The financial burden for the surgical management of osteoradionecrosis

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In brief

- Provides an insight into the cost of treating severe ORN.
- Shows the associated risk and complications associated with invasive dental treatment.
- Highlights a condition that has been sidelined but requires attention.

Osteoradionecrosis (ORN) remains a difficult clinical problem. In large refractory cases surgery appears to be the only option but it does not guarantee a cure and is expensive. Cost analysis of 31 patients who had resection with or without reconstruction of their mandible was £892,357. The largest cost was in-patient stay, which accounted for 62% of the total. This article explores in detail the expenditure associated with major ORN surgery and its subsequent implications.

Introduction

Osteoradionecrosis (ORN) is a well-known complication of head and neck radiotherapy (RT) and although it is nearly a century since the condition was first recognised[1] there is no reliable treatment for the condition. The introduction of a novel and targeted delivery RT via intensity modulated radiation therapy (IMRT) raised the prospect of a reduction in ORN but this does not seem to have transpired. The problem has been compounded by the increased use of chemo-radiation which accentuates the risk of ORN[2] and the fact that a trigger such as dental extraction is no longer necessary as ORN is now more often a spontaneous event.[3] Also the pool of patient at risk of ORN is increasing in the community as cancer therapy becomes more successful. The risk of ORN is life-long.

ORN has been graded into three categories;[4] the most severe consists of exposed bone with a painful oro-cutaneous fistulae and frequently in combination with a pathological fracture of the mandible or invasion of the sinus in the maxilla. These presentations do not respond to conservative measures and at present surgical excision with the introduction of new tissue is the standard of care. However, surgery is not without risk for by definition the surrounding tissues are scarred with dense fibrous tissue and in many instances the postoperative period is replete with complications and a prolonged hospital stay. This detracts from the patient's quality of life. The cost associated with the surgical management of grade III ORN is often overlooked. The intention of this retrospective study is to analyse the cost of surgical management of grade III ORN.

The problems induced by jaw necrosis are undervalued. Despite calls from the dental profession as to the potential problem posed by the condition little resource has been allocated to this issue. The population at risk is increasing as more patients with cancer are being cured or their life extended. At the same time with increasing age the heavy metal generation and their heavily restored dentitions are vulnerable to failing. This together with the fact that ORN has a high rate of spontaneous occurrence indicates this problem will persist. ORN is integral to dentistry and dental provision. The dental team remains a constant in the patient's head and neck journey playing an important role pre-RT and post RT even after they have been discharged from the cancer services.

The cost of ORN has not been estimated previously largely due to the complexities of finance in the NHS. We aimed to determine the financial burden of ORN to provide an insight into the difficulties of managing complex ORN.

Method

The electronic surgical records at Guy's Hospital between 2008–2014 were reviewed and patients undergoing surgical treatment for ORN were identified. ORN was defined according to the Notani[4] grading system.

A list of resources required to treat ORN was compiled (Table 1) and the costs elicited

Table 1 Shows the five main categories used and within them some of the more commonly occurring interventions

Categories	Sub-categories
Out-patient appointments	Head & Neck
	Dietetics
	SALT
	Physiotherapy
Imaging	CT
	MRI
	Angiography
	Ultrasound
Surgery	Pre-surgical assessment
	Theatre time
	Surgical team
In-patient stay	ITU stay
	Ward stay
Miscellaneous	PEG placement
	Hyperbaric oxygen therapy

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from the hospital finance department. Data was collected for each patient as they passed along the 'ORN surgical journey'. The costing exercise started when the patient agreed to surgery for their ORN. It is acknowledged that conservative treatment frequently preceded surgery by a number of years but outpatient costs before this point were outside the scope of this analysis.

The objective in this study was to cost only the surgical journey.

Results

In the period 2008-2014 a total of 31 patients were admitted to hospital for surgical resection of ORN. This cohort of patients underwent a total of 53 independent and discrete surgical procedures amounting to 387 hours of operating theatre time. A total of 19 (61%) patients underwent one surgical intervention and 12 (39%) more than one operation. The mean operating time was nine hours (range 3–15 hours). Operative costs were calculated as an amalgam of theatre running costs per hour (inclusive of anaesthetic staff), senior and junior surgical staffing costs and pre-assessment charges. These amounted to a total of £246,051 with a mean of £7,937 (range: £1,944–£29,183) per procedure.

The mean in-patient stay per admission was 38 days (range 4–161 days). The mean stay for patients who required only one surgical procedure was 31 days. In those patients requiring two, three and four operations, the mean stay was 21, 57 and 108 days, respectively. Average cost for ward stay was £14,440 (range £1,520–61,180). When Intensive Critical Care Unit (ICCU) costs were included in the hospital stay calculation the mean cost per admission was £18,253 (range £5,040–£89,180).

Imaging modalities used in preparation for ORN surgery were CT and MRI scans, angiograms, cone beam CT of jaws and ultrasound evaluation of the vessels in the neck. The mean number of imaging episodes was two (range 1–9) with a mean cost per patient of £222. Patients undergoing three or more surgeries had a mean cost at £470 with an average of four imaging episodes per patient.

Out-patients appointments were costed from the date a decision was made for surgical intervention. Collectively (n = 31 patients) it amounted to £62,555 with a mean of £1,955 per patient (Table 2). The largest contribution to outpatient cost was attendance on the head and neck review clinic (£40,800), followed by dietetics (£10,550), speech and language therapy (£4,658) and physiotherapy (£3,640). Complementary therapies and dental specialties accounted for £2,907 of the total. Additional miscellaneous costs are numerous when managing ORN and cannot all be included in the calculations. Examples include in- and out-patient pharmacy prescription and histopathology analysis. Two interventions particularly stood out, one was the provision of feeding tubes (a percutaneous endoscopic gastrostomy [PEG] or [RIG] radiologically inserted gastrostomy). In all 11/31(34%) patients had 20 RIG or PEG procedures at a cost of £1,818 per insertion (£36,360). The other was hyperbaric oxygen therapy (HBOT). Four patients were referred for HBOT (30 dives pre-op) at a cost of almost £7,000 per patient per regime (£27,656). Not all patients completed the recommended prescription.

The five main categories of in-patient admission, imaging, surgery, out-patient appointments and miscellaneous costs gave a total expenditure of £892,357 (range £6,140–£137,658) for treating 31 patients with ORN. The average cost per patient was £27,866. Ward and ICCU fees contributed to 62% overall treatment costs.

In the series 5/31 (16%) patients had persistent ORN. The mean cost per person was £52,679 compared to £27,866 calculated for the group as a whole. One patient planned for further surgery was cancelled due to poor medical health. If this patient is excluded then the remaining four patients had an average cost of £63,963 for their unresolved ORN treatment journey (Table 3).

The in-patient stay and total cost of patients undergoing one, two and more than two surgical interventions is shown in Table 4 with mean cost per patient rising as expected as number of surgical interventions increases.

Resolution was defined as no recurrence of exposed bone or symptoms resembling ORN at the surgical site for a year following surgery. According to this category 26/31 patients had resolution with a mean treatment time of 85 weeks (range 52–286 weeks)

Table 2 Shows the total, mean and range for the number of visits for each out-patient services for the 31 patients

Out-patient service	Total	Mean	Minimum	Maximum
Head & Neck	408	13	1	54
Physiotherapy	65	2	0	47
Speech & Language	34	1	0	12
Dietetics	87	2	0	32
Miscellaneous	17	1	0	6

Table 3 Resolved versus unresolved ORN costs

	Resolved ORN (n = 27)	Unresolved ORN (n = 5)
Total	£628,927	£263,394
Mean	£23,294	£52,679

Table 4 Shows the five main cost areas for a surgical ORN journey when the three patients are sub-categorised according to the number of surgeries they underwent

No. of surgical interventions	1	2	>2
No. of patients	19	8	4
Mean length of in-patient stay (days)	31	21	108
Total cost (ward, imaging, surgery, OPD, misc.)	£383,597	£185,139	£316,079
Mean total cost (ward, imaging, surgery, OPD, misc.)	£20,189	£23,142	£79,020

Discussion

ORN is a well recognised entity but numerically the number of cases in the population is small and attracts little attention from health regulators. On the contrary the condition looms large in the minds of dental surgeons trying to manage these cases as many operations prove a harrowing experience for both the clinical team and patient alike. The incidence of ORN when radiotherapy is used in isolation is reported to

be 2-8% of cases treated.[5,6] National Statistics data for England predict that around 4,000 patients each year with head and neck cancer undergo a course of radical radiotherapy.[7] If a conservative incidence of ORN is selected (2-4%) then in the region of 80–160 patients will develop ORN each year in England.

Until recently it has been universally accepted that ORN was triggered by a dental event such as an infection or extraction and so it could be prevented by careful dental care. The dental care of head and neck cancer patients has been transformed in the last decade with provision is built into the treatment pathway. However, the incidence of ORN is not reducing and may even be increasing. This is because ORN has become a spontaneous event in at least 50% of cases.[3] The reasons are unclear but could be due to the improved conformity of radiation dose with IMRT and an obvious candidate is the introduction of concomitant chemo-radiotherapy as part of the treatment regime for mouth cancer.

The current management of advanced (grade III) ORN depends on the clinician's preferred pathophysiological explanation for ORN. Marx's[8] theory of hypoxia-hypovascular-hypocellular has led to the use of HBOT either alone or as an adjunct to surgery. The consensus is for 30 sessions before surgery and ten sessions post-operation at 2.4 atmosphere pressure with each session lasting 90 minutes.[9] A more recent theory of ORN induction has been proposed by Delanian.[10] It emphasises the importance of radiation induced fibrosis as the force behind ORN with hypo-cellularity and hypo-vascularity as the sequalae. If Delanian is correct, then the advantage is that radiation induced fibrosis can be modulated by pharmacological means via pentoxifylline and tocopherol (PVe).

Experience shows that no treatment strategy (HBOT, surgery, HBOT + surgery or pentoxifylline/vitamin E) carries a guarantee of success especially with grade III disease. Historically surgery has played an important role and will do for the foreseeable future in the management of ORN. It does not have to be extensive in design. In early disease minimal approaches include sequestrectomy or reduction of sharp bony edges. More invasive approaches included debridement of necrotic bone with primary closure. However once ORN is established with fistulae and pathological fractures the only viable surgical option for a patient plagued by infection and uncontrolled pain is resection of the affected portion of the jaw with or without free vascularised free tissue transfer. Microvascular transposition is an ideal solution if the transfer is successful. However, it is not uncommon for the scarred and damaged tissue of the neck to break down and expose underlying structure.

The largest cost identified in this study (62% of the total cost) was the number of days resident on the ward and ICCU. The charges totalled £554,080 for the 31 patients. The range varied from £5,040 to £89,180 depending on the complexity of surgery and the unfolding complications thereafter. It is well recognised that irradiated tissue has poorer healing potential and increased risk of further fibrosis upon surgery. This was clearly significant regarding the cost of ward stay where it had been noted that patients suffered from complications either directly related to surgery such as infection or wound break down or a complication secondary to their surgery such as chest infections from aspiration due to effects on swallowing. One patient with one of the lowest cost of care (£6,140) was admitted twice for a total of four nights only. The two operative procedures (three and two hours respectively) involved initially resection of ORN bone and on the second occasion the application of a bone plate. The simple treatment plan minimised complications and costs. This pathway is in contrast to the majority of patients who were managed with microvascular reconstruction of the jaw. As a result of current experience, simpler reconstructive treatment plans are being adopted. Wherever possible with lateral ORN lesions of the body or angle of the mandible the damaged bone is removed and the defect repaired with bulky axial muscle flaps such as pectoralis major or latissimus dorsi. The mandible is held in correct occlusion by inter-maxillary fixation screws and elastic traction for two or three months while the new scar tissue forms and hold the jaw in the correct position. Any break down of neck skin is inconsequential as a highly vascularised muscle flap seals the neck and will accept split skin graft quite reliably.

In contrast a traditional surgical approach (resection and microvascular reconstruction) to replace damaged bone and soft tissue carries significant cost and morbidity. More than two attempts at surgery carries physical and financial penalties. The mean duration of admission for first surgery is 31 days and more than two surgeries 108 days. In this study the oral function of patients was not assessed but the number of patients requiring permanent PEG is a testament to poor oral function.

In this series, 26 cases have long term follow up. The longest time to ORN resolution was 286 weeks. The patient had four surgical admissions and an associated long in-patient stay. One patient died at 33 weeks and if this case is excluded the remaining four unresolved cases had a mean treatment time of 182 weeks (range 84–276 weeks).

This recalcitrant group of patients with unresolved ORN cost at least £25,000 more per person than the resolved group and the mean duration of treatment was extended by almost 100 weeks. There was an increase attendance on SALT and dietetics services. If the data presented are correct then it begets the surgeon on occasion to stop and review the case for each intervention can compound the situation. The four patients with unresolved ORN in this series are now being treated conservatively with PVe and antibiotics at an approximate cost of £375/year. The ORN has not resolved but all four patients are largely asymptomatic.

In terms of manpower and resources, 387 hours of operating time equates to almost one operating list per week for just under a year devoted to ORN. Furthermore a total of 408 appointments for ORN were attended among a busy head and neck cancer clinic.

The costing of these 31 patients reveals an insight into the complexities of managing ORN. The condition is difficult to treat. Prevention or early treatment is the optimal strategy. Prophylactic extraction of 'at risk' teeth before radiotherapy will help reduce a trigger for ORN but still does not provide a guarantee. Post-RT the GDP has an important role for managing the vulnerable retained dentition as well as identifying early ORN. Guidance by the Royal College of Surgeons has been provided for all phases of radiotherapy and highlights the importance of prevention via regular review, high fluoride toothpaste and early intervention.[12] GDPs should be aware that the risk of ORN does not diminish with time but increases with time as fibrosis continues throughout life. It remains important for GDPs to understand the cost of ORN, length and extent of treatment, the potential of failure for resolution and the difficult journey a patient experiences when considering invasive dental treatment for head and neck RT patients. There seems no way of avoiding the spontaneous induction of ORN. Prophylactic use of pentoxifylline and vitamin E (PVe) has been proposed as a possible solution.[11] The use of these medications has shown promising results in both established ORN and as prophylaxis for dental extractions.[3,11] If it were prescribed for three months prior and for a year following surgery this would add £460 to the cost of

surgical treatment and compares favourably to HBOT treatment (£10,000). The role of HBOT as prophylaxis against ORN is also being investigated in a randomised control trial (HOPON trial).[13] The results of this are being eagerly awaited.

Limitations

The authors recognise the retrospective analysis of costs is not comprehensive in detail. There also remains additional costs that have not been included such as plain film radiography, blood assays, in-patient and out-patient prescriptions and histopathological examination of the specimen. It is also possible that in other institutions some of the complication encounter may have been avoided.

Conclusion

ORN is still a persistent feature of head and neck cancer treatment. Surgery appears the only effective treatment for advanced grade 3 ORN. In the present series 84% of cases were cured while 16% had unresolved ORN. This success came at a cost with prolonged recovery times due to poor wound healing. Functional outcomes were also less than ideal with 35% of patients with permanent PEG feeding.

GDPs have a key role in head and neck cancer management and its subsequent events and outcomes. They may be the first health professional to identify an oral cancer and once diagnosed and treated continue to have a role in maintaining and caring for the patient's dentition. GDPs are already aware of the complication of ORN and should consider dental extraction in post-radiotherapy patients with caution and where appropriate a referral for prompt assessment in secondary or tertiary care. Where established ORN is diagnosed then an immediate referral should be considered with the aim to commence management with some urgency to restrict progression, as this paper highlights that the cost implications are particularly high for the management of severe ORN where surgical management may be implicated. In contrast the cost of managing stage I and stage II is likely to be lower reinforcing the need for GDP awareness. This is particularly salient in the current financial climate within the NHS but more importantly to improve patient's quality of life.

1. Regaud C. On the sensitivity of bony tissue to gamma rays and the mechanism of osteoradionecrosis (in French). *Comptes Rendus Hebdomadaires des Seances et Memoires de la Societe de Biologie* 1922; **87:** 629–932.
2. Jeraemic B, Shibamoto Y, Milicic B *et al.* Hyperfractionated radiation therapy with or without concurrent low-dose daily cisplatin in locally advanced squamous cell carcinoma of the head and neck: a prospective randomized trial. *J Clin Oncol* 2000; **18:** 1458–1464.
3. Patel V, Gadiwalla Y, Sassoon I, Sproat C, Kwok J, McGurk M. Use of pentoxifylline and tocopherol in the management of osteoradionecrosis. *Br J Oral Maxillofac Surg* 2016; **54:** 342–345.
4. Notani K, Yamazaki Y, Kitada H *et al.* Management of mandibular osteoradionecrosis corresponding to the severity of osteoradionecrosis and the method of radiotherapy. *Head Neck* 2003; **25:** 181–186.
5. Nabil S, Samman N. Incidence and prevention of osteoradionecrosis after dental extraction in irradiated patients: a systematic review. *Int J Oral Maxillofac Surg* 2011; **40:** 229–243.
6. Epstein J B, Wong F L, Stevenson-Moore P. Osteoradionecrosis: clinical experience and a proposal for classification. *J Oral Maxillofac Surg* 1987; **45:** 104–110.
7. National Cancer Registration and Analysis Service. Head and neck cancer resources. Public Health England. Available at http://www.ncin.org.uk/cancer_type_and_topic_specific_work/cancer_type_specific_work/head_and_neck_cancers/head_and_neck_cancer_hub/resources (accessed January 2017).
8. Marx R. Osteoradionecrosis: a new concept of its pathophysiology. *J Oral Maxillofac Surg* 1983; **41:** 283–288.
9. Marx R E, Johnson R P, Kline S N. Prevention of osteoradionecrosis: A randomized prospective clinical trial of hyperbaric oxygen *versus* penicillin. *J Am Dent Assoc* 1985; **11:** 49–54.
10. Delanian S, Lefaix J L. The radiation-induced fibroatrophic process: therapeutic perspective via the antioxidant pathway. *Radiother Oncol* 2004; **73:** 119–131.
11. Patel V, Gadiwalla Y, Sassoon I, Sproat C, Kwok J, McGurk M. Prophylactic use of pentoxifylline and tocopherol in patients who require dental extractions after radiotherapy for cancer of the head and neck. *Br J Oral Maxillofac Surg* 2016; **54:** 547–550.
12. The Royal College of Surgeons of England / The British Society for Disability and Oral Health. The Oral Management of Oncology Patients Requiring Radiotherapy, Chemotherapyand/or Bone Marrow Transplantation. Clinical Guidelines. 2012.
13. ISRCTN Registry. Hyperbaric oxygen for the prevention of osteoradionecrosis. Information available online at http://www.isrctn.com/ISRCTN39634732 (accessed January 2017).