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Hyperbaric Oxygen and Postradiation Osteonecrosis of the Mandible

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The clinical and dental records of 26 patients with the clinical diagnosis of postradiation osteonecrosis (PRON) managed with hyperbaric oxygen (HBO) were reviewed to determine the efficacy of HBO. 19 patients were male and 7 were female; age at the first HBO session ranged from 28 to 80 years (median 57.5 years). All but 8 patients reviewed had some form of surgical management; 7 had mandibulectomy for PRON. As part of management, a total of 9–84 HBO sessions (median 35 sessions) was administered. 18 of the 26 patients ultimately achieved persistent mucosal and cutaneous coverage 1–84 months (median 24 months) after the first HBO session. 13 of the 26 patients met strict criteria for resolution of their disease; fully 21 of 26 patients had improved PRON status following HBO therapy. HBO treatment as part of a comprehensive managment plan is safe and effective in the management of PRON.

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INTRODUCTION

POSTRADIATION OSTEONECROSIS (PRON) of the mandible is an uncommon but potentially serious complication of high dose radiotherapy for carcinoma of the head and neck. Its reported incidence ranges from 2.6 to 22% [1–7] in modern series, most commonly 5–15%. Its clinical course is highly variable. With conservative measures, 8–48% [1, 4, 6, 8, 9] of patients might be expected to heal, the remainder being left with residual necrosis which may be symptomatic and/or progressive.

Rankow and Weissman [7] introduced the first widely accepted indications for mandibulectomy for PRON: (1) intractable pain, (2) persistent bone exposure unhealed with medical therapy after 1 year, (3) orocutaneous fistula formation, and (4) pathological fracture of the mandible.

In 1973, Mainous and colleagues [10] reported the first series of cases of PRON of the mandible treated with hyperbaric oxygen (HBO). Other series from Long Beach [11–13] and other centres [9, 14–20] confirmed that HBO could effect healing of soft tissue defects in cases that were otherwise refractory to treatment. The Wilford-Hall protocol [9, 20] represented the first systematic combination of HBO and surgery in the management of PRON. All 70 patients in the series of Marx *et al.* satisfied strict criteria for resolution, specifically: (1) freedom from pain, (2) retention or reconstruction of mandibular continuity, (3) restoration of mandibular function, and (4) maintenance of intact mucosa over bone. Such results are impressive in a highly selected group of patients, most of whom had been refractory to previous treatment. However, in the Wilford-Hall series, 73% of patients progressed through all three stages of the protocol, receiving a total of up to 100 sessions of HBO, in conjunction with mandibular resection and reconstruction.

Our objective was to review the experience in the treatment of PRON with HBO in a primary care oncology centre and to determine whether satisfactory results can be obtained with fewer HBO sessions and less frequent mandibulectomy.

PATIENTS AND METHODS

A retrospective review was undertaken of the medical and dental records, and treatment records and films, of all patients with the clinical diagnosis of PRON of the mandible that were referred from the British Columbia Cancer Agency, Vancouver Clinic, to the Hyperbaric Unit at the Vancouver General Hospital, and received HBO treatment. Where possible, an estimate of the dose of irradiation that had been administered to the necrotic defect was made, and then converted to a parameter for Biologically Effective Dose (BED) as described by Fowler [21] (e.g. 60 Gy in 30 fractions, BED = 100 Gy_3).

The extent and nature of necrosis of soft tissue and bone both before and after treatment was defined after the classification of Epstein *et al.* [1] which is outlined in Table 1. Complete resolution of PRON was defined following the strict criteria of Marx *et al.* [9].

All patients were managed in a multidisciplinary head and neck oncology clinic with the participation of experienced radiation oncologists, surgeons, and dentists. All patients were treated with conservative measures, with the addition of HBO and surgery when it was deemed necessary; these included:

—counselling to stop smoking and limit alcohol consumption,
—rigorous oral hygiene measures including hydrogen peroxide and/or chlorhexidine oral rinses,
—comprehensive dental care including gentle sequestrectomies, when necessary,
—oral antibiotics (usually tetracycline),

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Table 1. Clinical classification of osteoradionecrosis of the mandible (Epstein, Wong and Stevenson-Moore, 1987)

Resolved, healed
(a) No pathological fracture
(b) Pathological fracture
Chronic persistent (non-progressive)
(a) No pathological fracture
(b) Pathological fracture
Active progressive
(a) No pathological fracture
(b) Pathological fracture

—analgesics and other symptomatic measures.

Vigorous efforts to rule out recurrent disease as a cause of mucocutaneous defects were made where possible, although biopsies were usually avoided if PRON was suspected clinically.

At our institution, approximately half of all PRON patients had HBO. The criteria for referral generally included progressive necrosis or symptomatic disease. In the study period, treatment policies at the Hyperbaric Unit did vary. HBO was delivered in a multiplace chamber at 2.5 ATA (atmospheres absolute), with 100% oxygen for 90 min per dive, with the total number of dives depending upon consultation between the referring and hyperbaric physicians, the response of the lesion, patient tolerance to treatment, and whether surgery was also to be performed.

RESULTS

Between 1975 and 1988, 26 patients received HBO for PRON of the mandible; relevant preHBO data are given in Table 2. 19 patients were males and 7 were females; age at the time of first session of HBO ranged from 28 to 80 years (median 57.5 years). Associated medical conditions included hypertension alone in 1 patient, non-insulin dependent diabetes mellitus in 1 patient, and chronic obstructive pulmonary disease, hypertension, and insulin dependent diabetes mellitus in 1 patient.

1 patient received irradiation at another centre and was referred to the B.C. Cancer Agency with the diagnosis of PRON; in the remaining 25 patients, radiotherapy had been administered at the Vancouver Clinic. The known tumour volume along with a 1.0 cm margin of normal tissue was usually included within the high dose volume (90% isodose surface). Although no effort was made to undertake prophylactic total nodal irradiation, most often at least ipsilateral first echelon nodes were included within this volume; in no patient was prophylactic neck dissection performed. Prescribed tumour doses are given in Table 2; BED ranged from 99 to 127 Gy_3 (median 109 Gy_3). 5 patients in whom brachytherapy was performed and treatment data were available were treated with single plane implantation. In 1 patient, technique and dose were unknown. A definite effort was made to exclude the mandible from the high dose volume in all brachytherapy patients. It was possible to estimate the dose that had been administered to the mandible that later became osteonecrotic in 17 of 26 patients. The BED to the osteonecrotic mandible was less than 100 Gy_3 in only 1 patient, and was higher than 120 Gy_3 in 5 patients (median 109 Gy_3).

Details of PRON management are given in Table 3. 19 of 26 patients also had surgery as part of management of PRON. 7 patients had mandibulectomy for necrosis; 1 other patient had previously had a mandibulectomy for recurrent disease. Surgery and HBO were combined in a planned approach in only 8 patients. Within this group, 2 patients were to have had HBO followed by surgery, 2 had surgery followed by HBO, and 3 had HBO both pre- and postoperatively, respectively. Of these, 1 patient refused surgery and further HBO, after an initial HBO course; another patient did not receive a postoperative second course due to lack of funds.

22 patients received a single course of HBO therapy. 3 patients received two series of treatments, 2 in a planned pre- and postoperative setting, and 1 for progressive, recurrent PRON. 1 patient received three courses of HBO therapy, the first being discontinued because of claustrophobia and the second and third administered pre- and postmandibulectomy. In 4 patients, the HBO course was clearly incomplete, 1 for "inconvenience", 1 for lack of funds, 1 for patient noncompliance and 1 because of claustrophobia.

In only 3 patients was reconstruction attempted postmandibulectomy. Patient no. 1 had an iliac and Dacron graft applied, with HBO therapy pre- and postoperatively, and remains healed at 26 months after surgery. Patient no. 11 had an ileocutaneous flap which later necrosed, despite postoperative HBO; subsequent to sequestrectomy and further conservative management, there was complete mucosal healing and pain relief at 25 months postreconstruction. Patient no. 12 had an initial rib graft which necrosed and a second ileocutaneous flap which was successful, neither under cover of HBO complete healing persisted at 46 months after the second surgery; osseointegrated implants were later inserted without complication.

Patients were followed for 8 to 156 months (median 38 months) after HBO treatment. Patient nos 1, 14 and 25 were lost to follow-up. Patient nos 5, 20, 22 and 23 died of carcinoma of the prostate, cerebrovascular accident, alcoholic liver disease, and carcinoma of the lung, respectively. Patient nos 6 and 7 died of local and distant recurrences of their head and neck malignancies, respectively. There was no morbidity of HBO therapy, apart from 1 patient with complaints of transient minor blurring of vision.

18 of 26 patients achieved consistent mucosal and cutaneous coverage 1 to 84 months (median 24 months) after the first HBO session. 16 of the 26 patients were completely pain free, and 13 of them met the strict Wilford–Hall criteria for resolution of PRON. Of these, 11 were managed with conservative surgery and HBO. 21 patients had an ultimately improved PRON status, after the classification of Epstein *et al.* [1].

Table 4 gives the preHBO and ultimate PRON status. In this series, there was no apparent relationship between the probability of healing and time between onset of PRON and first HBO session, total number of HBO sessions, or use and type of surgery in management of necrosis. However, it appeared that there was a reduced probability of resolution of PRON in association with the presence of active progressive disease or pathological fracture.

Qualitatively it was noted that pain relief and hastening of healing of mucosal and cutaneous deficits occurred as early as the first few HBO sessions in many patients. This also applied to many of the patients in whom signs and symptoms of PRON had persisted with many months of other medical conservative therapies.

Patient no 25, in whom complete healing occurred 15 months after HBO treatment, developed recurrent pain and

Table 2. PreHBO patients' characteristics

Patient no.	Tumour histology/ site	TNM stage*	XRT type	XRT† dose	PRON precipitant	Time XRT to PRON (months)	Time PRON to HBO (months)
1	SCC Tongue	T2NOMO	TELE	52.5 Gy/ 15‡	Surgery	4	2
2	SCC Tongue	T1NIMO	BRACHY	67.5 Gy in $6\frac{1}{2}$ days	Spontaneous	4	4
3	SCC FOM	T2NIMO	TELE	64.0 Gy/ 25‡	PostXRT extraction	24	72
4	SCC FOM	T2N3MO	TELE	60.0 Gy/ 25‡	Surgery	3	2
5	SCC Buccal Mucosa	T2NOMO	TELE	65.0 Gy/ 25‡	Surgery	5	6
6	SCC Tongue	T3NOMO	TELE	60.0 Gy/ 25‡	Spontaneous	19	1
7	SCC FOM	T2NOMO	TELE	60.0 Gy/ 25‡	Surgery	5	0
8	SCC Tongue	T2NOMO	BRACHY	64.9 Gy in 6 days	Spontaneous	20	5
9	SCC FOM	T2NOMO	TELE	55.0 Gy/ 15‡	PostXRT extraction	28	17
10	SCC Tonsil	T1NOMO	TELE	60.0 Gy/ 25‡	PostXRT extraction	7	12
11	SCC Lower alveolus	T4NOMO	TELE	52.5 Gy/ 15‡	PreXRT extraction	0	22
12	SCC FOM	T2NOMO	TELE	62.4 Gy/ 26‡	Surgery	4	1
13	Pleomorphic adenoma palate	N/A	TELE	55.0 Gy/ 15‡	PostXRT extraction	60	18
14	SCC Lower alveolus	T2N1MO	TELE	60.0 Gy/ 25‡	Surgery	3	0
15	SCC FOM	T1NOMO	BRACHY	72.0 Gy at infinity	Surgery	12	48
16	SCC FOM	T2N1MO	TELE	60.0 Gy/ 25‡	PostXRT extraction	9	22
17	SCC Lower alveolus	T2NOMO	TELE	60.0 Gy/ 25‡	PreXRT extractions	2	2
18	SCC Tongue	T4N2MO	TELE	55.0 Gy/ 15‡	Surgery	60	12
19	SCC FOM	T2NOMO	TELE + BRACHY	?	Spontaneous	25	48
20	SCC Tonsil	T1NOMO	TELE	64.8 Gy/ 27‡	Spontaneous	72	3
21	SCC Soft palate	T2NOMO	TELE	60.0 Gy/ 25‡	Spontaneous	96	12
22	SCC Tonsil	T2NOMO	TELE	60.0 Gy/ 25‡	Spontaneous	34	11
23	SCC Lower alveolus	T3N1MO	TELE	60.0 Gy/ 25‡	Surgery	38	13
24	SCC FOM	T1N1MO	BRACHY	87.7 Gy/ at infinity	PostXRT extraction	26	1
25	SCC FOM	T1NOMO	BRACHY	74.5 Gy/ at infinity	PostXRT extraction	26	1
26	SCC FOM	T2N1MO	TELE	55.0 Gy/ 16‡	PostXRT extraction	5	90

*UICC/AJCC, 1987. †Prescribed tumour dose; for brachytherapy, at 0.5 cm treating distance. ‡Fractions (one per day, five per week, all fields daily). SCC = squamous cell carcinoma. FOM = floor of mouth. XRT = radiotherapy.

Table 3. HBO treatment details and results

Patient no.	PreHBO PRON stage*	Number HBO sessions	PRON surgery	Time HBO start to healing (months)	Follow-up (months)	Final PRON stage*
1	IIA	71	Mandib	1	39	IA
2	IIA	15	Alveol	14	168	IA
3	IIA	43	None	N/A	84	IIA
4	IIA	37	None	20	20	IIA
5	IIA	12	None	24	108	IA
6	IIA	16	Seq	3	60	IA
7	IIA	12	Mandib	3	11	IA
8	IIA	23	Seq	13	46	IA
9	IIIA	20	Mandib	7	37	IA
10	IIIB	39	Mandib	68	68	IA
11	IIIB	39	Mandib	27	39	IA
12	IIA	84	Mandib	3	76	IA
13	IIA	30	None	N/A	72	IIB
14	IIIA	47	Closure OCF	N/A	21	IIIB
15	IIA	43	Alveol	2	35	IA
16	IIIA	15	None	38	38	IA
17	IIB	20	Mandib	6	37	IA
18	IIIB	17	Seq	N/A	35	IIA
19	IIA	59	Alveol	N/A	34	IIA
20	IIA	47	Alveol	6	9	IA
21	IIIB	23	None	N/A	42	IIB
22	IIIB	34	Alveol	8	53	IB
23	IIIB	38	None	N/A	6	IIB
24	IIA	53	Alveol	84	156	IA
25	IIA	35	Seq	15	25	IA
26	IIB	9	Seq	12	38	IA

*Epstein–Wong classification [1]. Mandib = mandibulectomy. Alveol = alveolectomy. Seq = sequestrectomy. OCF = orocutaneous fistula.

Table 4. PreHBO and final osteoradionecrosis stages

	Initial stage	IIA	IIB	IIIA	IIIB
Final stage	IA	11	2	2	2
	IB	—	—	—	—
	IIA	3	—	—	1
	IIB	1	—	—	2
	IIIA	—	—	—	—
	IIIB	—	—	1	—

mucosal defects another 18 months later and awaits further treatment. Patient nos 13, 18 and 19 healed completely 48, 6 and 17 months after HBO treatment, respectively,and developed recurrent signs of PRON a further 2, 12 and 10 months later, respectively. Osteonecrotic disease has persisted in these 3 patients despite further medical therapy.

DISCUSSION

Osteonecrosis was first reported in 1922 by Regaud [22], but mandibular osteonecrosis was not seem with any frequency until the 1950s when irradiation of head and neck malignancies became more common. The mandible has been thought to be particularly susceptible to PRON due to its blood supply and the dense configuration of its bone structure.

The pathology of irradiated rhesus monkey mandible has been examined [23], histological preparations revealed a decreased number of osteocytes and decreased vascularity of the periosteum, with fibrosing endarteritis of the inferior alveolar artery and of blood vessels in the bone marrow and haversian canals. Other authors have seen similar changes in human specimens [24]. Until recently, the most widely accepted hypothesis for the pathogenesis of osteonecrosis was that radiation rendered tissue susceptible to trauma which results in a portal for introduction of bacteria into relatively avascular tissue [25]. It has since been shown in histological sections and bacterial cultures that although microorganisms are present on the surface of necrotic bone, the necrotic bone itself is sterile [26]. Marx has summarised the concept of the development of hypoxic–hypovascular–hypocellular tissue, in which the tenuous equilibrium between the demand and supply of energy, oxygen and other metabolic needs may be disturbed by surgery, denture trauma or dental extractions [9, 26, 27]. Necrotic sites have been found to be hypoxic by transcutaneous measurements [28]. Infrared spectroscopy has suggested that such sites may also be associated with decreased amounts of deoxygenated haemoglobin [29].

Certain treatment factors appear to influence the risk of PRON. Primary radiotherapy of tumours adjacent to the mandible or clinically invading it [2, 5] appears more likely to result in necrosis. There also appears to be a positive relationship between dose [2, 3, 5, 30], high dose volume [8, 31], and risk of necrosis. In our series certainly, osteonecrotic sites appeared to be within the high dose volume in the vast majority of patients. The use of orthovoltage irradiation in large part may account for reported incidences of osteonecrosis before 1970 as high as 35% [5]. The use of brachytherapy [5] and particular teletherapy field arrangements [3] may also influence the risk of PRON. Patient factors which may also influence this risk include presence or absence of dentition [5],

periodontal disease, dental caries [8] and concurrent systemic disease, specifically hypertension, diabetes mellitus, and other conditions that may have effects on systemic microvasculature.

Efforts to prevent PRON have been important in reducing its incidence. Dental hygiene measures including the discontinuation of tobacco products and alcohol during and after irradiation are likely also to be of benefit. Thorough dental assessment before treatment may optimise dentition and reduce the potential for denture trauma. Although many authors agree that postradiation extractions should be avoided if possible [6, 30], many feel that dental extractions are safe if done judiciously and at least 2–3 weeks before commencement of irradiation [30]. If surgery later becomes necessary in the management of malignant disease, irradiated tissue should be handled as gently as possible. Efforts may be made during the planning phase of irradiation to avoid the use of orthovoltage apparatus, the use of brachytherapy in lesions immediately adjacent to the mandible, the inclusion of large volumes of the mandible in the high dose volume, and the administration of very high doses to any portion of the mandible. Lesions that involve bone may best be managed surgically. Careful follow-up to prevent trauma is likely also to reduce the probability of ultimate development of osteonecrosis.

Despite such efforts, the incidence of PRON of the mandible after iradiation of the oral cavity is not negligible. It has been reported that 11–74% of patients who develop PRON have no identifiable contributory traumatic factors, i.e. are "spontaneous" cases [1, 5, 8]. Therefore, in any centre that treats head and neck malignancies with irradiation, there will be patients with PRON who require assessment and treatment.

The clinical course of PRON is highly variable. Most cases present within the first year following irradiation, but many others may develop many years later [1, 6, 8]. The risk of PRON after radiation treatment must therefore be considered to be permanent. Some patients have minimal bone exposure while others may have extensive bone exposure with considerable rarefaction of mandibular bone. Similarly, osteonecrosis may remain stable for many years or may progress rapidly with the development of pathological fracture and/or orocutaneous fistula. Many patients with necrosis have pain which may be severe while still others may be entirely asymptomatic. A clinical classification of osteoradionecrosis was recently introduced [1]; it is hoped that this may facilitate the development of protocols for treatment of osteonecrosis, the choice of treatment in a particular patient, and the comparison of the results at different centres.

Selection of treatment of PRON must be contingent upon its presentation, the response to general conservative measures, the prognosis of the primary malignancy, and the general condition and wishes of the patient. Following the development of bone exposure with or without radiological evidence of bone loss, it is important to rule out recurrent malignancy as definitively as possible. In most cases, clinical and radiological findings are characteristic of true PRON, so that biopsy can be avoided. Conservative measures for necrosis that are commonly instituted include optimisation of oral hygiene, irrigation with saline or chlorhexidine oral rinses, oral antibiotics, local wound care for orocutaneous fistulas in the form of dressings or packing, and encouragement to discontinue such irritants as alcohol and tobacco products. Early reports on the use of pentoxyfylline [32] and electrotherapy [33] have also been published. Most published series suggest that such measures will facilitate complete healing in 31–61% of cases [1, 2, 4, 6, 8] and that stabilisation or improvement of disease may occur in a significant proportion of remaining patients. The Wilford–Hall group, however, found that 92% of these patients failed to heal with such conservative treatments [9].

Surgical management has played a role in the treatment of patients with PRON and may include sequestrectomy, alveolectomy with primary closure, closure of orocutaneous fistulae, or hemimandibulectomy. In an analysis of a group of his own patients, Marx outlines potential disadvantages to the approach recommended by Randow and Weissman, which include substantial financial expense, continuous pain with narcotic addiction, and loss of time from family and workplace [9].

The mechanism by which HBO facilitates healing in PRON has yet to be fully elucidated. In non-irradiated animal models, it has been established that a profoundly hypoxic dead space exists within skin wounds [34], and that capillary ingrowth into this space is dependent upon hypoxia and influenced by concentration of inspired oxygen [35]. In another similar model, it was shown that HBO increased healing in devascularised wounds [36]. Histological confirmation of healing has been obtained in a rat mandible model [37] and postradiation specimens from HBO-treated patients [9, 20]. Moreover, transcutaneous oxygen tensions in irradiated tissue have been shown to increase with the 8–12th HBO sessions, plateauing at 80% of control values thereafter [9]. With hyperoxia in a rabbit model, Hunt and Pai [37] found increased collagen synthesis which may facilitate capillary ingrowth.

Initial reports of benefit of hyperbaric oxygen in the management of PRON have now been confirmed by several centres [9, 11–19, 27]. One prospective trial [39] and another non-randomised series [40] suggest that HBO may be effective in preventing osteonecrosis in irradiated patients who later require dental extractions. Osteonecrosis has been recognised by the Ad Hoc Committee on Hyperbaric Oxygen Therapy of the Undersea Medical Society as worthy of third party payment [41]. Nevertheless, controversy continues as to what role, if any, hyperbaric oxygen should play in the management of PRON [17, 42–46].

The skilled and careful use of HBO was safe in our series. Side effects are uncommon. These include a transient myopia, seizures, an otic or pulmonary barotrauma, the latter potentially leading to air embolism. Concern has been expressed that hyperbaric oxygen may exacerbate a variety of autoimmune and immunosuppressive disorders, and viraemia [46]. Enhancement of risk of development of a second malignancy has not been found to be a problem clinically or in animal models [9]. Untreated pneumothorax is the only absolute contraindication to HBO therapy. Relative contraindications include upper respiratory tract infection, chronic sinusitis, seizure disorders, chronic obstructive lung disease with CO_2 retention, uncontrolled high fever, history of spontaneous pneumothorax or thoracic or ear surgery, viral infections, congenital spherocytosis and history of optic neuritis [46]. Risks of HBO may be minimised by a careful pretreatment assessment including chest X-ray and electrocardiogram; some centres routinely request otolaryngological and opthamological assessment before instituting HBO [46].

In our series, HBO appeared to have a positive effect on PRON in many patients. However, there is concern that conservative treatment alone with HBO alone may not be sufficient. Necrotic bone requires removal as its presence impairs healing. Marx *et al.* [9] reported that half of the 26% of their patients who did heal with HBO therapy returned with recurrent bone exposure within 2 years, requiring additional HBO. Many of the remaining patients improved symptomatically, but all of them later required further HBO therapy, some logging up to as many as 300 sessions. This led to the development of the Marx–Wilford–Hall USAF Medical Centre Protocol for PRON. Published results are impressive, with resolution of necrosis in all patients treated on the protocol.

The British Columbia Cancer Agency and Vancouver Geneal Hospital treated 26 patients with PRON. 18 ultimately achieved persistent mucosal and cutaneous coverage and 13 satisfied strict Wilford–Hall criteria for resolution of their disease, despite the fact that fewer HBO sessions were administered and only 7 patients required mandibulectomy for necrosis, 12 others requiring lesser surgical intervention. 21 patients had improved PRON status, several with satisfactory functional capabilities despite pesistent bony exposure. Only 4 of 26 patients healed and later developed recurrent bony exposure 2–18 months later. Active progressive disease and the presence of pathological fracture seemed to predict ultimate recurrent or persistent osteoradionecrosis.

Limitations of our study include short follow-up in some patients and small patient numbers. While these may make drawing definitive conclusions difficult, nevertheless we believe that it demonstrates that satisfactory results may be obtained in many patients with HBO and other conservative management, without the need for mandibulectomy with or without reconstruction. The difference between our results and the early Wilford–Hall experience may be that many patients in the latter institution had previously been treated elsewhere and represented a selected, referred patient population. Our study represents the experience of a general, multidisciplinary cancer centre serving a large geographical region, and therefore a non-selected patient population.

Treatment must always be individualised but the combination of HBO, other conservative management, and surgery will optimise treatment results in many patients; surgery may include sequestrectomy, alveolectomy, or mandibulectomy. Thirty sessions of HBO should be offered to any patient with chronic persisting symptomatic disease for more than 6 months, any active progessive disease, and any pathological fracture. In any patient in whom disease is unchanged or worse at the end of these sessions, surgery with primary closure followed by 10 postoperative HBO sessions should be offered. Any patient with active progressive disease and/or pathological fracture should be offered mandibulectomy after 30 sessions of HBO, again to be followed by 10 postoperative sessions. Mandibular reconstruction with titanium or bone grafting should be encouraged in patients who have mandibulectomy, but clearly this should be influenced by the functional capabilities and wishes of the patient. If reconstruction is undertaken, HBO sessions should be administered in the pre- and postoperative period.

In conclusion, we support the combined approach implicit in the Wilford–Hall protocol but believe that in the setting of most radiation oncology facilities, satisfactory results may be obtained with less frequent need for mandibulectomy, and fewer HBO sessions. Hyperbaric oxygen with or without surgery appears to be effective adjunct in the treatment of post-radiation osteonecrosis.

1. Epstein JB, Wong FLW, Stevenson-Moore P. Osteonecrosis: clinical experience and a proposal for classification. *J. Oral Maxillofax Surg* 1987, **45**, 104–110.
2. Bedwinek JM, Shukovsky LJ, Fletcher G, *et al.* Osteonecrosis in patients treated with definitive radiotherapy for squamous cell carcinomas of the oral cavity and naso- and oro-pharynx. *Radiology* 1976, **119**, 665–667.
3. Cheng VST, Wang CC. Osteonecrosis of the mandible resulting from external megavoltage radiation therapy. *Radiology* 1974, **112**, 685–689.
4. Morris RB, Chan E, Silverman S, *et al.* Osteonecrosis in patients irradiated for head and neck carcinoma. *Cancer* 1981, **47**, 1980–1983.
5. Murray DG, Herson J, Daly TE, *et al.* Radiation necrosis of the mandible: a 10 year study. Part I—Factors influencing the onset of necrosis. *Int J Radiat Oncol Biol Phys* 1980, **6**, 543–548.
6. Murray CG,Herson J, Daly TE, *et al.* Radiation necrosis of the mandible: a 10 year study. Part II—Dental factors: onset, duration, and management of necrosis. *Int J Radiat Oncol Biol Phys* 1980, **6**, 549–553.
7. Rankow RM, Weissman B. Osteonecrosis of the mandible. *Ann Otol* 1971, **80**, 603–611.
8. Beumer J, Harrison R, Sanders B, *et al.* Osteonecrosis: predisposing factors and outcomes of therapy. *Head Neck Surg* 1984, **6**, 819–827.
9. Marx RE. Osteonecrosis of the jaws: a review and update. *HBO Rev* 1984, **5**, 78–127.
10. Mainous EG, Boyne J, Hart GB. Elimination of sequestrum and healing of osteoradionecrosis of the mandible after hyperbaric oxygen therapy. *J Oral Surg* 1973, **31**, 336–339.
11. Hart GB, Mainous EG. Treatment of radiation necrosis with hyperbaric oxygen. *Cancer* 1976, **37**, 2580–2585.
12. Mainous EG, Boyne PJ. Hyperbaric oxygen in total rehabilitation of patients with mandibular osteoradionecrosis. *Int J Oral Surg* 1974, **3**, 297–301.
13. Mainous EG, Hart GB. Osteonecrosis of the mandible: treatment with hyperbaric oxygen. *Arch Otolaryngol* 1975, **101**, 173–177.
14. Daum REO, Negus TW. Hyperbaric oxygen in osteoradionecrosis of the mandible. *J Roy Nav Med Serv* 1988, **84**, 51–54.
15. Davis JC,Dunn JM, Gates GD, *et al.* Hyperbaric oxygen: a new adjunct in the management of radiation necrosis. *Arch Otolaryngol* 1979, **105**, 58–61.
16. Farmer JC, Shelton DL, Angelillo JD, *et al.* Treatment of radiation induced tissue injury by hyperbaric oxygen. *Ann Otol* 1987, **87**, 707–715.
17. Fattore L, Strauss RA. Hyperbaric oxygen in the treatment of osteoradionecrosis: a review of its use and efficacy. *Oral Surg Oral Med Oral Pathol* 1987, **63**, 280–286.
18. Mansfield MJ, Sanders DW, Heinbach RD, *et al.* Hyperbaric oxygen as an adjunct in the treatment of osteoradionecrosis of the mandible. *J Oral Surg* 1981, **39**, 585–589.
19. Tobey RE, Kelley JF. Osteoradionecrosis of the jaws. *Otolaryngol Clin N Am* 1979, **12**, 183–186.
20. Marx RE, Ames JR. The use of hyperbaric oxygen in bony reconstruction of the irradiated and tissue-deficient patient. *J Oral Maxillofac Surg* 1982, **40**, 412–420.
21. Fowler JF. The linear-quadratic formula and progress in fractionated radiotheraphy. *Br J Radiol* 1989, **62**, 679–684.
22. Regaud C. Sur la necrose des os attients par un processus cancereux et traités par les radiations. *Compt Rend Soc de Biol* 1922, **87**, 427.
23. Rohrer MD, Kim Y, Fayos JV. The effect of cobalt-60 irradiation on monkey mandibles. *Oral Surg* 1979, **48**, 424–440.
24. Pappas GC. Bone changes in osteoradionecrosis. *Oral Surg* 1969, **27**, 622–630.
25. Meyer I. Infectious disease of the jaws. *J Oral Surg* 1970, **28**, 17.
26. Marx RE. Osteoradionecrosis: a new concept of its pathophysiology. *J Oral Maxillofac Surg* 1983, **41**, 283–288.

27. Marx RE. A new concept in the treatment of osteoradionecrosis. *J Oral Maxillofac Surg* 1983, **41**, 351–357.
28. Marx RE, Johnson RB. Studies in the radiobiology of osteoradionecrosis and their clinical significance. *Oral Surg Oral Med Oral Path* 1987, **64**, 379–390.
29. Hutchison IL, Cope M, Delpy DT, Richardson CE, Harris M. The investigation of osteoradionerosis of the mandible by near infrared spectroscopy. *Br J Oral Maxillofac Surg* 1990, **28**, 150–154.
30. Epstein JB, ReaG, Wong FLW, *et al.* Osteonecrosis: a study of the relationship of dental extractions in patients receiving radiotherapy. *Head Neck Surg* 1987, **10**, 48–54.
31. Spanos W, Shukovsky LJ, Fletcher GH. Time, dose and tumour volume relationship in irradiation of squamous cell carcinoma of the base of tongue. *Cancer* 1976, **37**, 2591–2599.
32. Dion MW, Hussey DH, Doornbos JF, *et al.* Preliminary results of a pilot study of pentoxifylline in the treatment of late radiation soft tissue necrosis. *Int J Rad Oncol Biol Phys* 1990, **19**, 401–407.
33. King GE, Scheetz J, Jacob RF, *et al.* Electrotherapy and hyperbaric oxygen: promising treatments for post-radiation complications. *J Prosthet Dent* 1989, **62**, 331–334.
34. Silver IA. The measurement of oxygen tension in healing tissue. In Herzog *et al.* eds. *Progress in Respiration Research*. New York, Karger, 1969, **3**, 124–135.
35. Knighton DR, Silver IA, Hunt TK. Regulation of wound healing angiogenesis: effect of oxygen gradients and inspired oxygen concentration. *Surgery* 1981, **90**, 262–270.
36. Kiviisaari J, Ninikoski J. Effects of hyperbaric oxygenation and prolonged hypoxia on the healing of open wouds. *Acta Chir Scand* 1975, **141**, 14–19.
37. Nilsson P. Effects of hyperbaric oxygen on bone healing. *Swed Dent J Supp* 1989, **64**, 1–33.
38. Hunt TK, Pai MP. The effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. *Surg Gyn Obstet* 1972, **135**, 561–567.
39. Marx RE, Johnson RP, Cline RN. Prevention of osteoradionecrosis: a randomized prospective clinical trial of hyperbaric oxygen and penicillin. *J Am Dent Ass* 1985, **111**, 49–54.
40. Kraut RA. Prophylactic hyperbaric oxygen to avoid osteoradionecrosis when extractions follow radiation therapy. *Clin Prev Dent* 1985, 7, 17–20.
41. Myers RAM, Baker T, Cowley RA. Hyperbaric medicine: state of the art 1979. *Am Surg* 1982, **48**(a), 487–494.
42. Hudson JW. Letter. *Oral Surg* 1987, **64**, 413–414.
43. Kagan RA. Letter. *J Oral Maxillofac Surg* 1984, **42**, 141.
44. Marx RE. Letter. *Oral Surg* 1987, **64**, 414–416.
45. Schwartz HC. Letter. *J Oral Maxillofac Surg* 1984, **42**, 697.
46. Giebfried JW, Lawson W, Biller HF. Complications of hyperbaric oxygen in head and neck disease. *Otolaryngol Head Neck Surg* 1986, **94**, 508–512.