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Radical radiotherapy for treatment of malignant parotid tumours: A single centre experience 1995–2005

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Abstract

Radiotherapy is commonly used to reduce the risk of recurrence of malignant parotid gland tumours. We report our experience with radiotherapy for parotid malignancies at the Royal Marsden Hospital. We retrospectively reviewed the case notes of 90 patients with malignant parotid tumours who were treated with megavoltage irradiation between 1995 and 2005 at the Royal Marsden Hospital, and obtained details about age, sex, pathology, type of operation, type of radiotherapy, and outcome. Outcome data included date of recurrence, whether local or metastatic, date of death, and cause of death. Outcome for patients who had definitive operations compared with those who did not were analysed separately.

Forty-three patients (54%) had superficial parotidectomy, 26 (33%) had total parotidectomy, and 11 (13%) had fine needle aspiration (FNA). Adenocarcinoma, squamous cell carcinoma (SCC), and mucoepidermoid carcinoma were the most prevalent histologically confirmed tumours. Radiation was given most often by the lateral wedged pair field technique. Five-year locoregional control was better for patients who had definitive operations and postoperative radiotherapy than for those who did not (82% compared with 21%), disease-free survival was 58% compared with 29%, and overall survival was 68% compared with 0%, respectively.

Keywords: Postoperative radiotherapy; Malignant; Parotid; Tumours

Introduction

Parotid tumours are rare; they represent 3–6% of all head and neck cancers, and 0.3% of all cancers. After operation alone 20–70% of patients with malignant parotid gland tumours have local recurrences,[1–5] so radiotherapy is commonly used to reduce this risk. The use of adjuvant postoperative radiotherapy (PORT) for malignant parotid gland tumours has been reported in a series of retrospective studies of non-randomised trials that suggest that 20–50% fewer patients have local recurrence than those who have operation alone.[1–3,6,7] PORT is currently recommended for patients with T3–T4 disease, incomplete or close resection margins, high-grade tumours, recurrent disease, perineural invasion, nodal involvement, and adenoid cystic tumours.[6,8–11] Typically, a radiation dose equivalent to 60 Grays (Gy) in 30 fractions over 6 weeks is given to the parotid bed. When nodes are not invaded, high-grade tumours in the neck are treated with 50 Gy in 25 fractions over 5 weeks because of the risk of microscopic lymph node metastases. Primary radiotherapy for the malignant parotid is recommended in unresectable tumours or in patients who are not fit for operation. A radiation dose equivalent to at least 66 Gy in 33 fractions to the primary tumour and involved nodes is recommended.[8] We report our experience with radiotherapy for parotid malignancies at the Royal Marsden Hospital between 1995 and 2005.

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Materials and methods

We studied 90 patients with malignant parotid tumours who had megavoltage irradiation from 1995 to 2005 at the Royal Marsden Hospital. Six patients with primary lymphoma of the parotid gland and four who were treated with palliative radiotherapy were excluded. We retrospectively reviewed the case notes of the remaining 80 patients and obtained information about age, sex, pathology, type of operation, type of radiotherapy, and outcome. Data on outcome included date of recurrence, whether local or metastatic, date of death, and cause of death. Patients with squamous cell carcinoma (SCC) of the parotid were included in the analysis if there was no evidence or past history of SCC of the upper aerodigestive tract or skin. Those with SCC in the intraparotid lymph nodes were excluded.

Radiation technique

Most patients were treated with a lateral oblique wedge pair technique using photons. The gantry was angled so that the anterior oblique beam would not deliver an appreciable dose to the spinal cord and contralateral orbit. The posterior beam was angled to avoid the spinal cord and to cover the facial canal where appropriate. A few patients with superficial lobe tumours were treated with an applied electron field using energies ranging between 12 and 15 MeV depending on the depth at which treatment was required. Rarely when homogeneity of dose was an issue treatment was given with an applied mixed beam of photons and electrons. If required, areas around the lymph nodes were treated with 6 Mv photons using single applied field or two parallel-opposed fields, depending on the thickness of the patient's neck. The dose used was one of the two radiobiologically equivalent doses: 50 Gy in 20 fractions, or 60 Gy in 30 fractions. Patients with residual macroscopic disease (R2 M resection) were treated with a dose of 65 Gy in 30 fractions. The cervical lymph nodes were treated electively in high-grade tumours, and as an adjuvant to operation when nodes were invaded.

Statistical analysis

Local control, disease specific and overall survival rates were obtained using Kaplan–Meier survival curves. Data on patients who had postoperative radiotherapy compared with those who had primary radiotherapy alone, were analysed separately. The log rank test was used to compare the two groups. Data for patients who were lost to follow-up or whose follow-up did not reach 5 years were censored. The local control rate was defined as the proportion of patients who had no local recurrence at 5 years. Disease-specific survival defined the percentage of patients who were free from their head and neck cancer at 5 years. Univariate analyses were used to measure the effect of the following characteristics on outcome: T and N stage; age; histological results; grade; perineural invasion; and resection status. This was followed by a multivariate analysis. Cox proportional hazards regression analysis was used for the univariate and multivariate analyses. Statistical analysis was done using the Statistical Package for the Social Sciences (SPSS© 2006 Inc. Chicago, IL) Version 14.

Results

Median age was 67 years (range 18–95), there were 44 men (55%) and 36 women (45%). The type of operation was individualised and depended on several factors including tumour stage, patient's health, and coexisting conditions. Forty-three patients (54%) had superficial parotidectomy, and 26 (33%) had total parotidectomy. Eleven patients (14%) had fine needle aspiration (FNA) of whom six were medically unfit for operation, and five had unresectable disease. Twenty-two patients (28%) had neck dissection in addition to excision of the primary tumour, of whom eight (36%) had pathological cervical nodal disease. Eight other patients had clinical or radiological signs of cervical lymphadenopathy, but did not have neck dissection because of other medical conditions.

Adenocarcinoma, SCC, and mucoepidermoid carcinoma, were the most prevalent histologically confirmed tumours (Table 1). Twenty tumours (25%) were low-grade or well-differentiated, 26 (32%) were intermediate grade, and 34 (43%) were high-grade or poorly differentiated. Fifty-five patients (69%) had invaded (<1 mm) resection margins (R2), 16 (20%) had close (1–5 mm) resection margins (R1), and nine (11%) had complete excision (R0). Twelve patients (15%) had lymphovascular invasion and 22 (28%) had perineural invasion.

The lateral wedged pair field technique was used to treat 75 patients (94%), four (5%) were treated with applied electron fields, and one was treated using combined applied photons and electrons. Fifty-two (65%) were treated with one of the two radiobiologically equivalent doses: 50 Gy in 20 fractions, or 60 Gy in 30 fractions, which is the standard dose we use for sterilising microscopic disease. Twenty-eight patients (35%) who had pathological evidence of residual macroscopic disease (defined as R2 M) were treated with a dose of 65 Gy in 30 fractions. Forty-seven patients (59%) had radiotherapy to the cervical lymph nodes.

Table 1
Histological subtypes of parotid malignancies.

Type of carcinoma	No (%)
Adenocarcinoma	20 (25)
Squamous cell	14 (18)
Mucoepidermoid	14 (18)
Acinar cell	11 (14)
Poorly differentiated	6 (8)
Myoepithelial	4 (5)
Adenoid cystic	4 (5)
Salivary duct	3 (4)
Other	4 (5)
Total	80

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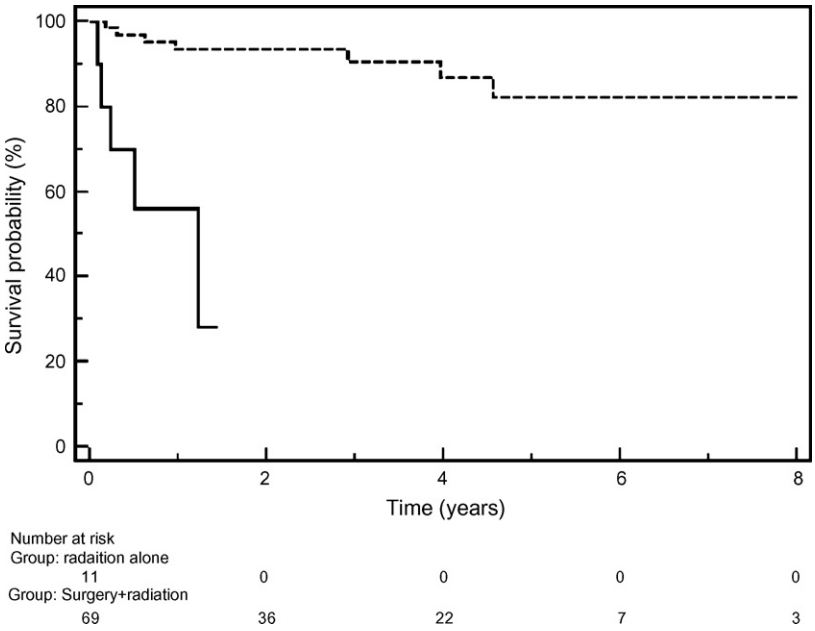

Fig. 1. Kaplan–Meier curve comparing locoregional control for patients who had radiotherapy alone (solid line) with those who had operation and radiotherapy (broken line).

Outcome analysis

Twenty-five patients (31%) had had a recurrence at the time of analysis, which was locoregional in 13 (16%), and distant in 12 (15%). Locoregional control at 2 and 5 years was 93% and 82%, respectively, for patients who had had definitive operations (Fig. 1). For those who had radiotherapy alone, the rates were 21% at both 2 and 5 years (Fig. 1). The difference between the two groups was significant ($p < 0.001$). Univariate followed by multivariate analysis of factors that affected local recurrence showed that age and T-stage were significant. Twenty-eight patients (35%) had died at the time of analysis, of whom 15 (19%) died of recurrent parotid carcinoma and 13 (16%) of other causes. For those who had definitive operations, disease-free survival at 2 and 5 years was 73% and 58%, respectively (Fig. 2), and for patients treated with radiotherapy alone it was 29% at both 2 and 5 years (Fig. 2). The difference between the two groups was

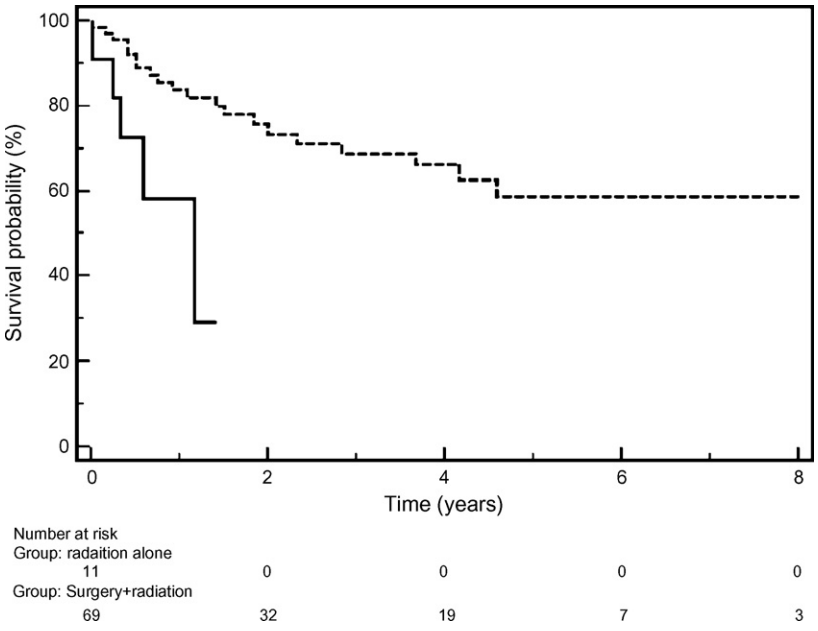

Fig. 2. Kaplan–Meier curve comparing disease-specific survival for patients who had radiotherapy alone (solid line) with those who had operation and radiotherapy (broken line).

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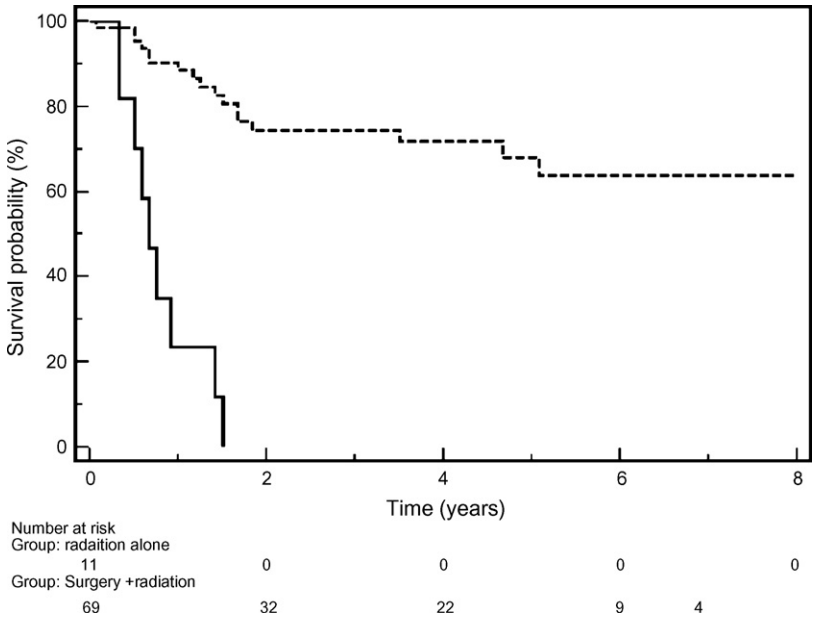

Fig. 3. Kaplan–Meier curve comparing overall survival for patients who had radiotherapy alone (solid line) with those who had operation and radiotherapy (broken line).

significant ($p = 0.004$). Univariate analysis of factors that affected disease-free survival showed that age and T-stage were significant. After adjusting for age, grade and T-stage, grade was no longer significant. Median overall survival was 9.5 years (range 3.4–15.3) for patients who had definitive operations compared with 0.6 years (range 0.3–1.5) for those who had radiotherapy alone (Fig. 3). For patients who had definitive operations, overall survival at 2 and 5 years was 74% and 68%, respectively (Fig. 3). No patient who had radiotherapy alone was alive at 2 years (Fig. 3). The difference between the two groups was significant ($p < 0.001$). Univariate analysis of survival showed that age, grade, histological subtype, and T-stage had a significant impact on survival. On multivariate analysis only age and T-stage were confirmed to have a significant impact on survival (details of the analyses can be obtained from the author). Unfortunately, the numbers of cases in the different histological subgroups were too small to determine a significant effect on outcome.

Discussion

Patients with malignant parotid tumours who had definitive operations and radical radiotherapy at our centre had locoregional control, disease-specific, and overall survival rates of 82%, 58%, and 68%, respectively, at 5 years. As expected rates were much lower for patients who had radical radiotherapy alone. Operation followed by radiotherapy is the standard treatment we give for such patients. Primary radiotherapy is given if the disease is inoperable. We know of no published randomised trials that show the benefit of postoperative radiotherapy. Most published evidence consists of retrospective case series. A summary of findings from some of these is listed in Table 2.

In our study, outcome for patients who had radiation alone is significantly worse than for those who had definitive operations and postoperative radiotherapy. This is not unexpected and is supported by other reports about the treatment of malignant parotid tumours.[1–3,6,7] However, our results should be interpreted with caution because of the low number of patients ($n = 11$) in the radiation alone group. They might have had a poorer outcome because of selection bias whereby a patient who was unfit for operation had radiotherapy alone. Patients in our study who had operation and radiotherapy had worse variables of outcome than most reported series.[6,7,12–16] No studies with better outcome than ours included patients with histologically confirmed SCC, whereas in our study 17% of the patients did. The published studies are also quite diverse. Most include patients who have had an operation with or without postoperative radiotherapy. Since the role of postoperative radiotherapy is well established in this setting, these studies will include patients with a good prognosis such as those with low-grade tumours and those who have a complete resection. We found two studies that reported only on patients who had postoperative radiotherapy.[6,13] Garden et al. did not include patients with residual macroscopic disease or signs of SCC, which is more likely to develop a secondary from an occult skin primary, and therefore has a worse prognosis.[6] Kirkbride et al. report only 10% of patients with SCC.[13] The only comparable study that included patients with characteristics similar to our study group showed lower locoregional control and overall survival.[17] The studies that included patients with SCC have outcomes that are comparable to our patients who had operation and postoperative radiotherapy.[17–19]

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Table 2
Summary of published data on operation and radiotherapy for management of malignant parotid tumours.

First author (year)	Reference no.	No. of patients	No (%) with invaded nodes	Predominant subtypes	No. (%) who had adjuvant radiotherapy	Prognostic factors	Outcome (years)		
							Disease-free survival	Local control	Overall survival
Spiro et al. (1993)	[7]	62	7 (11)	Mucoepidermoid, adenoid cystic, acinar cell, adenocarcinoma	57 (92)	Tumour spillage at operation, R2 resection, recurrent disease, facial nerve involvement	77% (5)	95% (5)	Not reported
Garden et al. (1997)	[6]	166	43 (26)	Mucoepidermoid, adenocarcinoma, adenoid cystic	142 applied electrons (86), 19 cobalt (11)	T-stage, grade, nodal status R1/R2 margins, perineural invasion	79% (5)	92% (5)	78% (5)
Leverstein et al. (1998)	[14]	65	10 (15)	Adenocarcinoma, adenoid cystic, acinar cell	51 (78)	T-stage, N stage ($p < 0.05$)	68% (5)	88% (5)	75% (5)
Magano (1999)	[18]	126		High-grade undifferentiated, squamous cell, adenoid cystic	81 (84)	Facial nerve involvement N stage, grade	47% (5)	77% (5)	54% (5)
Renehan et al. (1999)	[11]	103		Mucoepidermoid, adenoid cystic ex pleomorphic adenoma	66 (64)	T-stage, N stage, grade, perineural invasion, adenoid cystic carcinoma ($p < 0.05$)	78% (5)	75% (5)	Mean 61% (10)
Hocwald et al. (2001)	[9]	78		Mucoepidermoid, adenoid cystic, acinar cell, squamous cell	44 (56)	T-stage, N stage, grade, perineural invasion adenoid cystic carcinoma ($p < 0.05$)	69% (5)	92% (5)	Not reported
Kirkbride (2001)	[13]	159		Mucoepidermoid, azdenocarcinoma, adenoid cystic, acinar cell	159 (100)	Age ($p < 0.05$), T-stage ($p < 0.05$), N stage R1 resection, aggressive disease	76% (5)	80% (5)	68% (5)
Tulio (2001)	[20]	45		Adenocarcinoma, mucoepidermoid	21 (48)	T-stage, R1/R2 resection, N stage ($p < 0.05$)	81% (5)	81% (5)	55% (5)
Zbären (2002)	[16]	98	24 (25)	Mucoepidermoid, acinar cell, adenocarcinoma (high and low grade tumours)	63 (64)	Grade, T-stage	60% (5)	89% (5)	87% low grade (5) 56% high grade (5)
Bell (2005)	[12]	85		Mucoepidermoid	48 (56)	T-stage, N stage, age LN grade ($p < 0.05$)	77% (5)	86% (5)	–
Lima (2005)	[15]	126	22 (17)	Mucoepidermoid, adenocarcinoma, acinar cell, adenoid cystic	74 (59)	Age (>50 years), T-stage, N stage, grade, facial nerve involvement ($p < 0.05$)	72% (5)	84% (5)	Not reported
Pohar (2005)	[19]	163		Adenoid cystic, squamous cell, adenocarcinoma, acinar cell	91 (56)	Age (>55 years), T-stage	50% (5)	89% (5)	55% (5)
Terhard (2005)	[8]	317	120 (38)	Adenoid cystic, adenocarcinoma, mucoepidermoid	279 (88)	T-stage, R1/R2, N stage, perineural invasion ($p < 0.05$)	63% (5)	86% (5)	64% (5)
Koul (2007)	[17]	184	36 (20)	Mucoepidermoid, acinar cell, adenoid cystic, adenocarcinoma	102 (56)	Age (>60 years), local invasion, grade, T-stage ($p < 0.05$)	62% (5)	62% (5)	50% (5)

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Table 2 shows the different prognostic factors in the various case series, so the institutional guidelines for postoperative radiotherapy are likely to vary. Our study showed that T-stage was the most significant variable to affect locoregional control, disease-specific survival, and overall survival. Age also had a significant impact on locoregional control. Our study agrees with other studies that T-stage and age are significant prognostic factors, but other studies have shown that grade, N stage, perineural invasion, adenoid cystic disease, and whether an R1 or R2 resection was done are also prognostic factors. This difference could be because the low number of patients in the different subgroups of our study do not show significance, particularly those who had invaded nodes and those with adenoid cystic carcinoma. In summary, based on our study and other reports we recommend that patients with T3–T4 tumours, invaded nodes, R1 or R2 resection, perineural involvement, high-grade tumours, and adenoid cystic carcinomas should have postoperative radiotherapy.

Our study has shown good results in patients who have adjuvant postoperative radiotherapy to the parotid bed, in spite of the group being varied. Although postoperative radiotherapy improves outcome, the indications for this are not defined clearly and vary according to institutional protocols. Further studies are therefore required to define the indications. As malignant parotid tumours are rare, these studies must be multi-centre to ensure adequate statistical power.

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