

Mandibular Osteoradionecrosis

Dick Clarke, CHT

Mandibular Osteoradionecrosis

Review & Update

Primary Training in Hyperbaric Medicine
Columbia, South Carolina

“Late radiation tissue injury is a sign of success”

Sanders M, Dische S.
2002 ESTRO Meeting, Prague



Radiation tissue injury; “non-target” tissues

Acute effects: DNA damage, cell death-rapidly proliferating cells
self-limiting +/- RT pause

Late effects: chronic oxidative stress
dose-dependent > complex wounds/organ loss

“consequential vs. generic”

(3 - 7,400 cGy range)	No. Cases
< 5,000 cGy	5
5 - 6,000 cGy	24
6 - 7,000 cGy	33
> 7,000 cGy	42

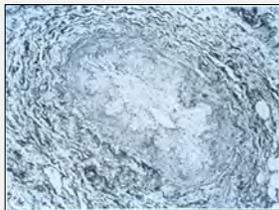
90% traumatically-induced

Table 2
The impact of the dose of radiotherapy (RT) on frequency of osteoradionecrosis. Data are No. (%).

Dose of RT (Gy)	Patients (percentage)
<40	8 (8.8)
40.1 - 45.0	5 (5.5)
45.1 - 50.0	4 (4.4)
50.1 - 55.0	5 (5.5)
55.1 - 60.0	15 (16.5)
>60	54 (59.3)

CLINICAL ARTICLES

Osteoradionecrosis: A New Concept of Its Pathophysiology
Khanlou N, et al. 2007



Marx RE, J Oral Maxillofac Surg 1983;41:283-288

CARNIVAL ARTICLES

A New Concept in the Treatment of Osteoradionecrosis
Khanlou N, et al. 2007

Marx ORN Protocol

- Stage I. HBO as primary therapy
- Stage II. Indication for surgery post-HBO ~ sequestrectomy
- Stage III. Mandible resection/fixation
- Stage III-R. Mandible reconstruction

Marx RE, J Oral Maxillofac Surg 1983;41:351-357

CLASSIFICATION AND TREATMENT STRATEGIES FOR OSTEORADIONECROSIS OF THE MANDIBLE

Investigator	Classification	Treatment Strategy
Marx RE	A new concept in the treatment of osteoradionecrosis. J Oral Maxillofac Surg 1983;41:351-357	Stage I: System of HBO used to allow natural healing Stage II: Grade 1 non-responsive after 1000 hyperbaric oxygenation treatments Stage III: Grade 2 non-responsive after 1000 hyperbaric oxygenation treatments Stage III-R: An additional 100 doses of HBO given to patients who needed a bone graft
Collin F	The incidence and management of osteoradionecrosis of the jaws following head and neck radiotherapy. Br J Oral Maxillofac Surg 1983;25:331-337	Major: Local sequestrectomy that may require osteotomy over several weeks Major: Bone exposure with debridement to the white thickness of the jaw, pathological fracture treatment protocol
Mason GC	Osteoradionecrosis: a study of the incidence in the North West of England. Br J Oral Maxillofac Surg 1983;25:338-342	Major: Bone exposure with debridement and a history of spontaneous healing bony sequestra Moderate-Major: Local sequestrectomy in patients with a residual spontaneously large area of exposed bone and sequestra, some fracture and fixation
Epstein D, et al	Osteoradionecrosis: clinical experience and a proposed classification. J Oral Maxillofac Surg 1983;41:338-342	Stage 1: Resected/fixated, with or without pathological fracture Stage 2: Osteotomy/sequestrectomy, with or without pathological fracture Stage 3: Active/sequestrectomy, with or without pathological fracture
Chen M, et al	Osteoradionecrosis: resection using osteoscopy. J Oral Maxillofac Surg 1983;41:338-342	Stage 1: Bone exposure with debridement and sequestrectomy Stage 2: Bone exposure with debridement and sequestrectomy, with or without pathological fracture Stage 3: Bone exposure with debridement and sequestrectomy, with or without pathological fracture
Stewart J, et al	Radionecrosis of the mandible: a retrospective analysis of the incidence and risk factors. Br J Oral Maxillofac Surg 1983;25:338-342	Stage 1: Bone exposure with debridement and sequestrectomy, with or without pathological fracture Stage 2: Bone exposure with debridement and sequestrectomy, with or without pathological fracture Stage 3: Bone exposure with debridement and sequestrectomy, with or without pathological fracture Stage 4: Bone exposure with debridement and sequestrectomy, with or without pathological fracture Stage 5: Bone exposure with debridement and sequestrectomy, with or without pathological fracture
Chen M, et al	Clinical outcomes in oral and maxillofacial surgery post bone. Management of dental extraction in	Type 1: Fracturing with bone grafts using bone grafts or tissue

Maxillary jaw: a protocol without hyperbaric oxygenation

Investigator	Classification	Treatment Strategy
Wong W, et al	Conservative management of osteoradionecrosis. J Oral Maxillofac Surg 1983;41:351-357	Type II: Bone exposure with secondary contamination, an aggressive fracture Stage 1: Bone exposure with debridement and sequestrectomy Stage 2: Bone exposure with debridement and sequestrectomy Stage 3: Bone exposure with debridement and sequestrectomy Stage 4: Bone exposure with debridement and sequestrectomy
Stewart J, et al	Mandibular osteoradionecrosis: clinical behavior and management aspects. J Oral Maxillofac Surg 1983;41:351-357	Stage 1: Radiological evidence of necrotic bone with intact mucosa Stage 2: Radiological evidence of necrotic bone with exposed mucosa Stage 3: Radiological evidence of necrotic bone with exposed mucosa and sequestra Stage 4: Radiological evidence of necrotic bone with exposed mucosa and sequestra
Schwartz JC, Page JA	Osteoradionecrosis of the mandible: a retrospective analysis. J Oral Maxillofac Surg 1983;41:351-357	Stage 1: Superficial involvement of the mandible only Stage 2: Isolated involvement of the mandible, with or without tooth loss Stage 3: Diffuse involvement of the mandible, with or without tooth loss Stage 4: Diffuse involvement of the mandible, with or without tooth loss
Stewart J, et al	Management of mandibular osteoradionecrosis: corresponding to the severity of osteoradionecrosis and the method of radiotherapy. J Oral Maxillofac Surg 1983;41:351-357	Stage 1: ORN limited to alveolar bone Stage 2: ORN limited to the alveolar bone and/or above the level of the inferior alveolar canal Stage 3: ORN under the lower part of the inferior alveolar canal, with tooth or bone fracture Stage 4: ORN under the lower part of the inferior alveolar canal, with tooth or bone fracture
Tan Y, et al	Osteoradionecrosis and radiation dose to the mandible in patients with oropharyngeal cancer. J Oral Maxillofac Surg 1983;41:351-357	Stage 1: Bone exposure with debridement and sequestrectomy Stage 2: Bone exposure with debridement and sequestrectomy Stage 3: Bone exposure with debridement and sequestrectomy

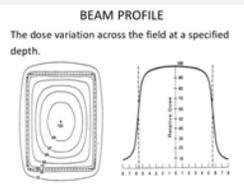
Management of mandibular osteoradionecrosis corresponding to the severity of osteoradionecrosis and the method of radiotherapy

Investigator	Classification	Treatment Strategy
Khanlou N, et al	Management of mandibular osteoradionecrosis corresponding to the severity of osteoradionecrosis and the method of radiotherapy. J Oral Maxillofac Surg 1983;41:351-357	Stage 0: Bone exposure more than 3, priority, no direct change in imaging Stage 1: Bone exposure with no radiological changes on imaging, with or without sequestra Stage 2: Bone exposure with distinct changes on imaging, with or without sequestra Stage 3: Radiologically bone involving the lower border of the mandible Stage 4: <3 cm length of bone affected, asymptomatic Stage 5: <3 cm length of bone affected, involving fracture or tooth fracture Stage 6: <3 cm length of bone affected, involving fracture or tooth fracture Stage 7: <3 cm length of bone affected, involving fracture or tooth fracture Stage 8: <3 cm length of bone affected, involving fracture or tooth fracture Stage 9: <3 cm length of bone affected, involving fracture or tooth fracture
Epstein D, et al	Osteoradionecrosis: a review of current concepts in defining the extent of the disease and a new classification proposal. Br J Oral Maxillofac Surg 1983;25:338-342	Stage 1: ORN limited to alveolar bone Stage 2: ORN limited to the alveolar bone and/or above the level of the inferior alveolar canal Stage 3: ORN under the lower part of the inferior alveolar canal, with tooth or bone fracture Stage 4: ORN under the lower part of the inferior alveolar canal, with tooth or bone fracture
Wong W, et al	Conservative management of osteoradionecrosis of the mandible: presenting a new concept in treatment and staging systems. J Oral Maxillofac Surg 1983;41:351-357	Type 1: Fracturing with bone grafts using bone grafts or tissue Type 2: Fracturing with bone grafts using bone grafts or tissue Type 3: Fracturing with bone grafts using bone grafts or tissue
Collin F, et al	Classification of osteoradionecrosis of the mandible. J Oral Maxillofac Surg 1983;41:351-357	Type 1: Fracturing with bone grafts using bone grafts or tissue Type 2: Fracturing with bone grafts using bone grafts or tissue Type 3: Fracturing with bone grafts using bone grafts or tissue
Stewart J, et al	Management of mandibular osteoradionecrosis: corresponding to the severity of osteoradionecrosis and the method of radiotherapy. J Oral Maxillofac Surg 1983;41:351-357	Type 1: Fracturing with bone grafts using bone grafts or tissue Type 2: Fracturing with bone grafts using bone grafts or tissue Type 3: Fracturing with bone grafts using bone grafts or tissue

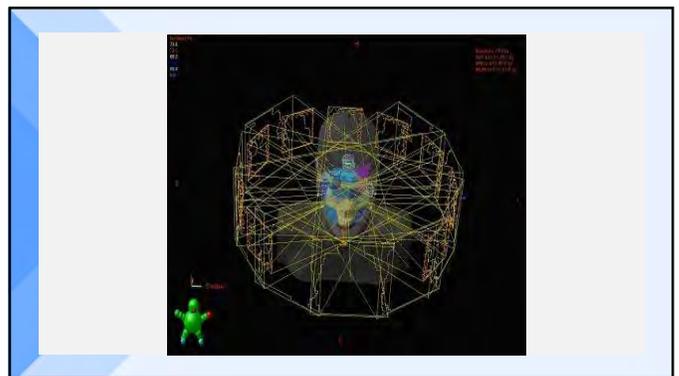
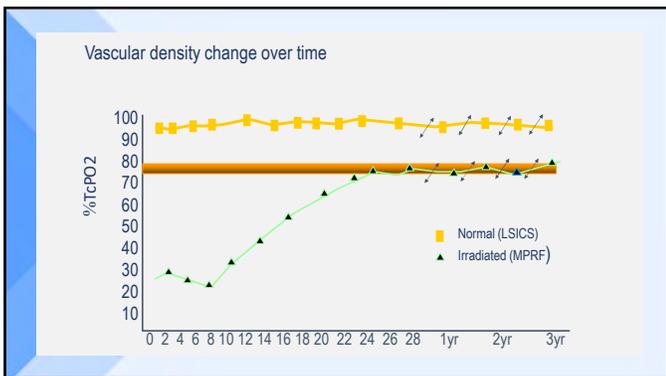
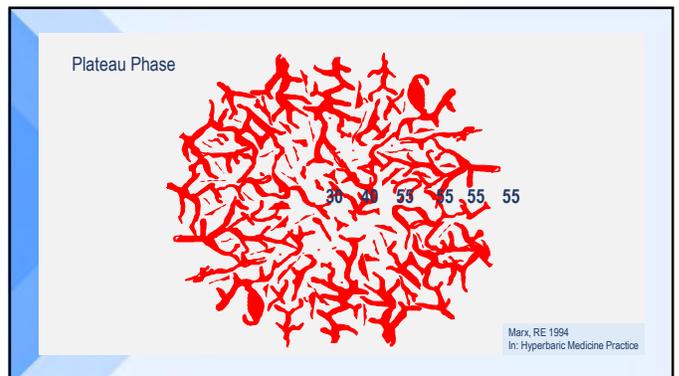
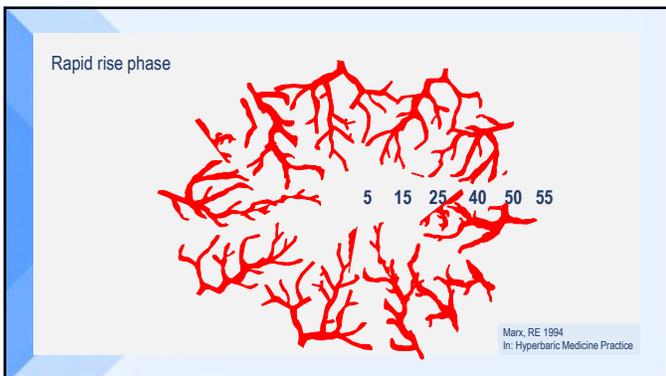
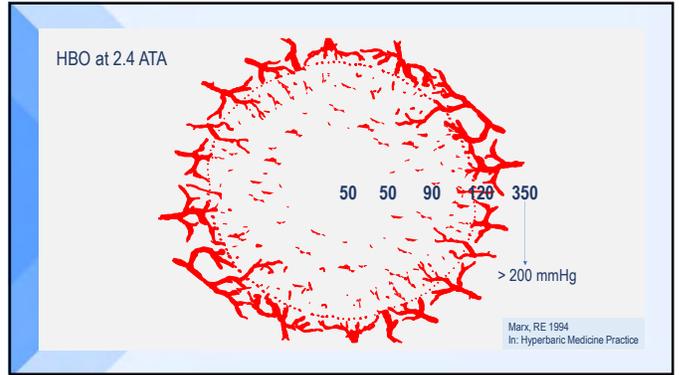
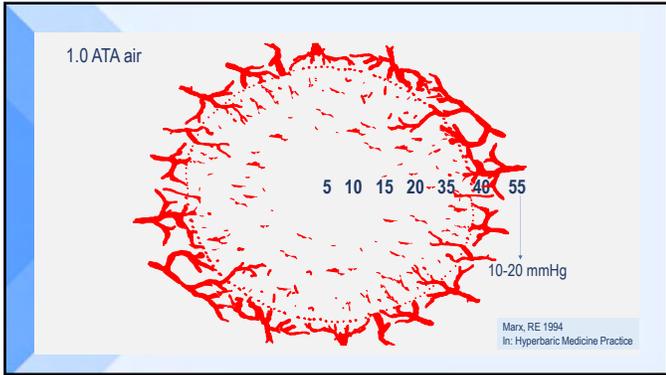
Radiation damaged tissue as a unique wound

Regulation of wound-healing # C_{60} - C_{70} angiogenesis - Effect of oxygen gradients and inspired oxygen concentration

BEAM PROFILE
The dose variation across the field at a specified depth.



Knighton DR, et al. Surgery 1981;90(2)

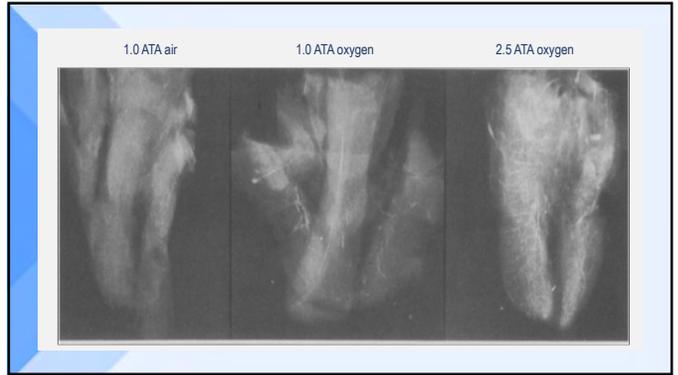


Micro-angiogenic vascular density

	Normobaric Air (N=7)	Normobaric Oxygen (N=14)	Hyperbaric Oxygen (N=14)
Maximum VDE	18	19	99
Minimum VDE	6	6	78
Mean VDE	13	13	93

Normobaric air vs. Normobaric O₂: $p < 0.89$
 Normobaric O₂ vs. Hyperbaric O₂: $p < 0.01$
 Normobaric air vs. Hyperbaric O₂: $p < 0.01$

Marx RE, et al. 1990
 Am J Surgery, 160



Effect of hyperbaric oxygen treatment on oxygen tension and vascular capacity in irradiated skin and mucosa

20 pts hx H/N RT 50-70 Gy.
 ORN or ORN prophylaxis

Randomly allocated HBO vs. no-HBO

Skin & mucosal tissue perfusion measurements
 Transcutaneous oximetry & Doppler flowmetry

pre-HBO & 6 months post-HBO
 controls 6 months apart

Svalestad J, et al. Int J Oral Maxillo Surg 2014;43

tcpO₂ measurements pre/post HBO vs. controls

	HBO group	3 months	6 months	Controls	6 months	
Forehead	Baseline	39.8 +/-15.75	39.87 +/-11.25	41.3 +/-10.5	43.6 +/-10.5	
	O ₂	140.3 +/-71.3	135.8 +/-37.5	137.3 +/-38.3	127.5 +/-55.5	113.3 +/-39.8
Cheek	Baseline	29.3 +/-13.5	42.8 +/-15.7 *	42.8 +/-7.5 *	31.5 +/-9	29.3 +/-11.3
	O ₂	105.0 +/-43.5	150.85 +/-63.8 *	148.5 +/-48.8 *	105.0 +/-37.5	95.3 +/-34.5
Intercostal	Baseline	54.0 +/-13.5	54.8 +/-15	59.3 +/-9.75	64.5 +/-18	62.3 +/-14.3
	O ₂	148.2 +/-52.5	156.8 +/-52.5	156.8 +/-43.5	116.3 +/-33	145.5 +/-45.0

* P < 0.05 compared to baseline

Effect of hyperbaric oxygen treatment on irradiated oral mucosa: microvessel density

Same 20 pts hx H/N

Buccal oral mucosa tissue samples

pre-HBO & 6 months post-HBO
 controls 6 months apart

Svalestad J, et al. Int J Oral Maxillo Surg 2015;44

Vascularization & cell proliferation

	HBO Group			Controls				
Blood vessels	Baseline	6 months	p	Baseline	6 months	p		
Sub-epithelial	MVD	45.4 +/- 13.9	98.0 +/- 15.9	0.002	45.6 +/- 15.7	49.3 +/- 10.5	NS	
	MVA	1.5 +/- 0.6	4.4 +/- 1.9	0.003	1.5 +/- 0.6	1.6 +/- 0.5	NS	
Deeper connective tissue	MVD	30.4 +/- 10.1	45.1 +/- 16.4	0.01	28.1 +/- 9.6	34.4 +/- 7.8	NS	
	MVA	2.5 +/- 1.3	3.7 +/- 1.3	0.041	2.2 +/- 0.9	2.7 +/- 1.4	NS	
Lymph vessels	Sub-epithelial	MVD	18.3 +/- 8.1	36.1 +/- 12.6	0.002	19.4 +/- 6.2	16.9 +/- 8.8	NS
		MVA	1.3 +/- 0.7	2.7 +/- 1.8	0.019	1.2 +/- 0.6	1.5 +/- 0.7	NS

Marx ORN protocol

Marx Stage I: Localized/early disease
30 HBO treatments

Stage I responder

- decreased amount of exposed bone
- resorption or spontaneous sequestration
- softening of exposed bone!



Marx Stage II:
Stage I "non-responder"

- Local surgical debridement or resection
- 10 HBO treatments post-operatively

Marx Stage III/III-R:

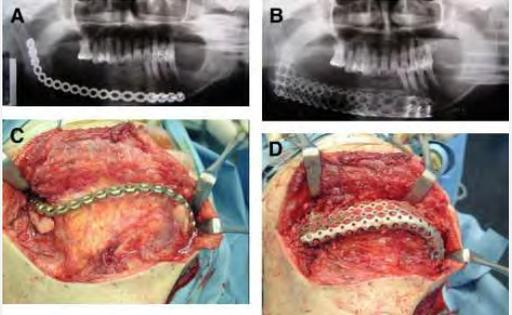
- Extensive mucosal loss & more necrotic bone
- Soft tissue fistula; pathologic fracture; bone resorption; Stage II non-responder

Following initial 30 treatments:

- Partial jaw resection; fixation; primary closure of any fistulae
- Resection of RT damaged soft tissue & skin flap repair
- Ten additional treatments

10-12 weeks after resection > formal reconstruction

- Titanium fixation plate; titanium/Dacron tray-filled cancellous bone chips
- +/- ten additional treatments



Prospective study; complications within irradiated soft tissue > 6,400 cGy

Wound Infections	N	Minor	Major	Total	
Non-HBO	80	6 (7.5%)	13 (16%)	19 (24%)	P= 0.001
HBO	80	3 (3.5%)	2 (2.5%)	5 (6%)	

Wound Dehiscence	N	Minor	Major	Total	
Non-HBO	80	12 (15%)	26 (33%)	38 (48%)	P= 0.001
HBO	80	6 (7.5%)	3 (3.5%)	9 (11%)	

Delayed Healing	N	Minor	Major	Total	
Non-HBO	80	44 (55%)			P= 0.005
HBO	80	9 (11%)			

Marx, RE 1994
In: Hyperbaric Medicine Practice



Study design

- 134 consecutive ORN pts assessed
- 12 centers; 1997-2001
- 68 randomized & analyzed
- 31 HBO - 37 sham
- Study stopped at 2nd interim analysis
- HBO 19% healed
- Sham 32% healed
- "Need for surgery = HBO failure"

Annane D, et al. J Clinical Oncology 2004;22(24)

Study design

97 ORN pts randomized
12 centers; 2008-2017

Required removal necrotic bone
"some pts reconstructed"

Randomly assigned per ITT
51 Surg + HBO vs. 46 Surg.

Primary outcome: ORN healing 1 yr.

70% Surg + HBO vs. 51% Surg.

"HBO did not significantly improve healing..."
"This effect not statistically significant"

Forner L, et al. Radiation & Oncology 2022;166

PENTOCLO
Pentoxifylline - Tocopherol - Clodronate

PENTO
Pentoxifylline - Tocopherol



Delanian S, et al. Int J Rad Oncol Biol Phys 2011

Management of osteoradionecrosis of the jaws with pentoxifylline-tocopherol: a systematic review of the literature and meta-analysis

Kolokythas A, et al. Int J Oral & Maxillofac Surg 2019; 48

The effect of combined application of pentoxifylline and Vitamin E for the treatment of osteoradionecrosis of the jaws: a meta-analysis

Zhang Z, et al. Oral Surg Oral Med Oral Pathol Radio 2020;129

Changing trends and the role of medical management on the outcome of patients treated for osteoradionecrosis of the mandible: experience from a regional head and neck unit

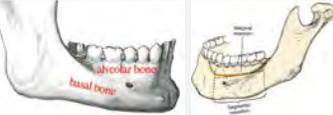
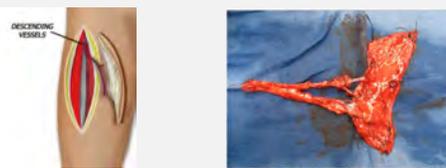
D'Souza J, et al. B J Oral Maxillo Surg 2014;52

	Before 2006			After 2006		
	Number (n=25)	ORN (n=25)	Total (n=50)	Number (n=25)	ORN (n=25)	Total (n=50)
ORN grade						
I	1	1	2	1	1	2
II	1	1	2	1	1	2
III	1	1	2	1	1	2
IV	1	1	2	1	1	2
V	1	1	2	1	1	2
VI	1	1	2	1	1	2
VII	1	1	2	1	1	2
VIII	1	1	2	1	1	2
IX	1	1	2	1	1	2
X	1	1	2	1	1	2
XI	1	1	2	1	1	2
XII	1	1	2	1	1	2
XIII	1	1	2	1	1	2
XIV	1	1	2	1	1	2
XV	1	1	2	1	1	2
XVI	1	1	2	1	1	2
XVII	1	1	2	1	1	2
XVIII	1	1	2	1	1	2
XIX	1	1	2	1	1	2
XX	1	1	2	1	1	2
XXI	1	1	2	1	1	2
XXII	1	1	2	1	1	2
XXIII	1	1	2	1	1	2
XXIV	1	1	2	1	1	2
XXV	1	1	2	1	1	2
XXVI	1	1	2	1	1	2
XXVII	1	1	2	1	1	2
XXVIII	1	1	2	1	1	2
XXIX	1	1	2	1	1	2
XXX	1	1	2	1	1	2
XXXI	1	1	2	1	1	2
XXXII	1	1	2	1	1	2
XXXIII	1	1	2	1	1	2
XXXIV	1	1	2	1	1	2
XXXV	1	1	2	1	1	2
XXXVI	1	1	2	1	1	2
XXXVII	1	1	2	1	1	2
XXXVIII	1	1	2	1	1	2
XXXIX	1	1	2	1	1	2
XL	1	1	2	1	1	2
XLI	1	1	2	1	1	2
XLII	1	1	2	1	1	2
XLIII	1	1	2	1	1	2
XLIV	1	1	2	1	1	2
XLV	1	1	2	1	1	2
XLVI	1	1	2	1	1	2
XLVII	1	1	2	1	1	2
XLVIII	1	1	2	1	1	2
XLIX	1	1	2	1	1	2
L	1	1	2	1	1	2
LI	1	1	2	1	1	2
LII	1	1	2	1	1	2
LIII	1	1	2	1	1	2
LIV	1	1	2	1	1	2
LV	1	1	2	1	1	2
LVI	1	1	2	1	1	2
LVII	1	1	2	1	1	2
LVIII	1	1	2	1	1	2
LVIX	1	1	2	1	1	2
LX	1	1	2	1	1	2
LXI	1	1	2	1	1	2
LXII	1	1	2	1	1	2
LXIII	1	1	2	1	1	2
LXIV	1	1	2	1	1	2
LXV	1	1	2	1	1	2
LXVI	1	1	2	1	1	2
LXVII	1	1	2	1	1	2
LXVIII	1	1	2	1	1	2
LXIX	1	1	2	1	1	2
LXX	1	1	2	1	1	2
LXXI	1	1	2	1	1	2
LXXII	1	1	2	1	1	2
LXXIII	1	1	2	1	1	2
LXXIV	1	1	2	1	1	2
LXXV	1	1	2	1	1	2
LXXVI	1	1	2	1	1	2
LXXVII	1	1	2	1	1	2
LXXVIII	1	1	2	1	1	2
LXXIX	1	1	2	1	1	2
LXXX	1	1	2	1	1	2
LXXXI	1	1	2	1	1	2
LXXXII	1	1	2	1	1	2
LXXXIII	1	1	2	1	1	2
LXXXIV	1	1	2	1	1	2
LXXXV	1	1	2	1	1	2
LXXXVI	1	1	2	1	1	2
LXXXVII	1	1	2	1	1	2
LXXXVIII	1	1	2	1	1	2
LXXXIX	1	1	2	1	1	2
LXXXX	1	1	2	1	1	2
LXXXXI	1	1	2	1	1	2
LXXXXII	1	1	2	1	1	2
LXXXXIII	1	1	2	1	1	2
LXXXXIV	1	1	2	1	1	2
LXXXXV	1	1	2	1	1	2
LXXXXVI	1	1	2	1	1	2
LXXXXVII	1	1	2	1	1	2
LXXXXVIII	1	1	2	1	1	2
LXXXXIX	1	1	2	1	1	2
LXXXXX	1	1	2	1	1	2
LXXXXXI	1	1	2	1	1	2
LXXXXXII	1	1	2	1	1	2
LXXXXXIII	1	1	2	1	1	2
LXXXXXIV	1	1	2	1	1	2
LXXXXXV	1	1	2	1	1	2
LXXXXXVI	1	1	2	1	1	2
LXXXXXVII	1	1	2	1	1	2
LXXXXXVIII	1	1	2	1	1	2
LXXXXXIX	1	1	2	1	1	2
LXXXXXX	1	1	2	1	1	2
LXXXXXXI	1	1	2	1	1	2
LXXXXXXII	1	1	2	1	1	2
LXXXXXXIII	1	1	2	1	1	2
LXXXXXXIV	1	1	2	1	1	2
LXXXXXXV	1	1	2	1	1	2
LXXXXXXVI	1	1	2	1	1	2
LXXXXXXVII	1	1	2	1	1	2
LXXXXXXVIII	1	1	2	1	1	2
LXXXXXXIX	1	1	2	1	1	2
LXXXXXXX	1	1	2	1	1	2
LXXXXXXXI	1	1	2	1	1	2
LXXXXXXXII	1	1	2	1	1	2
LXXXXXXXIII	1	1	2	1	1	2
LXXXXXXXIV	1	1	2	1	1	2
LXXXXXXXV	1	1	2	1	1	2
LXXXXXXXVI	1	1	2	1	1	2
LXXXXXXXVII	1	1	2	1	1	2
LXXXXXXXVIII	1	1	2	1	1	2
LXXXXXXXIX	1	1	2	1	1	2
LXXXXXXXX	1	1	2	1	1	2
LXXXXXXXXI	1	1	2	1	1	2
LXXXXXXXII	1	1	2	1	1	2
LXXXXXXXIII	1	1	2	1	1	2
LXXXXXXXIV	1	1	2	1	1	2
LXXXXXXXV	1	1	2	1	1	2
LXXXXXXXVI	1	1	2	1	1	2
LXXXXXXXVII	1	1	2	1	1	2
LXXXXXXXVIII	1	1	2	1	1	2
LXXXXXXXIX	1	1	2	1	1	2
LXXXXXXXX	1	1	2	1	1	2
LXXXXXXXXI	1	1	2	1	1	2
LXXXXXXXII	1	1	2	1	1	2
LXXXXXXXIII	1	1	2	1	1	2
LXXXXXXXIV	1	1	2	1	1	2
LXXXXXXXV	1	1	2	1	1	2
LXXXXXXXVI	1	1	2	1	1	2
LXXXXXXXVII	1	1	2	1	1	2
LXXXXXXXVIII	1	1	2	1	1	2
LXXXXXXXIX	1	1	2	1	1	2
LXXXXXXXX	1	1	2	1	1	2
LXXXXXXXXI	1	1	2	1	1	2
LXXXXXXXII	1	1	2	1	1	2
LXXXXXXXIII	1	1	2	1	1	2
LXXXXXXXIV	1	1	2	1	1	2
LXXXXXXXV	1	1	2	1	1	2
LXXXXXXXVI	1	1	2	1	1	2
LXXXXXXXVII	1	1	2	1	1	2
LXXXXXXXVIII	1	1	2	1	1	2
LXXXXXXXIX	1	1	2	1	1	2
LXXXXXXXX	1	1	2	1	1	2
LXXXXXXXXI	1	1	2	1	1	2
LXXXXXXXII	1	1	2	1	1	2
LXXXXXXXIII	1	1	2	1	1	2
LXXXXXXXIV	1	1	2	1	1	2
LXXXXXXXV	1	1	2	1	1	2
LXXXXXXXVI	1	1	2	1	1	2
LXXXXXXXVII	1	1	2	1	1	2
LXXXXXXXVIII	1	1	2	1	1	2
LXXXXXXXIX	1	1	2	1	1	2
LXXXXXXXX	1	1	2	1	1	2
LXXXXXXXXI	1	1	2	1	1	2
LXXXXXXXII	1	1	2	1	1	2
LXXXXXXXIII	1	1	2	1	1	2
LXXXXXXXIV	1	1	2	1	1	2
LXXXXXXXV	1	1	2	1	1	2
LXXXXXXXVI	1	1	2	1	1	2
LXXXXXXXVII	1	1	2	1	1	2
LXXXXXXXVIII	1	1	2	1	1	2
LXXXXXXXIX	1	1	2	1	1	2
LXXXXXXXX	1	1	2	1	1	2
LXXXXXXXXI	1	1	2	1	1	2
LXXXXXXXII	1	1	2	1	1	2
LXXXXXXXIII	1	1	2	1	1	2
LXXXXXXXIV	1	1	2	1	1	2
LXXXXXXXV	1	1	2	1	1	2
LXXXXXXXVI	1	1	2	1	1	2
LXXXXXXXVII	1	1	2	1	1	2
LXXXXXXXVIII	1	1	2	1	1	2
LXXXXXXXIX	1	1	2	1	1	2
LXXXXXXXX	1	1	2	1	1	2
LXXXXXXXXI	1	1	2	1	1	2

211-583
Evaluation of Anterolateral Thigh Fascia Lata Rescued Flap for Mandibular Osteoradionecrosis
 Ariangpour K, et al. JAMA Otol Head Neck Surg 2023;149(7):621-627

Notani Stages

1. ORN confined to alveolar bone
2. ORN limited to alveolar bone and/or above level of inferior alveolar canal
3. ORN under lower part of inferior alveolar canal, with fistula or bone fx.

50/52 MORN cases successfully managed
 2 progressed to fibular free flap
 Simple, reliable, low risk
 Low donor site morbidity - ease of harvest

Overview and Emerging Trends in the Treatment of Osteoradionecrosis
 Meleca JB, et al. Curr Treat Options in Oncol 2021;22

Hyperbaric Oxygen Therapy

Standard procedure: Pressures often vary between 2.0 & 2.5 ATA for 60-120 minutes once or twice daily for 30-60 sessions

Contraindications: Tumor recurrence; history of HBO complications

Complications: Tumor recurrence (theoretical, not substantiated by evidence); visual disturbance, barotrauma, oxygen toxicity

Special points: Evidence for HBO treatment & prevention of ORN mixed. Smaller uncontrolled studies have shown recovery with HBO alone or combined with surgery, however, few randomized controlled trials exist. The first showed ORN prevention for dental procedures. Subsequent RCTs have not supported HBO treatment or prevention efficacy. Cochrane Review suggested moderate-quality evidence for increased likelihood to achieve mucosal coverage & prevent post-op breakdown.

Cost-effectiveness: Expensive (often more expensive than surgery given number of visits required and cost of equipment/staffing).

Fasciocutaneous Flaps for Refractory Intermediate Stage Osteoradionecrosis of the Mandible—Is It Time for a Shift in Management?
 Gigliotti J, et al. J Oral Maxillofac Surg 2021;79

"Marx pioneered HBO, no RCTs have replicated his results"
 "Appears little benefit to addition of HBO for advanced stages"

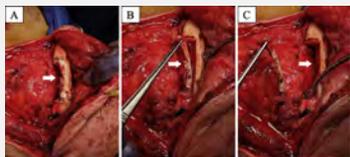
Concept of RT-induced fibro-atrophic theory
 Use of PENTOPENTOCLO promising - better data required



Osteoradionecrosis: Exposing the Evidence Not the Bone
 Frankart AJ, et al. Int J Rad Oncol Biol Phys 2021;109(5)

"The microvascular osteo-myo-cutaneous free flap, such as free fibular flap, has evolved to become a workhorse ..."

"Conservative management including the use of pentoxifylline-vit. E should be attempted before surgical procedures"

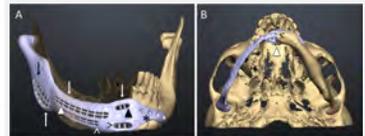


18 pts over 5 yrs

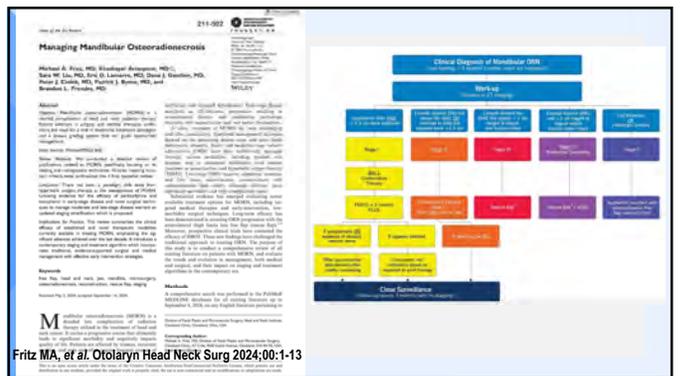
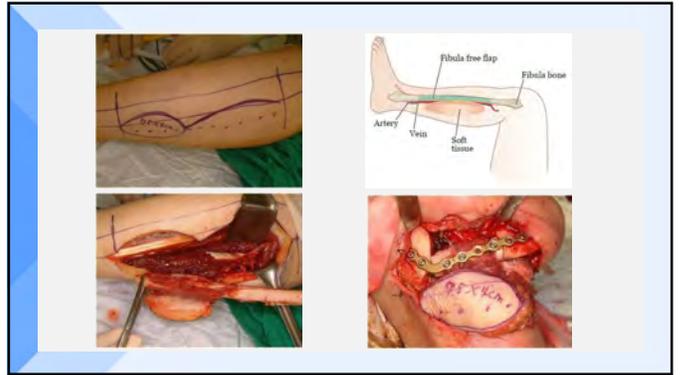
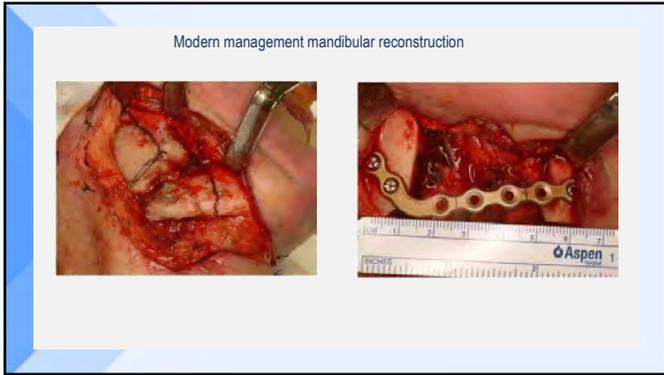
Primary outcomes at 1 yr. achieved in 14/18 (78%)

- absence of extrusion
- decrease/cessation of pain
- stability/increase in mouth opening
- resumption of oral feeding
- absence of fracture/displacement/screw loosening

MRONJ - 10 ORN - 2 SCC - 2 Other - 4



Bedogni A, et al. J Oral Oncology 2021;112



Where does HBO currently stand for ORN?

Stage I - localized

- Four decades clinical practice experience c/w Marx protocol
- Widely, although not exclusively reimbursed
- Not supported by efficacy/effectiveness evidence
- PENTOCLO <100 reported cases; no efficacy evidence
- Recent limited reporting of periosteal & ALT/FFF flaps promising

*Weight of existing evidence supports HBO ***

** Cochrane Database of Systemic Reviews, 2016

Stage III 'advanced'

- Introduction of Marx Protocol (1983) mandible reconstruction
 - ~ HBO reduced failure rates; optimized healing
 - ~ essential standard of care ~ two decades
- Advent of microvascular surgery another step change
- Single-stage radical resection & myo-cutaneous free fibular flap
 - ~ now considered "gold standard" for advanced ORN since 2000
 - ~ HBO occasionally employed for post-op complications
- Marx two-stage protocol in absence of microvascular surgeon



74 pts randomized to HBO or PCN

All high risk > 6,000 cGy

135 teeth extracted in 37 PCN pts
~ 29.9% unhealed sockets at 6 months

156 teeth extracted in 37 HBO pts
~ 5.6% unhealed sockets at 6 months

Marx RE, et al. JADA 1985;111:49-54

ORN prophylaxis protocol

- Basis for 20 pre-op. procedures
 - angiogenesis plateau
- Basis for 10 post-op. procedures
 - reduces dehiscence by promoting collagen production along incision lines




144 pts randomized; HBO vs. no HBO

10 facilities

55 received HBO + surgery

66 received surgery

Mean RT dose 6,300 cGy

Blinded assessors

Trial halted at interim analysis

Data relates to conformal/IMRT

Shaw, R.J., et al. Int J Rad Oncol Bio Phys 2019