**
- **Neutrophils (WBC oxidative killing)**
- **Osteoclasts**


5, 5, 10, 15, 20, 35, 40, 55 mm Hg
Δ ≈ 10 – 20 mm Hg


During HBO at 2.4 ATA
50, 50, 90, 120 – 350 mm Hg
Δ 230 mm Hg







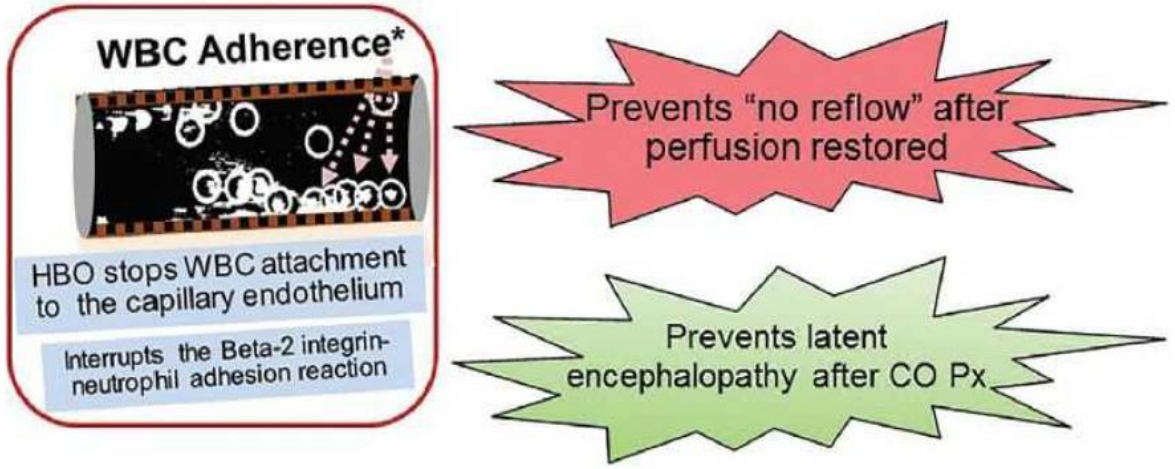
Hyperbaric medicine practice 4th edition

Microbiological effects (Secondary mechanism)

- Bacteriostatic and bacteriocidal effects
  - ≫Clostridial organisms (no killed but stop multiplying)
  - ≫Anaerobic streptococcus and peptostreptococcus are killed by hyperoxic condition
  - ≫Bacteroids species killed by hyperoxia
  - ≫Fungal infection by actinomyces species
- Cessation of the endotoxin formation produced by clostridial organisms
- Toxin inactivation has been best appreciated with the theta toxin produced by clostridial organisms
- Additive effect with certain antibiotics
  - ≫Aminoglycosides
  - ≫Amphotericin
  - ≫Possibly vancomycin

Mitigation of reperfusion injury

- Interrupt the neutrophil adherence to the endothelium by beta-integrin attachment mechanism inactivation
- Extreme hyperoxia environment triggers to generate oxygen free radical scavengers (superoxide, peroxidase)



LEGEND: Mitigation of neutrophil adherence to the capillary endothelium sensitized by hypoxia reduces/eliminates the release of toxic O_2 radicals (peroxides and superoxides) that cause the harmful effects of the reperfusion injury.

In addition, this prevents the cascade of reactive oxygen species with nitric oxide (NO)--in hypoxic environments--from forming highly toxic degradation products such as peroxynitrite (-OON).

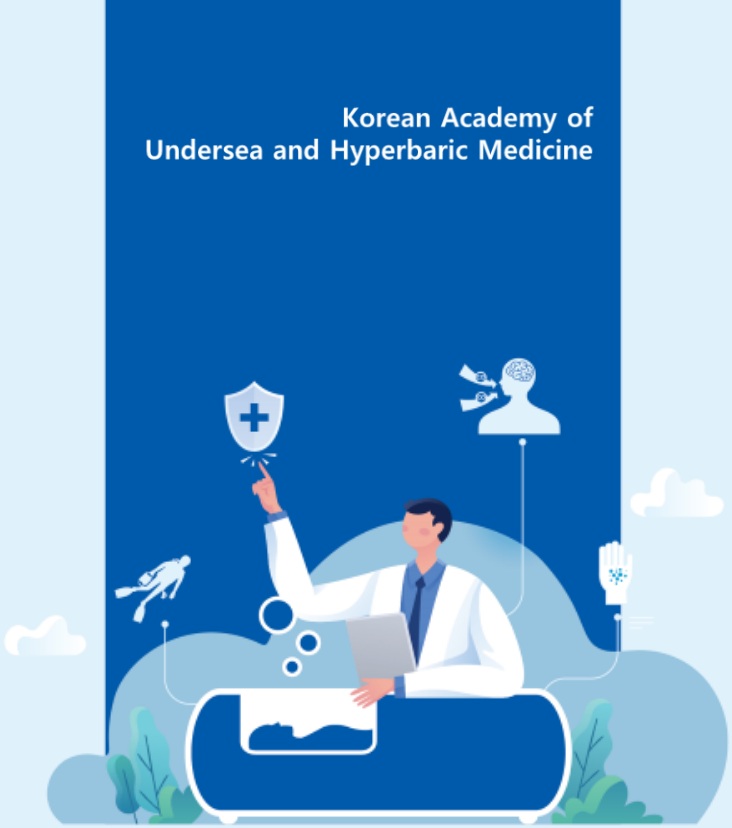
NOTES & KEY: *Neutrophils adhering to the sensitized capillary endothelium are so indicated by white circles around them (Zamboni[10]); CO Px = Carbon monoxide poisoning, HBO_2 = Hyperbaric oxygen, WBC = White blood cell

Figure 35. Morphology of the reperfusion injury and roles of HBO_2 in mitigating its effects.

- Recommend starting HBO as soon as possible after an extended period of ischemia in critical tissue such as the brain and heart as well as skeletal muscles and perhaps in other organs such as the liver, kidney, pancreas, etc.

- HBO should be considered after revascularization surgeries associated with long ischemia times
  - Re-implantations
  - Threatened flaps
  - Other situations where there is a possibility that reperfusion injury will contribute to more morbidity.

급성기 창상



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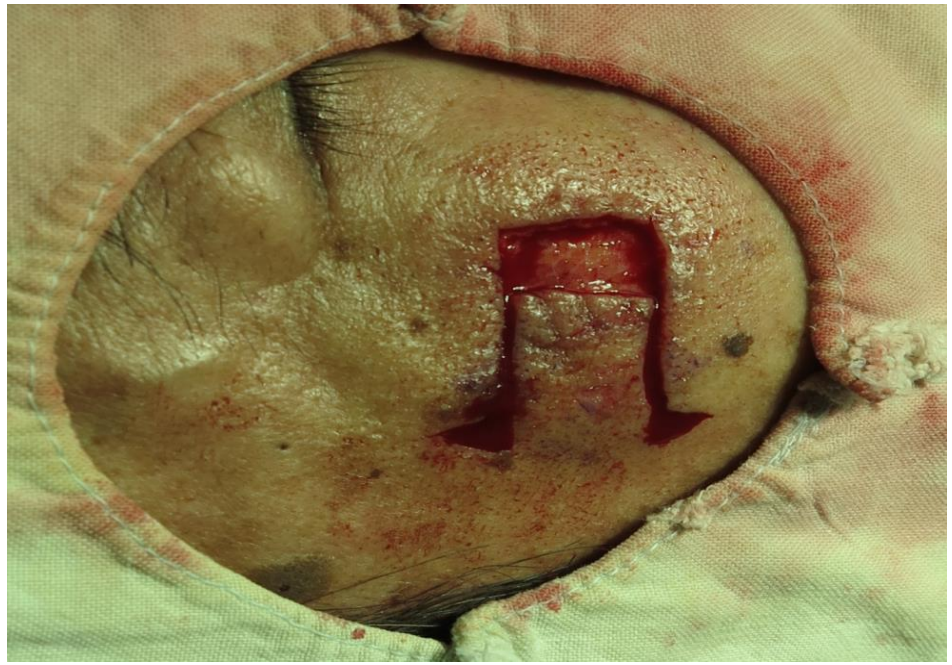
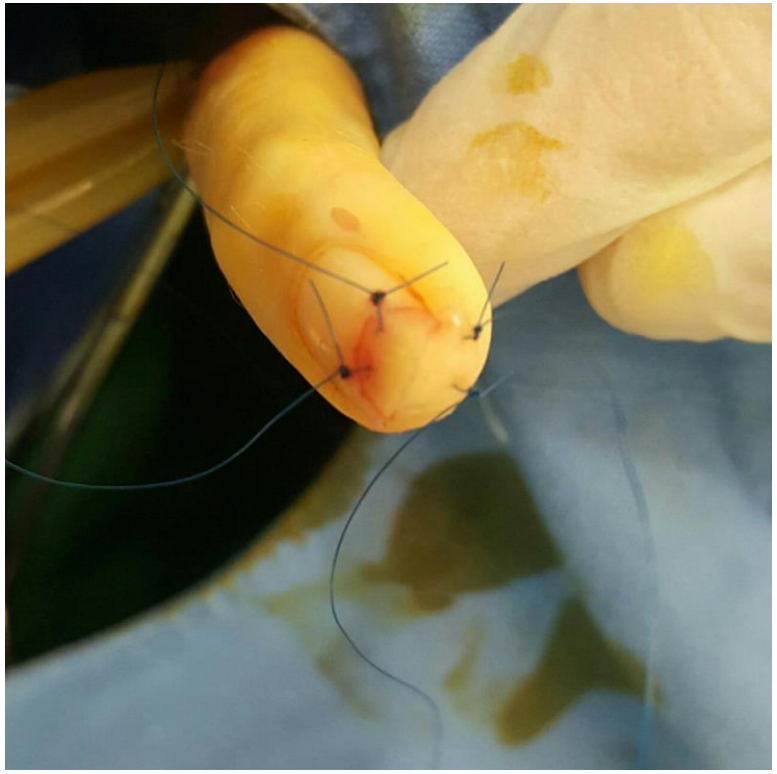
Flap

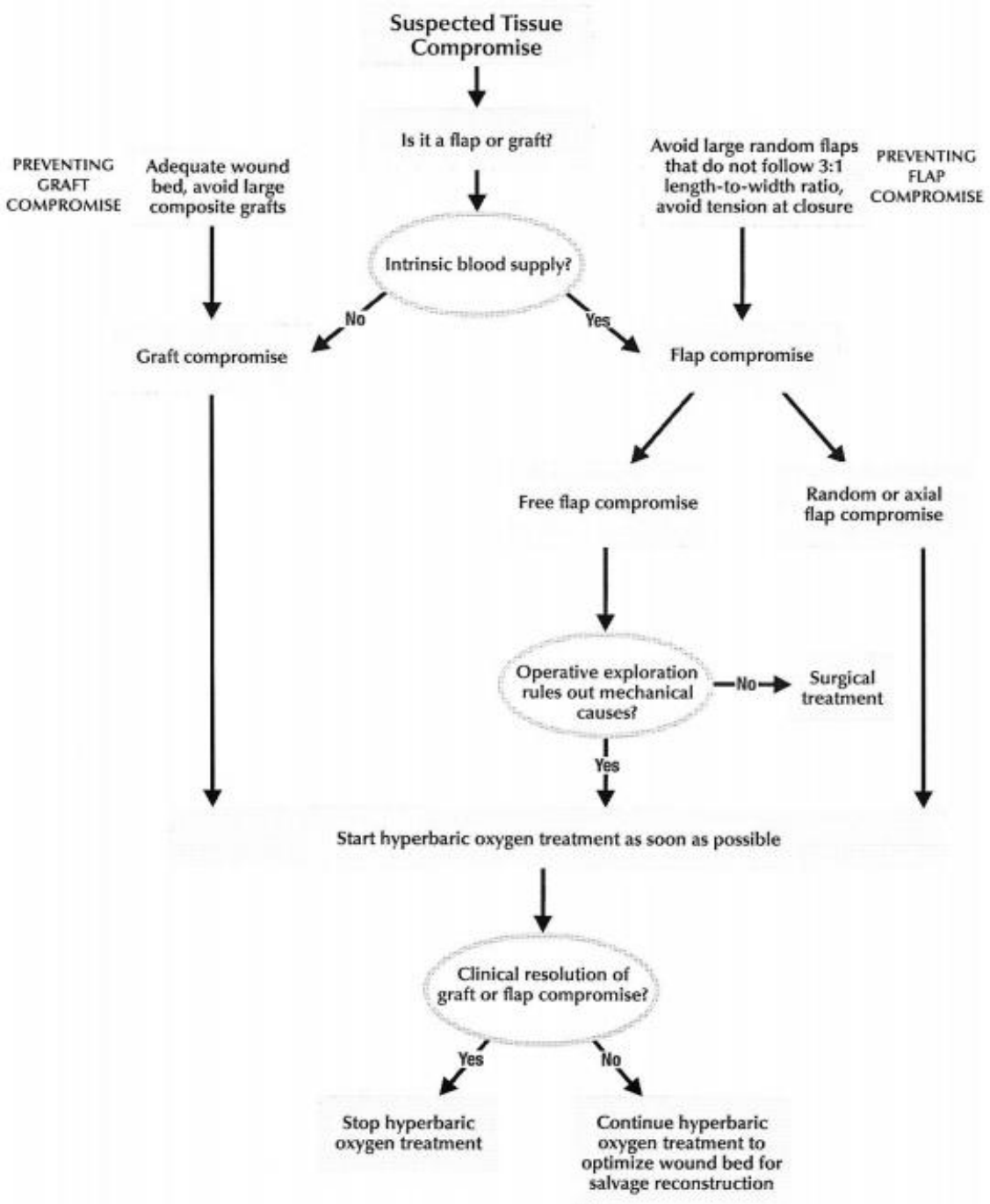


Graft

Graft



Compromised Flap


Suspected Tissue Compromise
Is it a flap or graft?
PREVENTING GRAFT COMPROMISE
Adequate wound bed, avoid large composite grafts
Avoid large random flaps that do not follow 3:1 length-to-width ratio, avoid tension at closure
PREVENTING FLAP COMPROMISE
Intrinsic blood supply?
No
Yes
Graft compromise
Flap compromise
Free flap compromise
Random or axial flap compromise
Operative exploration rules out mechanical causes?
No
Surgical treatment
Yes
Start hyperbaric oxygen treatment as soon as possible
Clinical resolution of graft or flap compromise?
Yes
No
Stop hyperbaric oxygen treatment
Continue hyperbaric oxygen treatment to optimize wound bed for salvage reconstruction

Protocol

- 2~2.5 ATA
- 90~120 min
- Initial : 2/day
- Stable / viable : 1/day

Thermal burns

Figure 11. Burn Victim's Recovery

A. 23-year-old white female with facial burns from flaming gasoline and tar 12 hours after injury.

B. 24 hours later (36 hours after injury) after two HBO_2 treatments. Note resolution of edema.

C. 72 hours later (84 hours after injury) after six HBO_2 treatments.

D. Shortly before discharge.

E. Four years after discharge.

Note: Consent to use these photos was obtained prior to publication.

HBOT on Burn wounds?

- Inflammatory Cell Reduction
- Angiogenesis
- Increased Epithelialization

Indications

- Burns that extend into the dermis and beyond
: 2nd / 3rd degree

- Inhalation burn

- Impaired wound healing

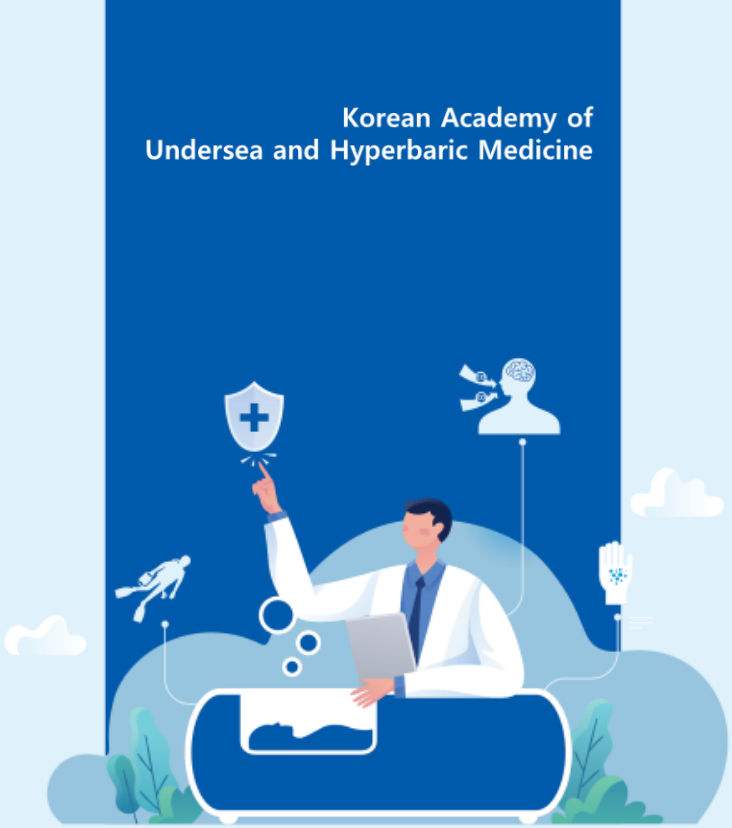
- Extensive edema

- A large skin area envolved

Techniques

- As soon as possible !!
- 1st 24hr : 3 times : 90min with 2.0~2.4 ATM
- 2nd day ~ : twice / day
- total 20~30 sessions.
- No. of treatments : wound response and extends

허혈성 질환



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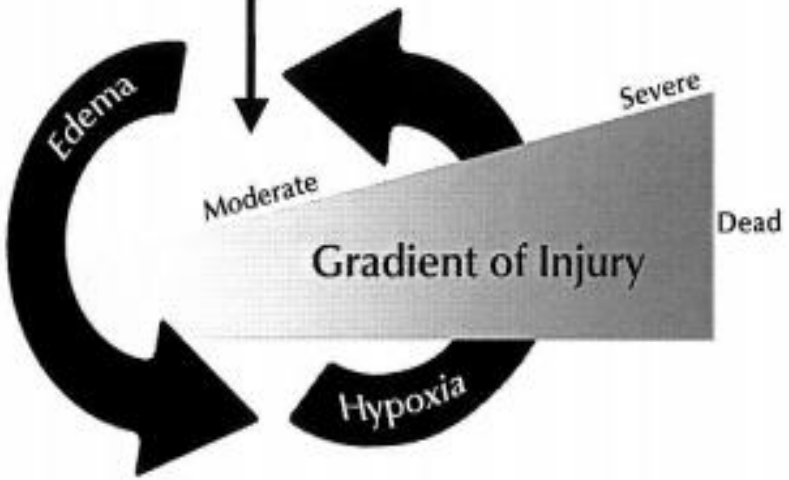
Traumatic Ischemias Crush Injuries and Compartment Syndromes

Etiology

Trauma
+
Ischemia

Pathophysiology
Vicious Cycle



Findings

Table 1. The Health Status Score—Quantifying Health and Function

Assessment	2 Points	1 Point	0 Points
	Use half points if mixed or intermediate between 2 grades		
Activities of daily living	Full	Some	None
Ambulation	Community	Household	None
	Subtract ½ point if aids are used.		
Comorbidities	No significant	Impaired	Decompensated
	Omit neurological deficits which is separate assessment below.		
Inhibitors smoking, collagen vascular diseases, and immunosuppressors	None	Past	Current
Neurological deficits	None	Some/Minor Sensation, imbalances	Major Cognitive, paralysis

Notes: Five assessments (considered to be the most important to determine how healthy and functional the patient is) are each graded from 2 points (best) to 0 points (worst) and summated to generate a 0 to 10 score. "Healthy" patients generate scores in the 7½ -10 range, "impaired" patients in the 3½-7 range and decompensated patients in the 0-3 range.

Table 2. Guidelines for using Hyperbaric Oxygen in Crush Injuries using the Gustilo Classification Paired with the Patient's Wellness Score[30]

Gustilo Type	Findings Soft tissue injury with the fracture	Outcomes in Healthy Hosts	HBO_2 Indications paired with Wellness Score[1]		
			Healthy	Impaired	Decompensated
I	Minimal (<1 cm wide) puncture wound from inside to out	Usually no different from a closed fracture of the same severity			Yes
II	Laceration with minimal deep soft tissue damage	Same as above			Yes
III	Crush Injuries	Depend on Subtypes A, B, and C			
A	Sufficient soft tissue to close the wound (after debridement)	~10% completion rate[2]		Yes	Yes
B	Flaps and/or grafts needed for bone coverage	≥50% incidence of complications[2]	Yes	Yes	Yes/No[3]
C	III-B injuries with major vascular damage		Yes	Yes/No[3]	Yes/No[3]

Notes: Table 2 shows how the Wellness Score is combined with the Gustilo open fracture grading system to add objectivity to the indications for using hyperbaric oxygen in crush injuries.

Scores greater than 4 points support the decision for doing everything possible to salvage the injured tissue including the adjunctive use of hyperbaric oxygen.

Compartment syndromes

Figure 2-a. Indications for HBO_2 in the Skeletal Muscle-Compartment Syndrome

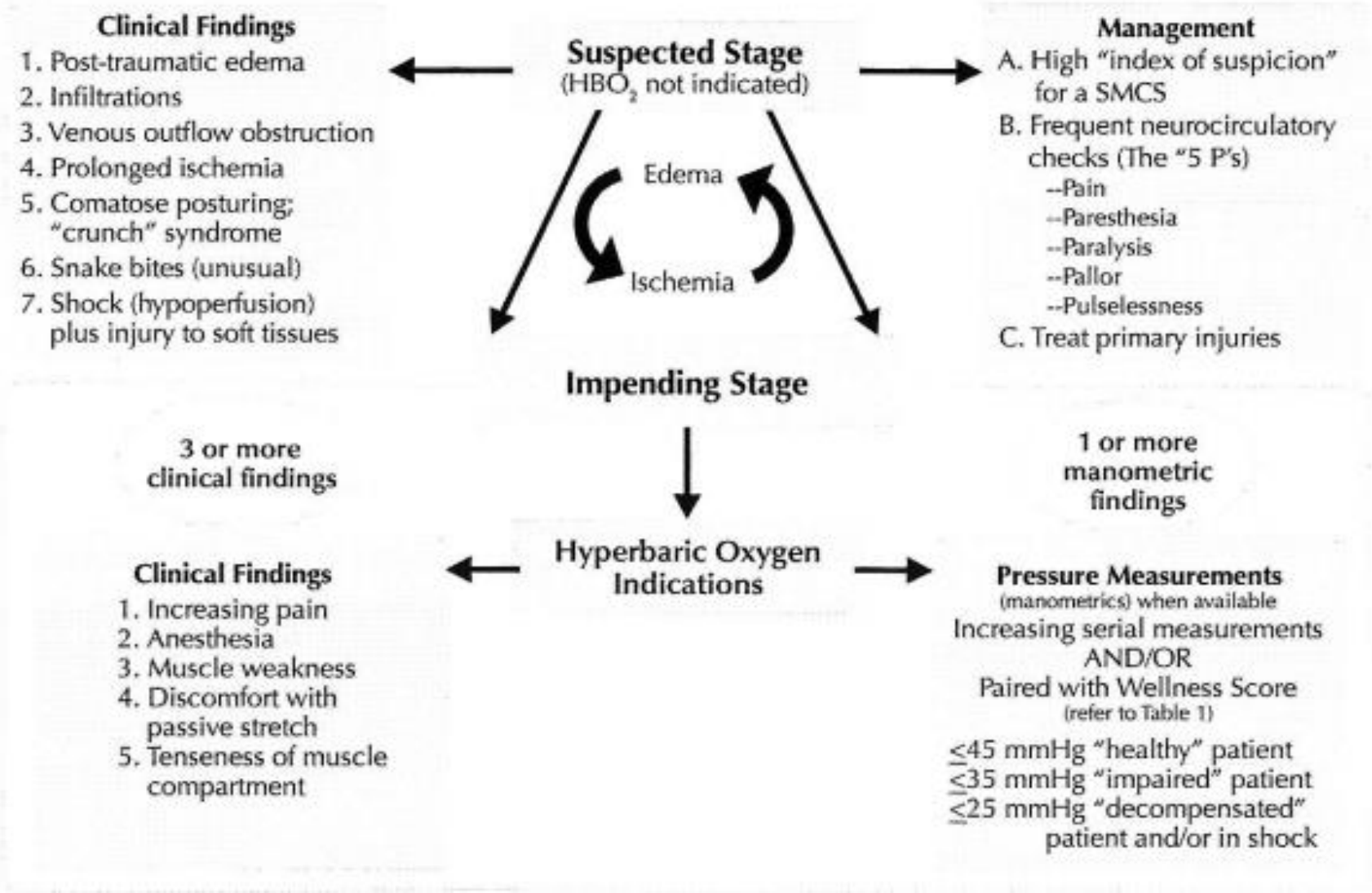
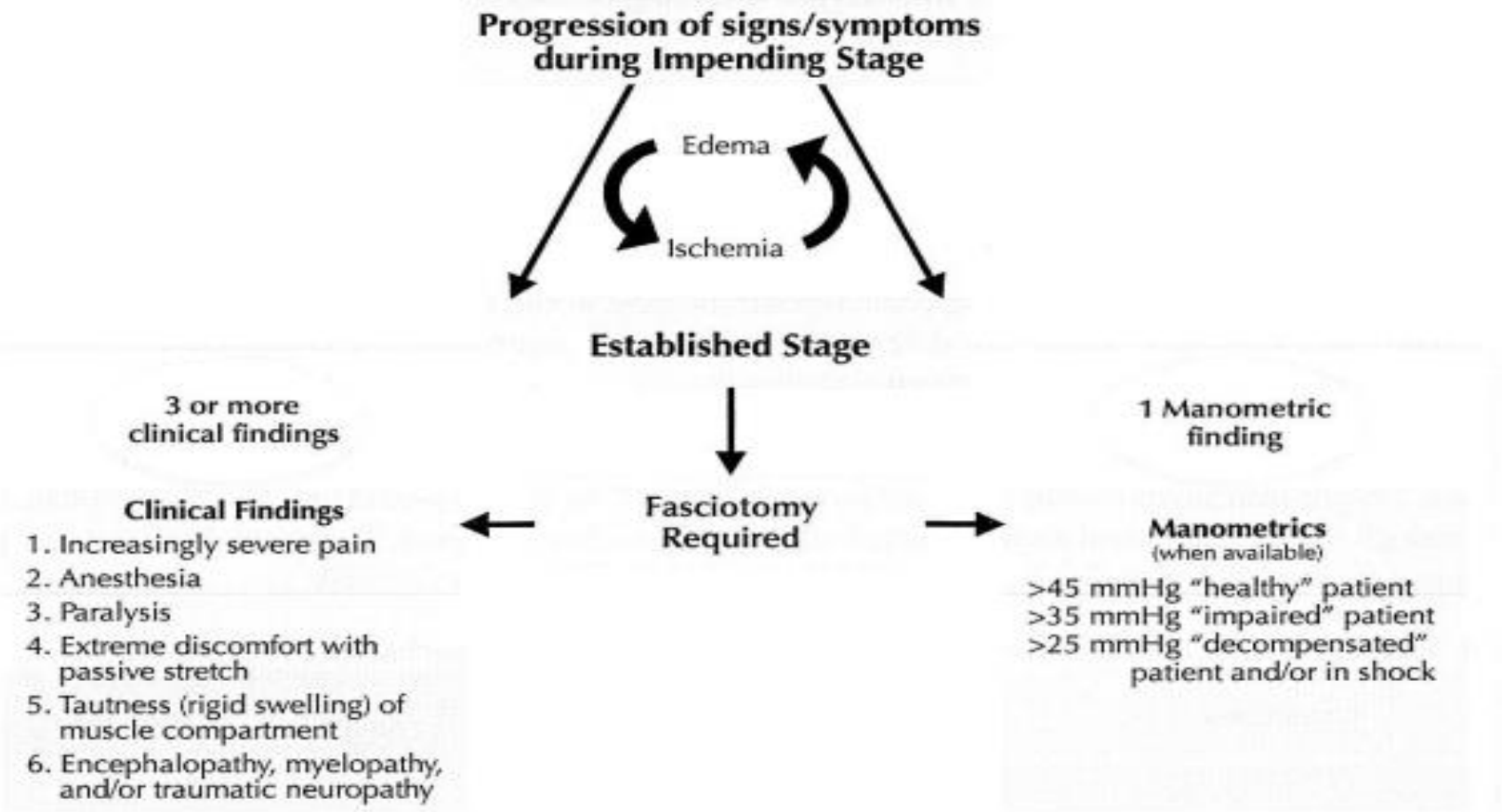


Figure 2-b. Requirements for Fasciotomy in the Skeletal Muscle-Compartment Syndrome and Indications for Hyperbaric Oxygen Post-Fasciotomy



Indications for HBO_2 Post-Fasciotomy

- Ischemic muscle
- Demarcation between viable and non-viable tissue is unclear
- Massive swelling/prolonged ischemia time
- Threatened skin flap or graft
- Residual neuropathy
- Markedly impaired or decompensated patient

Table 3. Treatment Recommendations and Peer Review when using Hyperbaric Oxygen for Crush

Conditions	Peer Review[1] Obtain after # of Rxs	Comments
Primary Conditions		
1. Reperfusion injury	1-2 treatments	Minimal tissue trauma, e.g. after free flaps, revascularizations, and transient edema
2. Crush injury	9 (TID 1st 24 hours; BID 2 days and daily 2 days)	If deterioration noted when HBO_2 treatments are decreased, resume the previous schedule
3. Compartment Syndromes	3 (BID day 1 and single treatment day 2)	HBO_2 is not a substitute for fasciotomy; use it for the impending stage of the SMCS
Residual Problems and/or Complications		
1. Threatened flaps and grafts	14 (BID for 7 days)	If site remains tenuous, consider an additional week of twice a day treatments
2. Problem wounds/infected wounds	21 (BID for 7 days, daily for 7 days)	Refer to Problem Wounds section of this Hyperbaric Oxygen Committee Report
3. Refractory osteomyelitis	30 (Daily for 21 days; possible extension to 40 treatments)	HBO_2 must be integrated with a combined antibiotic and surgical strategy
4. Post-fasciotomy concerns after SMCS	14 (BID for 7 days)	Concerns include massive swelling, threatened flaps, unclear demarcation, neuropathy, etc.

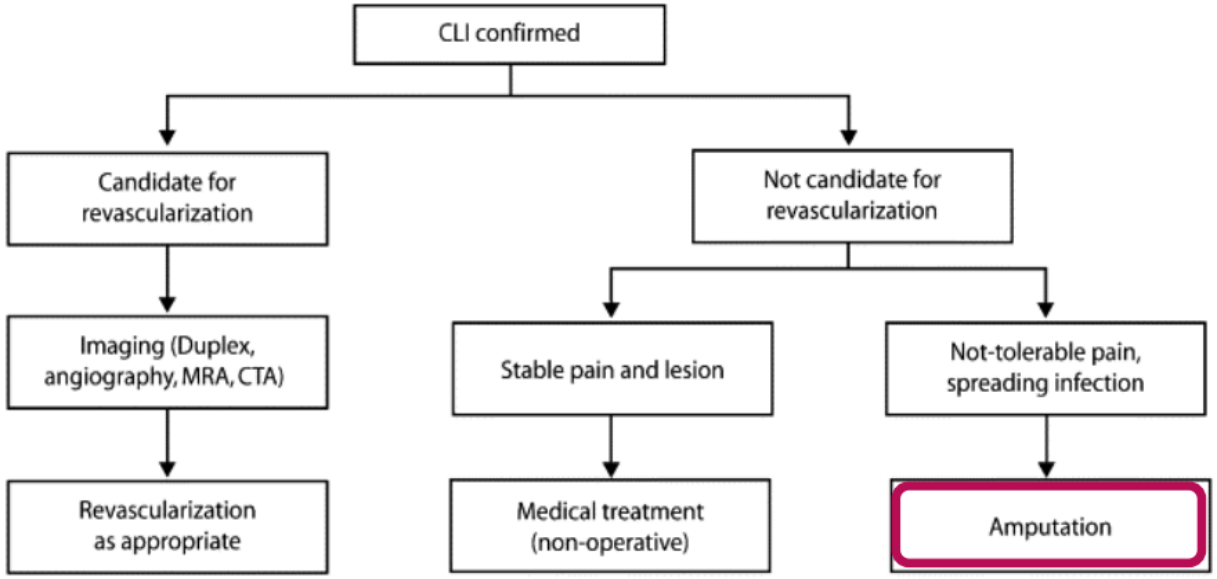
Notes: [1]Peer review should be done by two or more of the following: 1) Hyperbaric medicine physician; 2) Trauma/orthopedic/plastic surgeon requesting HBO_2 and/or patient's primary care physician to decide whether to continue or stop hyperbaric oxygen treatments.

Abbreviations: BID = Twice a day, HBO_2 = Hyperbaric oxygen, # = Number, Rxs = Treatments, SMCS = Skeletal muscle-compartment syndrome, TID = Three times a day.

PAOD

Critical Limb ischemia

- Defined by the presence of PAOD in combination with rest pain, gangrene, or a lower limb ulceration > 2 weeks duration



Eur J Vasc Endovasc Surg 2019; 58:S1.

- Numerous unexpected and unwanted outcomes generated by reperfusion
- PAOD patients experience **delay in recovery after successful therapy** due to further tissue damage

Reperfusion paradox

Postreperfusion syndrome

- Restoring blood flow to these ischemic areas paradoxically results in further injury
- Local complications of postreperfusion syndrome result
  - Amputation or severe dysfunction in the salvaged limbs

Restricted Blood Flow

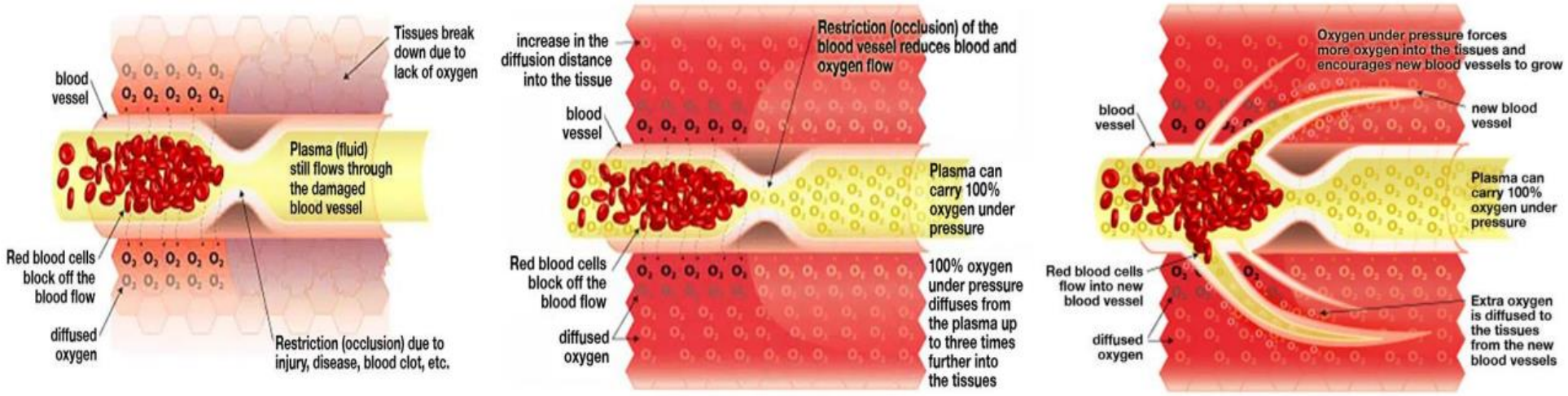
Restriction (occlusion) in blood flow due to surgery, illness, or injury,

Hyperbaric Oxygenation

oxygen-rich plasma is able to travel past the restriction, diff-using up to 3 times

Neurovascular Regeneration

HBOT mobilizes the body's circulating stem cells.



What Is Hyperbaric Oxygen Therapy HBOT

Guideline about HBOT

Hyperbaric therapy significantly reduced the risk of major amputation in patients with diabetic ulcer.

because of methodological shortcomings. Other patholo-
gies related to PAD and diabetes were not evaluated using
this kind of treatment. Therefore, given the absence of
prove
recom
consid
have
revasc

Hyperbaric oxygen may be considered in selected patients with ischemic ulcers who have not responded to, or are not candidates for, revascularization.

〈보험 적용 적응증〉

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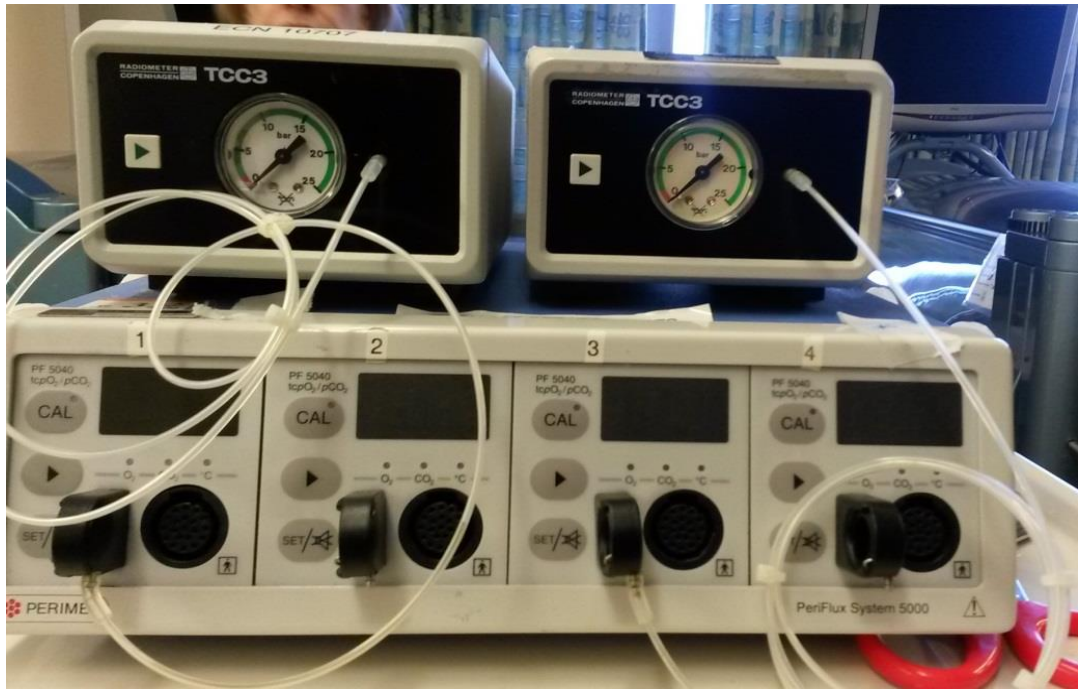
〈보건복지부, 2019. 01〉

Tissue Perfusion

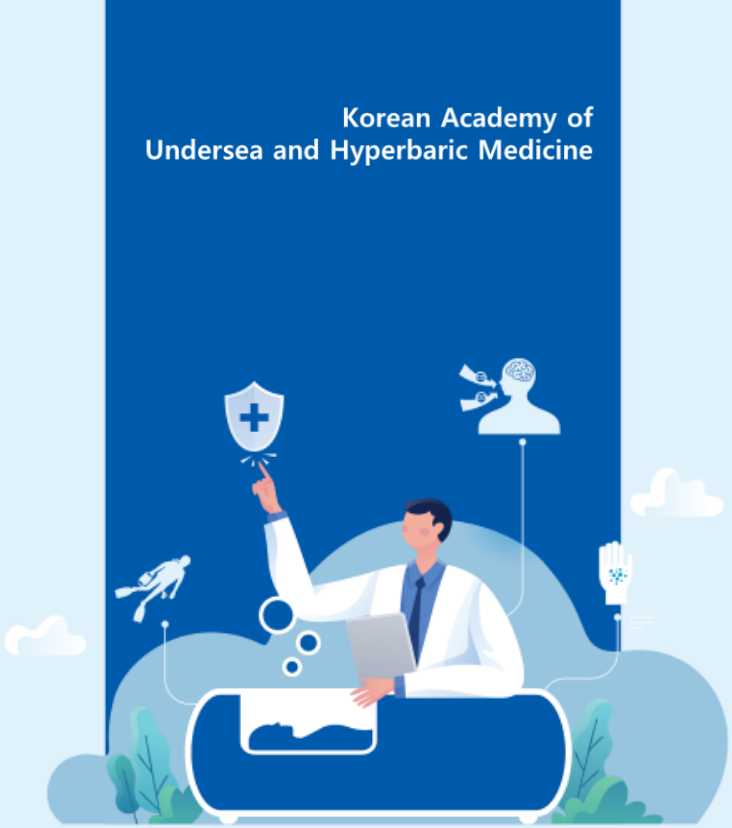
Measurement of Wd. hypoxia

Transcutaneous oxygen tension (PtcO2) : most useful



PtcO2 < 40mmHg : HBOT

만성 골수염



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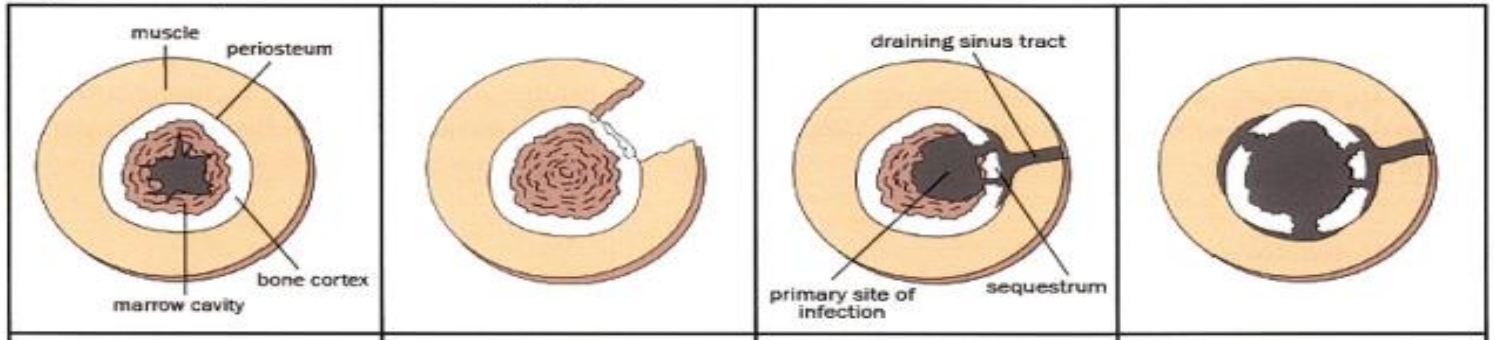
- Neutophils require tissue oxygen tensions of 30~40 mmHg to destroy bacteria by oxidative killing mechanisms
- Antibiotic fx. ⬆
- Cefazolin and HBOT produced a 100-fold greater reduction in bacterial counts
- Osteoclast enhancement
- Angiogenesis

Refractory Osteomyelitis

- Definitive surgical debridement + appropriate antibiotic Tx. (4~6 weeks)

Figure 1. Cierny-Mader's Anatomic Staging.



Stage 1: Medullary osteomyelitis	Stage 2: Superficial osteomyelitis	Stage 3: Localized osteomyelitis	Stage 4: Diffuse osteomyelitis
Anatomic Characteristic: Infection confined to bone intramedullary surfaces **Typical Etiology:** Hematogenous seeding, infected intramedullary hardware **Primary Management:** Culture directed antibiotics, hardware removal for refractory infection of stable bone	**Anatomic Characteristic:** Surface infection of periosteum and cortical bone **Typical Etiology:** Bone coverage defect allowing infection spread from overlying soft tissue wounds **Primary Management:** Culture directed antibiotics, superficial debridement of necrotic bone & tissue	**Anatomic Characteristics:** Localized full thickness involvement of cortical bone, ± sequestration **Typical Etiology:** Penetrating trauma, surgical contamination, infected hardware **Primary Management:** Culture directed antibiotics, debridement of necrotic bone & tissue, adjunctive HBO_2 therapy for refractory/progressive infection	**Anatomic Characteristics:** Through-and-through bone involvement (i.e. combined Stage 1, 2 and 3 characteristics), ± sequestration, with mechanical instability either before or after debridement **Typical Etiology:** Penetrating trauma, surgical contamination, infected hardware **Primary Management:** Culture directed antibiotics, debridement of necrotic bone & tissue, bone stabilization, adjunctive HBO_2 therapy for refractory /progressive infection

항생제 항생제+변연절제술 Adjunctive HBOT

Table 1. Host Physiologic Class

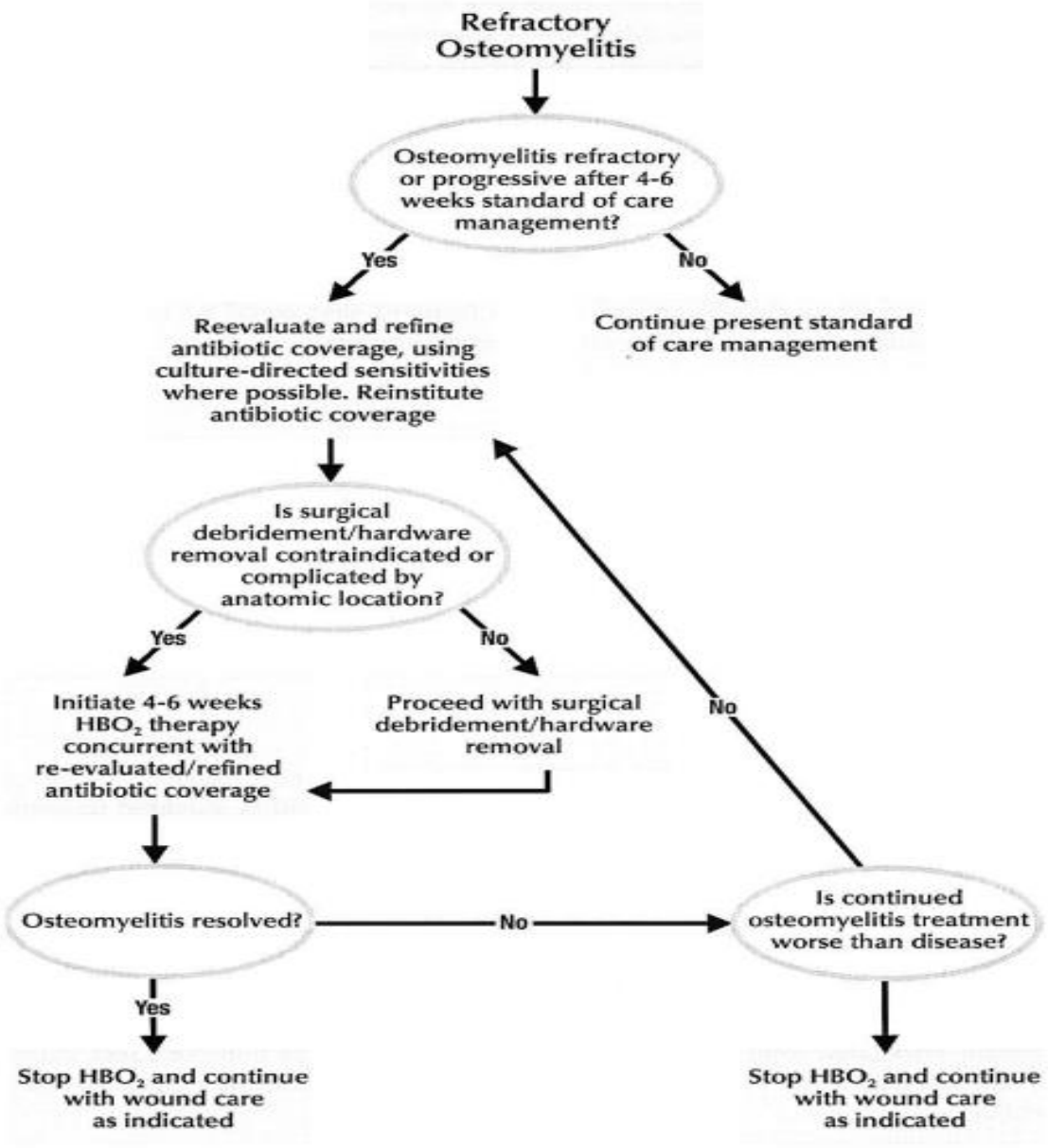
A Host	B Host	C Host
Normal Physiology	Systemic Compromise (B_S)	Osteomyelitis treatment or physiologic outcome is worse for host than ongoing disease
	Local Compromise (B_L)	
	Concurrent Local and Systemic Compromise (B_{LS})	

Table 2. Class B Host Compromising Factors

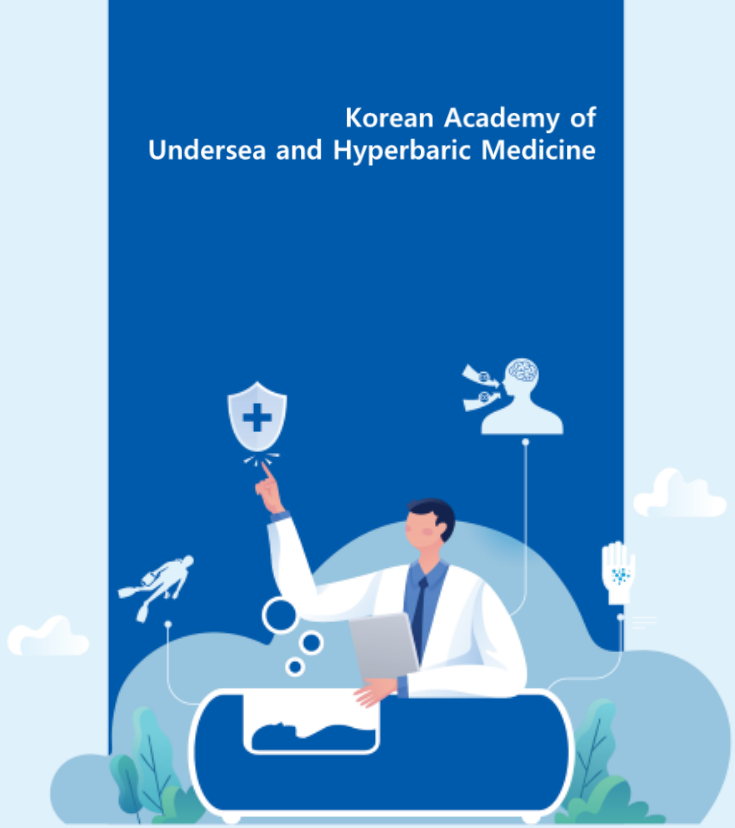
Systemic Factors (B_S)	Local Factors (B_L)
Malnutrition	Chronic lymphedema
Renal failure	Venous stasis
Diabetes mellitus	Major vessel compromise
Chronic hypoxia	Arteritis
Malignancy	Extensive scarring
Immune deficiency	Radiation fibrosis
Immunosuppression	Small vessel disease
Extremes of age	Complete loss of local sensation
Tobacco abuse	

* Specific areas (sternum, vertebrae, cranium, and other central bony)

Figure 2. Flowchart for HBO_2 Management of Refractory Osteomyelitis
Details of management are described in the text.



Delayed Radiation Injuries



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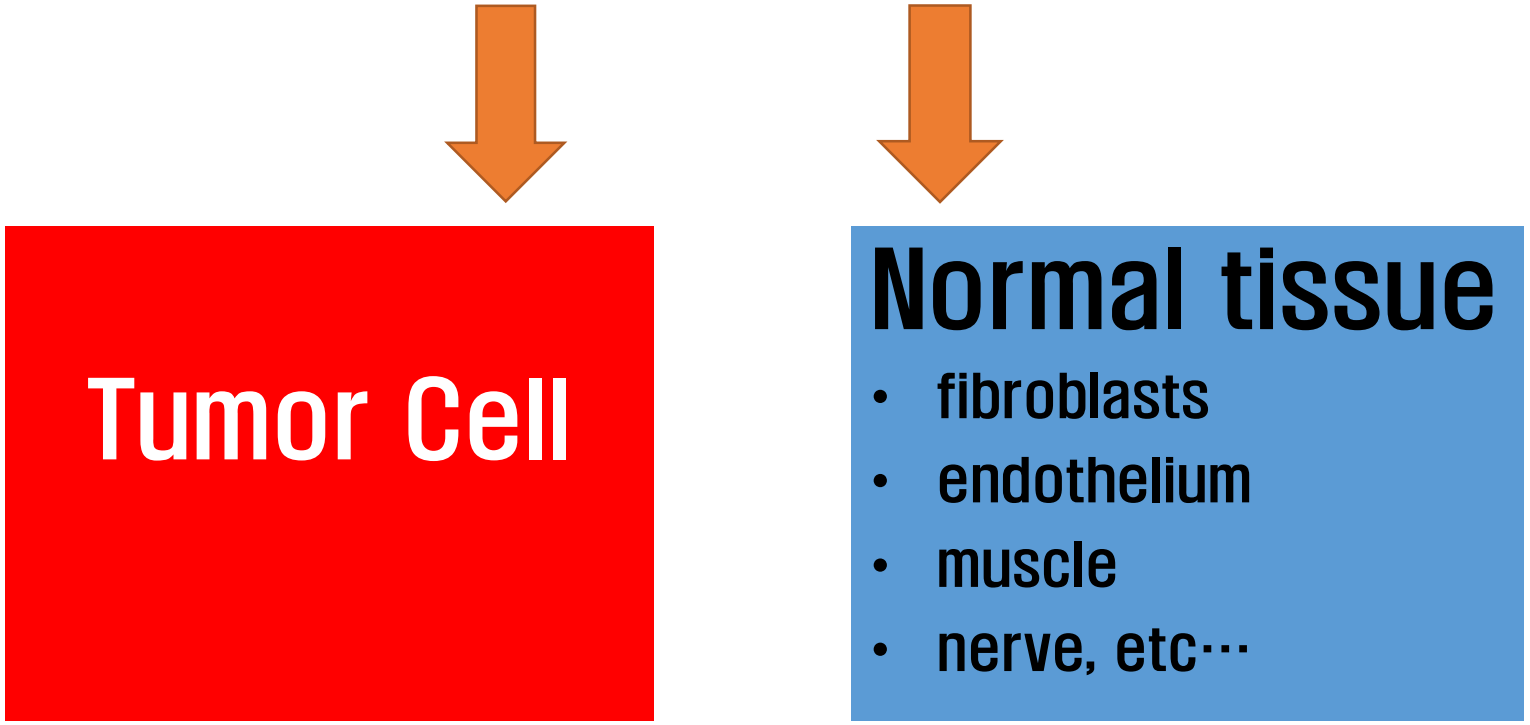
Radiation


Tumor Cell
Normal tissue
• fibroblasts
• endothelium
• muscle
• nerve, etc…

Radiation

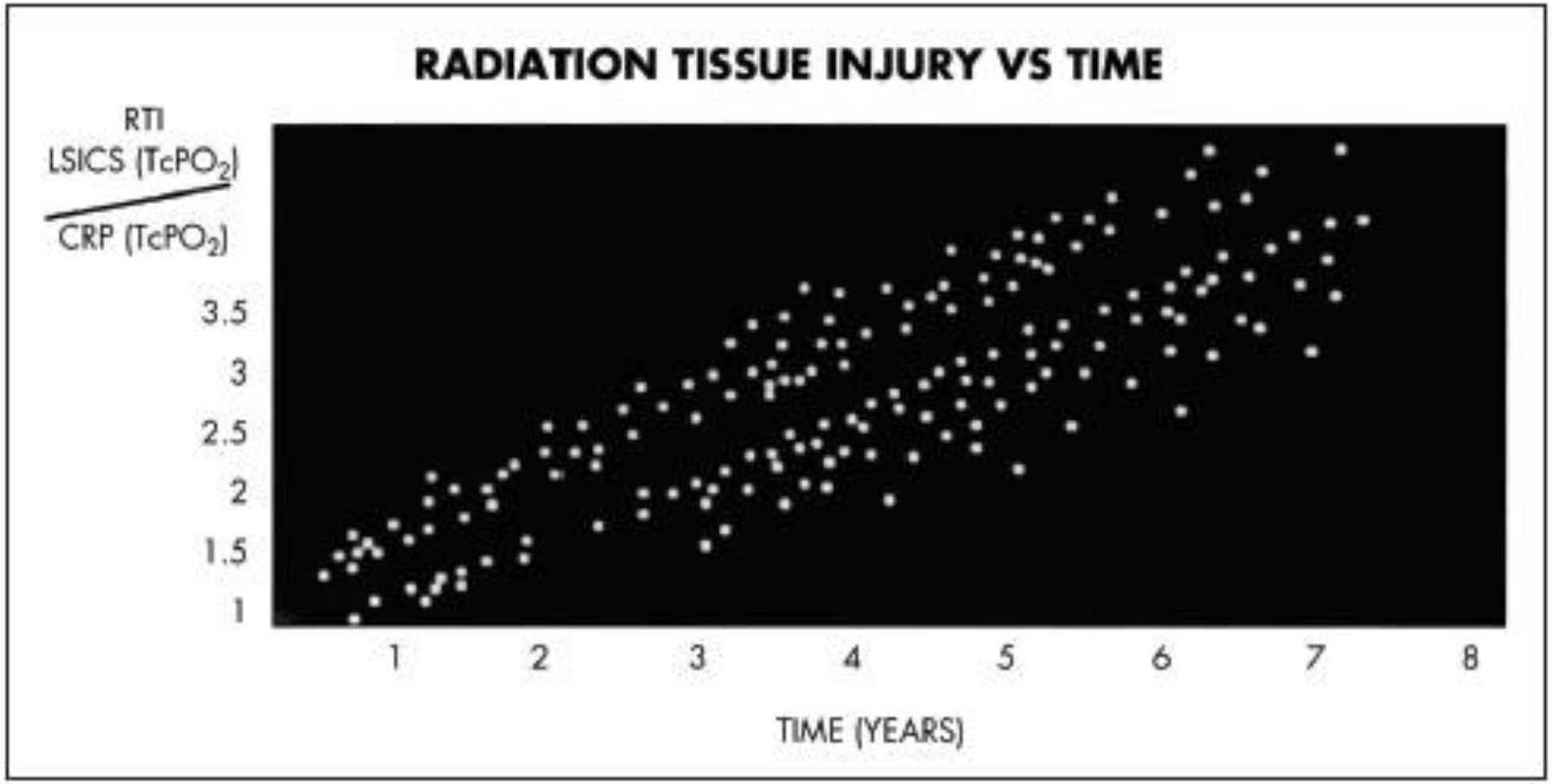
Cell Necrosis

Functional Damage

produce

- Daughter cells
- Collagen
- Regulatory enzyems

Progressive radiation fibrosis, capillary loss



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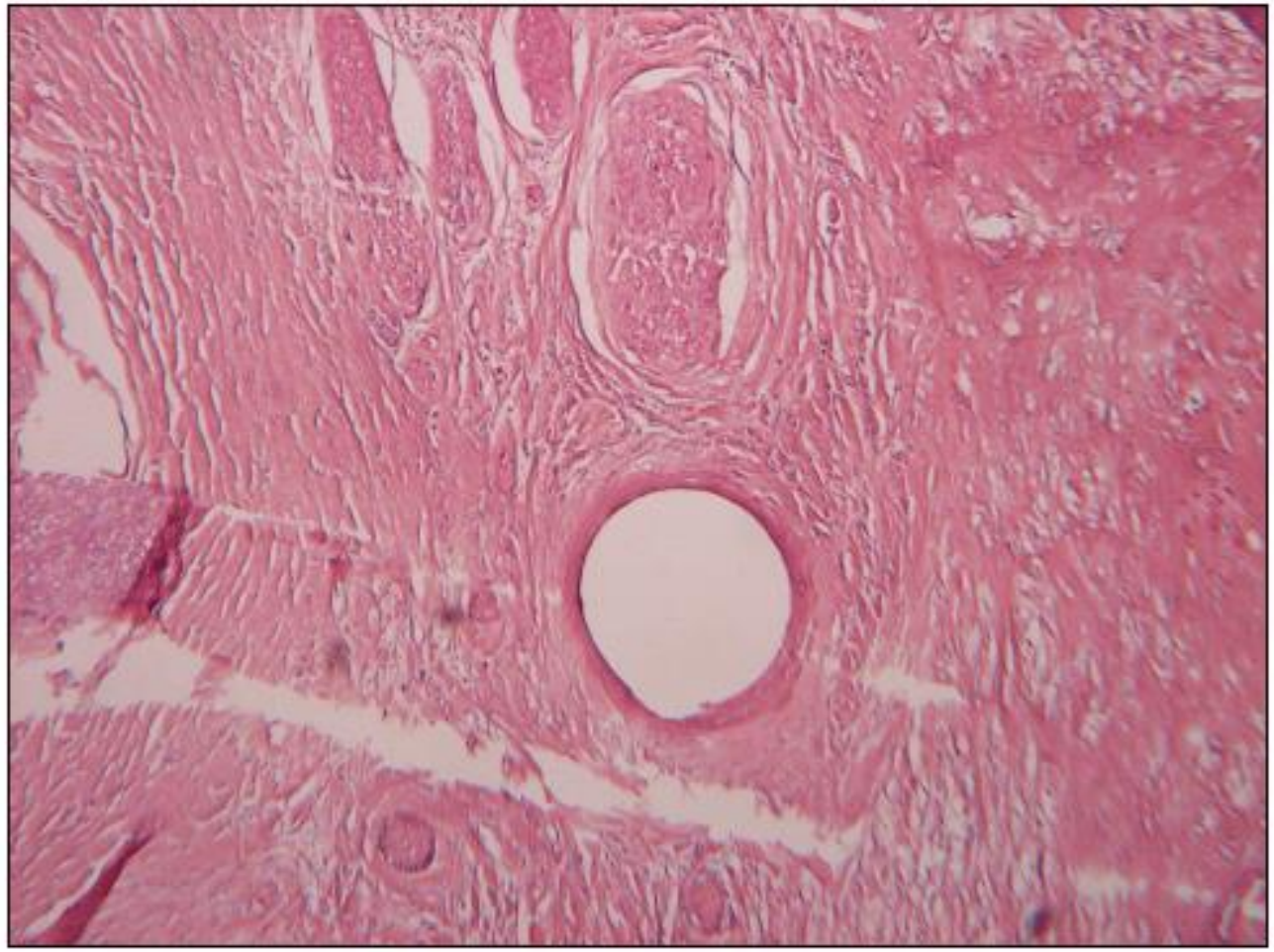
3H Tissue

- Hypovascular
- Hypocelluar
- Hypoxic



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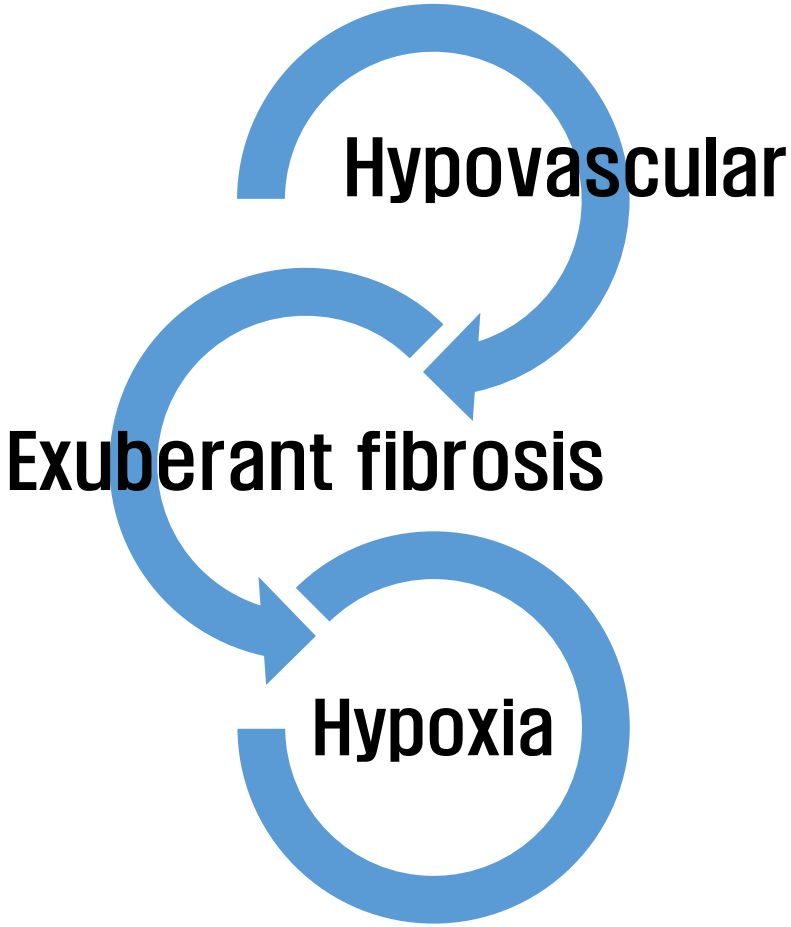

Hypovascular
Exuberant fibrosis
Hypoxia

Restricted Blood Flow

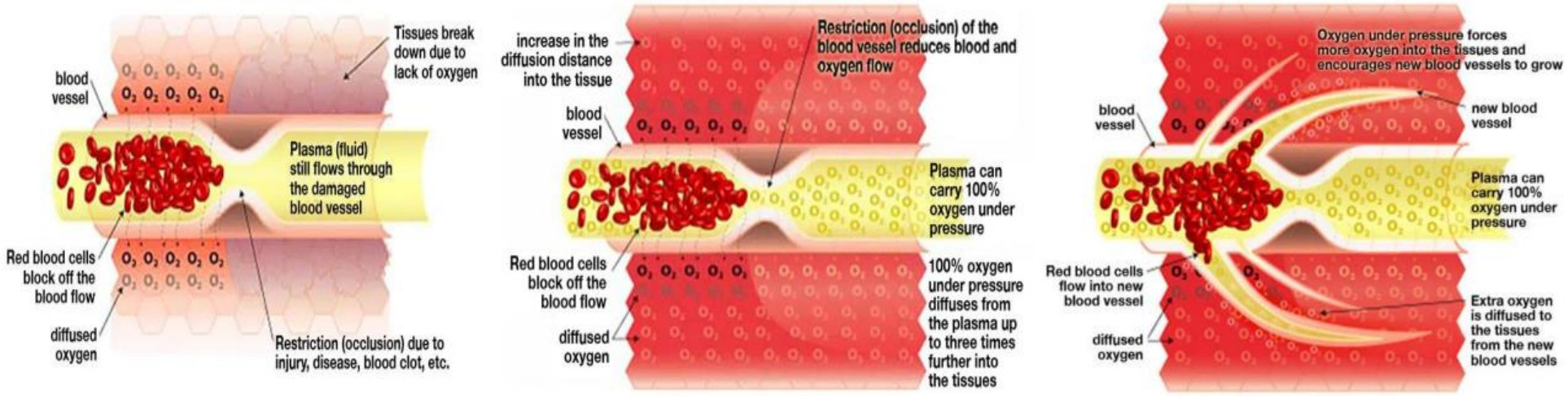
Restriction (occlusion) in blood flow due to surgery, illness, or injury,

Hyperbaric Oxygenation

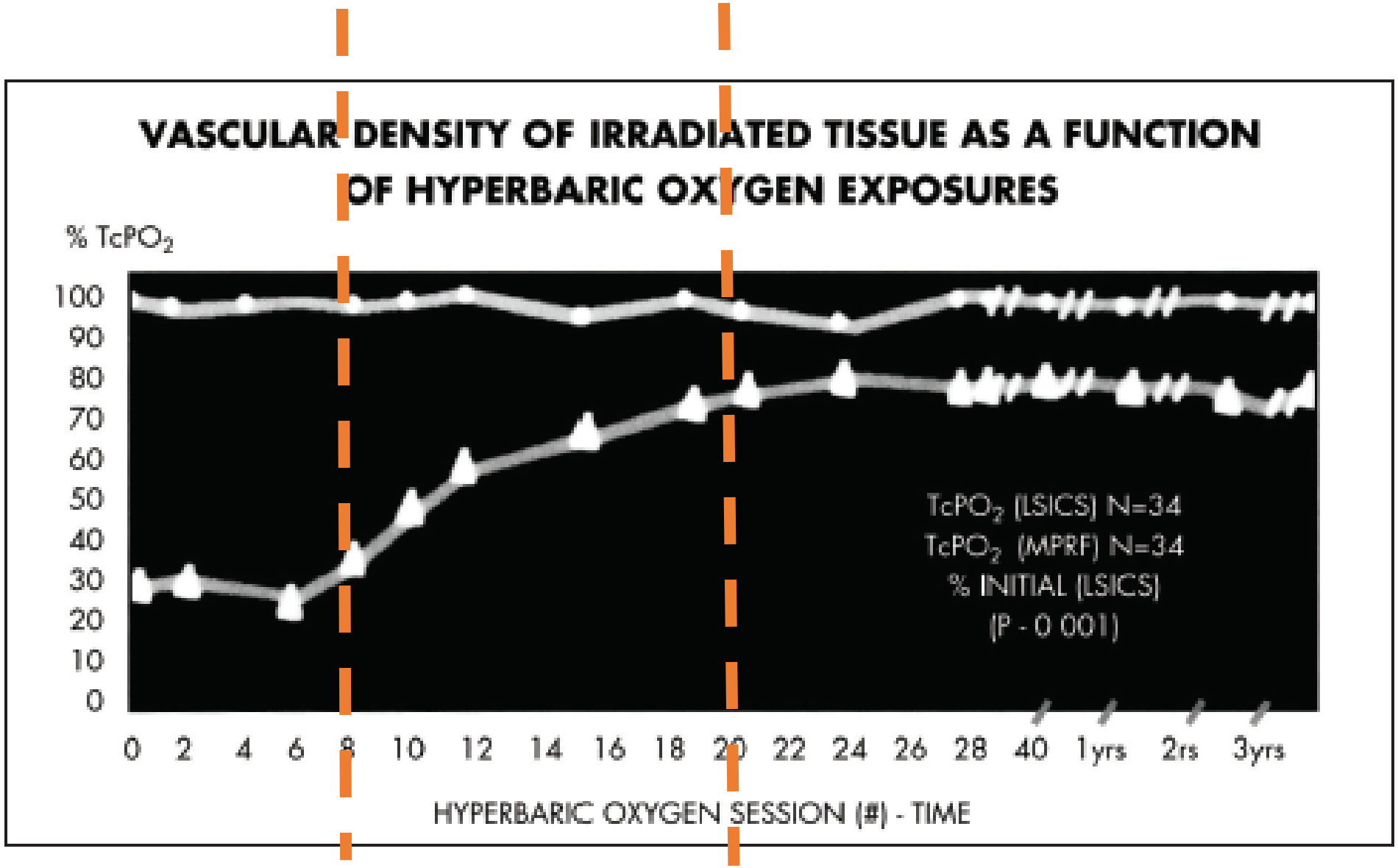
oxygen-rich plasma is able to travel past the restriction, diff-using up to 3 times

Neurovascular Regeneration

HBOT mobilizes the body's circulating stem cells.



What Is Hyperbaric Oxygen Therapy HBOT



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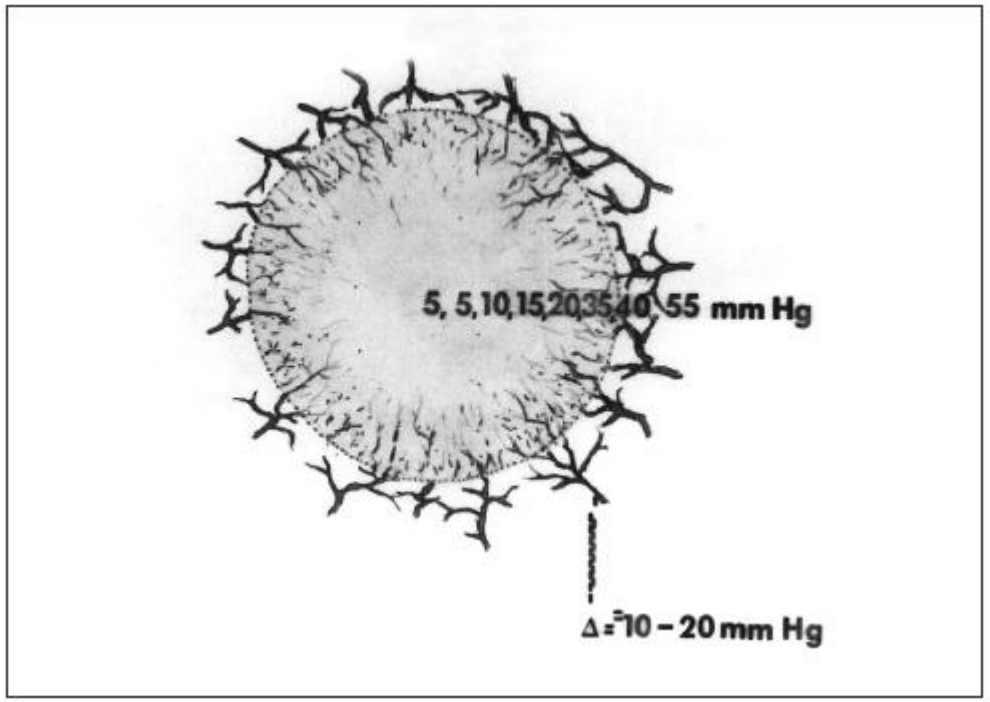
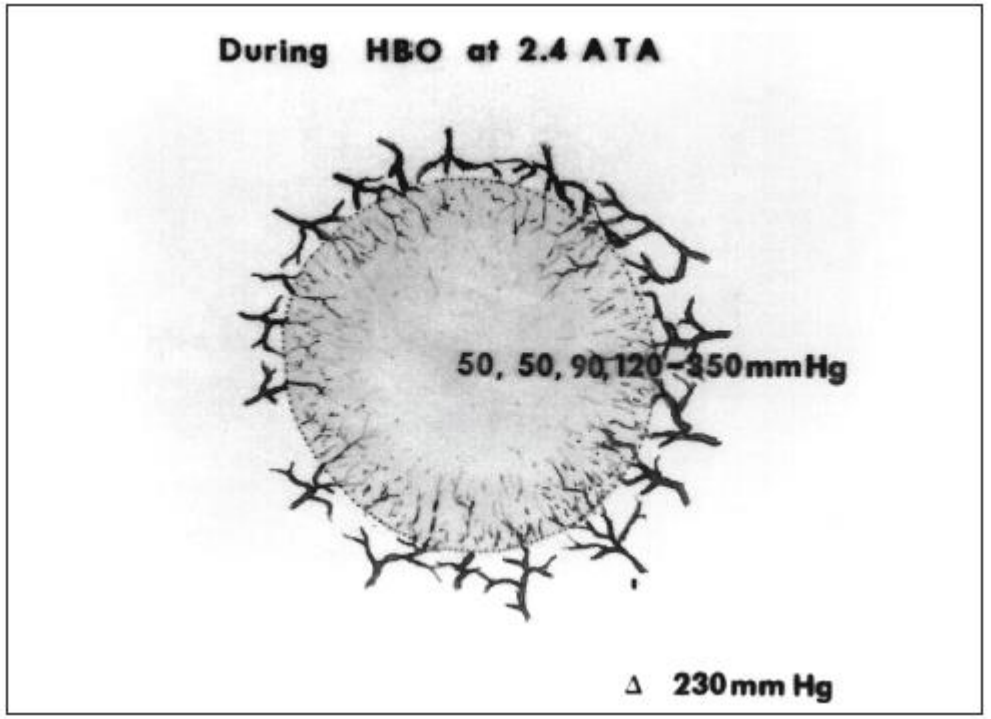
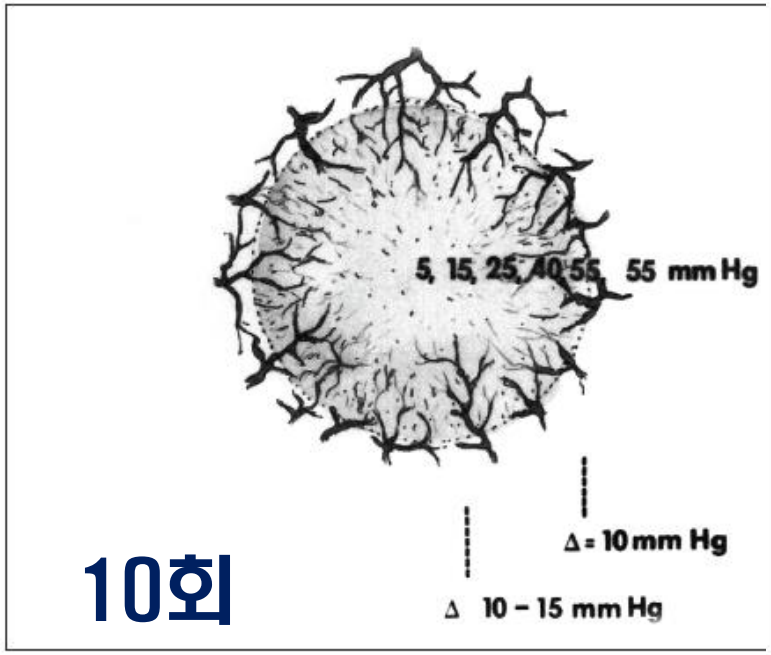
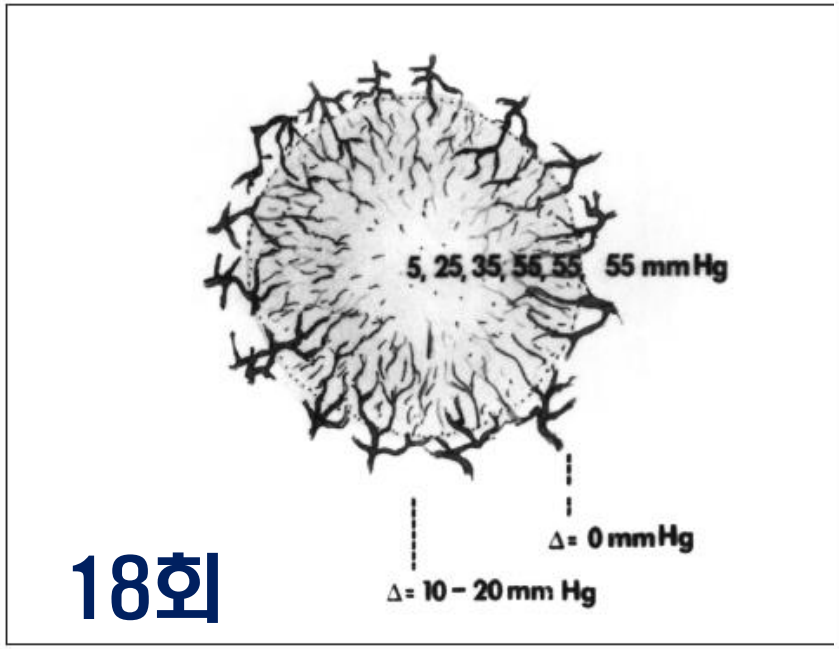
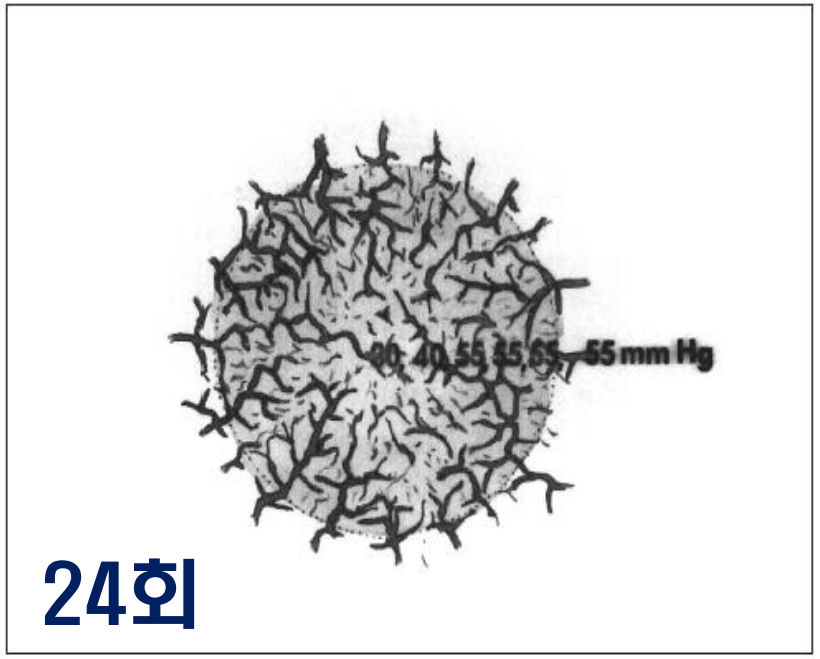

5, 5, 10, 15, 20, 35, 40, 55 mm Hg
Δ ≈ 10 – 20 mm Hg


During HBO at 2.4 ATA
50, 50, 90, 120 – 350 mm Hg
Δ 230 mm Hg







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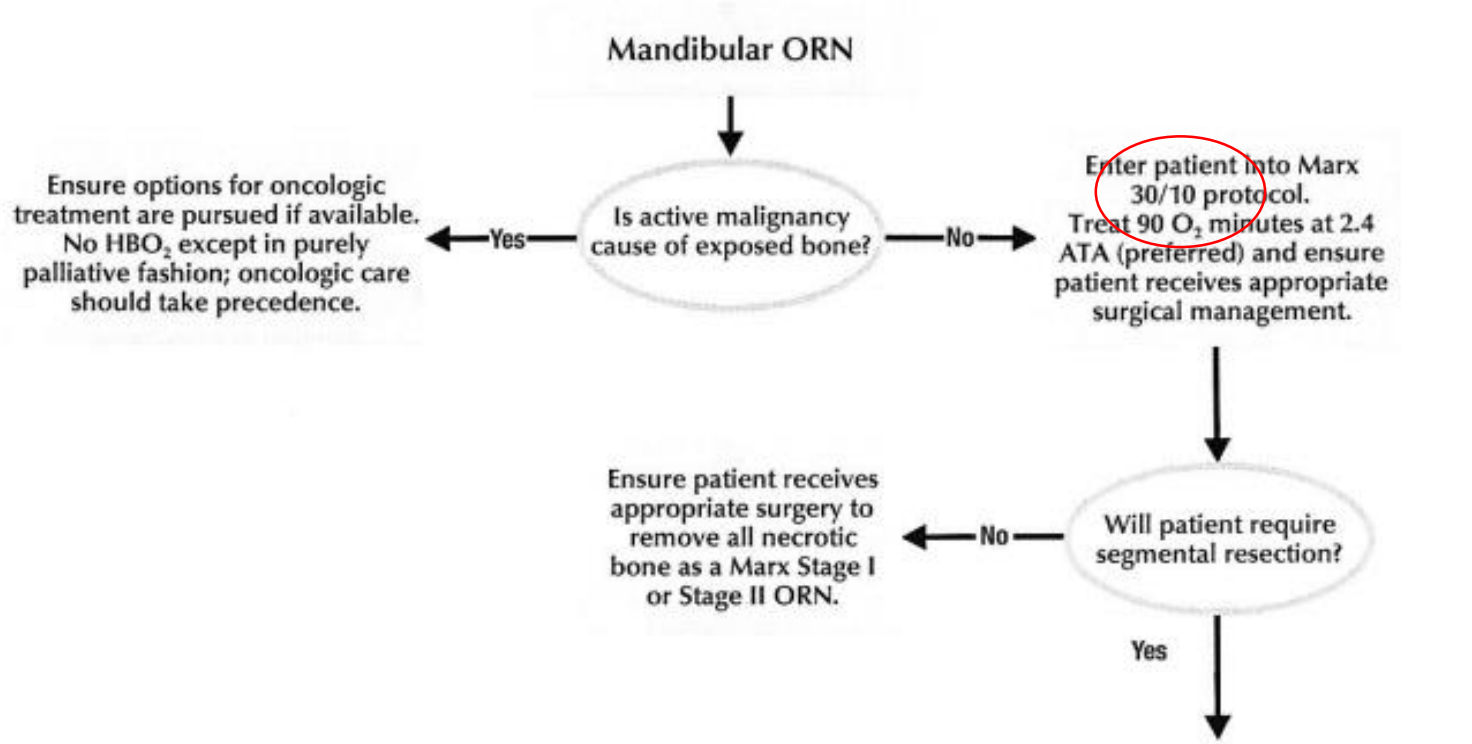
HBOT

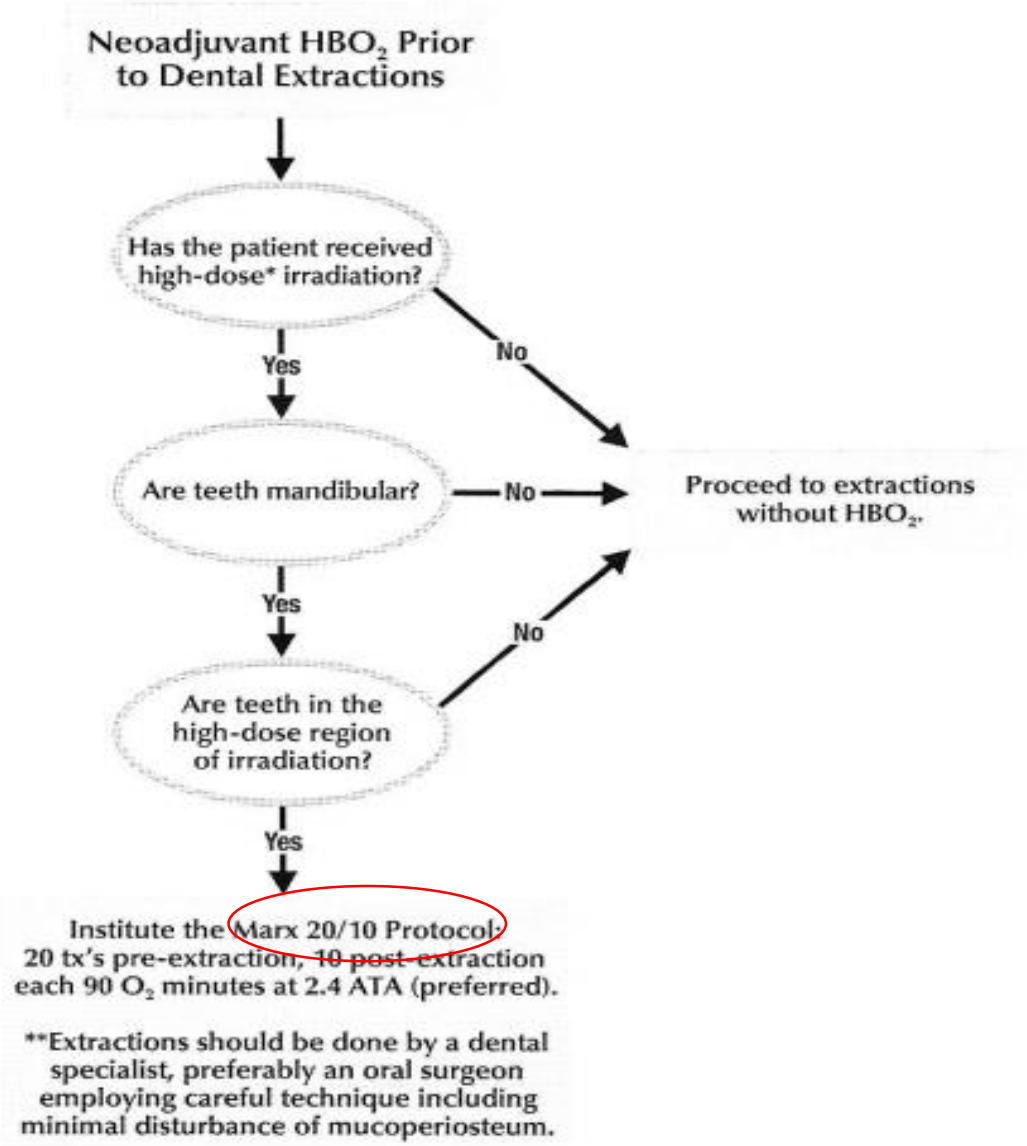
- Stimulates angiogenesis → improve tissue oxygenation
- Reduces fibrosis
- Mobilizes and induces and increase of stem cells (can differentiate)

Figure 1.



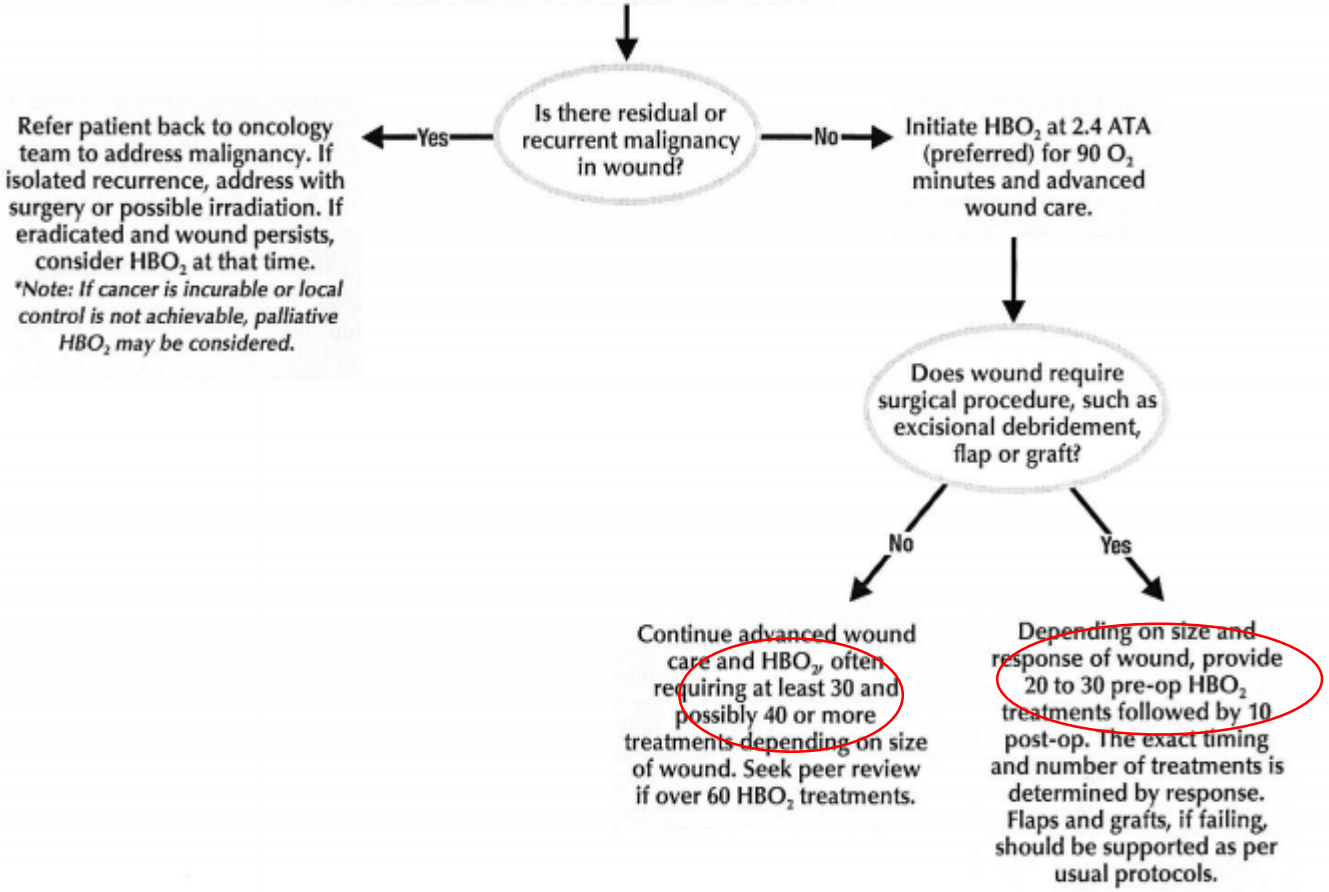
Note: Surgical experience and skills play an important role in accomplishing a successful course of treatment. Reconstructive surgery may take several forms including free flaps, when soft tissue is also needed. To complete reconstruction, pedicle flaps or free flaps may be appropriate.

This flowchart, though referring to mandibular ORN, with slight modification, may be applied to ORN at other anatomic sites.



* Doses of at least 60 Gy with likely risk of ORN showing significant increase at doses at 68 Gy or over.

Radiation Necrosis with External Wound, Including Head and Neck, Trunk and Extremities



Late Radiation Injury to Internal Organ Such as Bowel or Bladder

↓

Is recurrent/persistent tumor present?

Yes →

Cancer treatment should take precedence; if no effective oncologic treatment available, palliative HBO_2 should be considered.

No →

Document extent and severity of radiation injury by imaging. If accessible to endoscopy, direct visualization and/or biopsy is ideal. Address need for intervention for anemia or obstructive symptoms. Cystitis patients may require continuous bladder irrigation.

↓

Initiate HBO_2 preferably at 2.4 ATA for 90 O_2 minutes. Recommend initial 40 treatments unless early responder. Document response as patient approaches these 40 treatments. If there is response but improvement has not yet plateaued, consider another 10 to 20 treatments. If 60 treatments are to be exceeded, seek peer review.

**Note: Several cases of radiation cystitis have recurred but responded to a second course of treatment.*

CNS Radiation Necrosis

Is malignancy the cause of neurologic damage?

Both necrosis and tumor may show mass effect on anatomic imaging; may also need functional imaging such as PET or MRI spectroscopy to make diagnosis.

Yes →

Refer patient back to oncology team for cancer treatment if reasonable options are available. If none are possible, HBO_2 may be considered for palliation.

No →

Initiate HBO_2 preferably at 2.4 ATA for 90 O_2 minutes. Recommend initial 40 treatments unless early responder. Additional treatments can be considered. If exceeding 60 treatments, peer review is indicated. CNS imaging improvement (commonly by MRI), clinical improvement and decrease in steroid requirements often indicates response.

Generalized Approach to HBO_2 for Delayed Radiation Injury

Rule out persistent or recurrent malignancy as source of symptoms

Malignancy present?

Yes

Patient should be referred back to oncology team for management of malignancy, which will take priority if effective treatment is available. If none available, HBO_2 as palliative treatment should be considered since necrosis and tumor may both be present. HBO_2 cannot be expected to have benefit for tumor except potentially as adjuvant to concomitant radiation injury.

No

In most cases HBO_2 should be initiated. 2.4 ATA is preferred for 90 minutes of O_2 per treatment. Typically, 40 treatments are required. In some instances, up to 60 treatments are appropriate, especially for brain. Rarely, HBO_2 may exceed 60 treatments, though peer review should be obtained. If initially responsive but then recurrent symptoms, a repeat course is likely appropriate. HBO_2 should be combined with other appropriate medical or surgical interventions. Prior to surgery in a radiated field, 20 to 30 pre-operative treatments should be given. If there is a wound, wound care as in other hypoxic tissues is needed. A team effort including oncologists, surgeons and endoscopists will optimize patient outcome.

Case

- 37/M
- Rt. Maxillary sinus sarcoma : 중입자가속기 치료 (일본)
- 2018년 4월 본원 방문
- 본원 방문 전 저압산소치료…

Further progression of treatment-related necrosis in right maxillary sinus with bony erosions/defects.

Further progression of diffuse T2-high signal edematous change with enhancements in adjacent right masticator muscles and facial soft-tissue, right PPF, and in bone marrows in adjacent maxilla, sphenoid bone and skullbase.
Increased extent of sinusitis.
-> overall, treatment-related change
NC or sl. more increased size of multiple enhancing LNEs in covered both neck.
-> DDx. 1> immune therapy-related changes >
2> metastasis still cannot be excluded

환자 분은 상기 소견으로 치료 중이신 분으로 rt maxillary sinus cancer 치료 부위에 광범위한 염증 및 괴사 소견 보여 추가적인 고압산소 치료를 고려하실 수 있을 것으로 판단됩니다. 부디 고진선처 부탁드립니다. 감사합니다.

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Thank you

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