Outcomes following management of Squamous Cell Carcinoma of the Scalp: a retrospective series of 235 patients treated at the Peter MacCallum Cancer Centre.

Vanessa Estall[1,2], Angela Allen[3], Angela Webb[1], Mathias Bressel[1,] Chris McCormack[1], John Spilane[1, 2]

[1]Liverpool Hospital Cancer Therapy Centre, Sydney NSW 2071, Australia

[2]University of Melbourne, Parkville VIC 3010, Australia

[3]Waikato Regional Cancer Centre, Hamilton, New Zealand

[43]PeterMacCallum Cancer Centre, Melbourne VIC 3002, Australia

Abbreviated Title: Outcomes following management of SCC scalp.

Key terms: cutaneous squamous cell carcinoma, scalp, immunosuppression, outcomes

Word count: Title page 140, Abstract 197, Capsule Summary 93, Manuscript 2468, References 872

Number of figures and tables: Figures 7, Tables 8

Number of references: 30

Corresponding author: Dr Vanessa Estall BHB MBChB, FRANZCR, MD
Liverpool Hospital Cancer Therapy Centre
Locked bag 7103
PO Box 149
Liverpool 1871
Phone: +61 2 87389806
Fax: +61 2 87389819
Email: vjestall@hotmail.com

Disclosure statement: Funding sources: None
Conflicts of interest: None declared

Received Date : 19-Jan-2016
Revised Date : 26-Apr-2016
Accepted Date : 29-Apr-2016
Article type : Original Research

Abstract

Background

Squamous cell carcinoma (SCC) of the scalp is a common clinical problem in an aging population. Despite its high incidence, little has been documented regarding treatment or outcomes.

Methods

We retrospectively analysed 235 cases treated with curative intent at Peter MaCallum Cancer Centre, between 1998 and 2010. The cohort was analysed for demographics, management, survival and prognostic factors.

Results

The patients were primarily male (88%) with a median age of 79yrs (range 53-98). There was a high proportion of patient immunosuppression (29%) and stage T2 (48%) tumours. Management included surgery (45%), radiotherapy (28%) and surgery and adjuvant radiotherapy (26%). Median follow up from treatment was 4.5yrs. Estimated 5yr overall survival (OS), disease specific survival (DSS) and progression free survival (PFS) were 59%, 94% and 51% respectively. The 5yr cumulative incidence of local and regional relapse was 11.1% and 6.9% respectively. There were 4 patients who developed distant metastases and died of their disease. Statistically significant prognostic factors identified for poor outcomes for OS and PFS were T2 stage (Hazard ratio 1.7 and 2.1) and immunosuppression (Hazard ratio 3.3 and 3.4).

Conclusions

We conclude the presence of immunosuppression and T2 stage is prognostic for survival. Further research to establish treatment principles is warranted.

Introduction

Squamous cell carcinoma (SCC) of the scalp is a significant issue in Australia (1, 2). Lesions on the scalp account for 2% of all skin cancers and 10-20% of lesions in the head and neck region (3, 4). The incidence of SCC is significant in the elderly population (2) with men at particular risk of primary lesions on the scalp due to chronic sun exposure of this area. Clinical outcomes are assumed to be similar to SCC involving other parts of the head and neck region, with most series reporting all head and neck SCC's in the same cohort.

Few studies address the challenges of management and outcomes in the treatment of SCC of the scalp. In a large review of the Finnish cancer registry from 1967 to 1981, men with SCC of the scalp had a worse overall survival compared to the general cohort (80.2% vs. 87.8%) (5). Multiple publications have proposed the scalp as a high-risk site for SCC (6, 7, 8, 9), however the number of scalp cases analysed were small. The 7th edition of the Tumour Node Metastases (TNM) classification for NMSC by the American Joint Committee on Cancer (AJCC) incorporates risk factors for nodal metastases disease into the T stage in addition to tumour size (10). The scalp has not been included as a 'high-risk' site in the updated AJCC staging system. The National Comprehensive Cancer Network (NCCN) recommends SCC be stratified into a low or high risk of recurrence based on a tiered classification of anatomical sites, defining scalp SCC's as medium risk (11).

Due to the limited data available in the literature on this topic and inconsistency of recommendations, we performed a retrospective review of our practice to determine outcomes for patients with scalp SCC particularly with respects to patients with immune-suppression.

Methods

We conducted a retrospective review of patients with histologically proven, primary SCC of the scalp treated with curative intent between 1998 and 2010 at the Peter MacCallum Cancer Centre (PMCC), which is a large tertiary referral cancer hospital.

Patients were identified using the hospital's Division of Pathology and Radiation Oncology databases. Patient demographics, primary tumour characteristics and outcomes were recorded. We considered immuno-suppression as; co-existing haematological malignancy (including Hodgkin's/non-Hodgkin's lymphoma, chronic lymphocytic leukemia), immunosuppressant use (defined as prednisolone 5mg or more a day and/or other immunosuppressive agents for longer than one year), and end stage renal failure requiring dialysis. Tumour factors collected are reported in Table 1 and included SCC grade defined as G1 (well differentiated), G2 (moderately differentiated) and G3 (poorly differentiated). T stage was defined using the 7th edition TNM staging for NMSC (9), which allows T1 tumours <2cm in diameter to upstaged to T2 if they have 2 of the following features; >2mm thickness, Clark level >IV, perineural invasion, primary site ear or hair bearing lip, poorly differentiated or undifferentiated.

Primary treatment was recorded as surgery, radiotherapy or surgery followed by adjuvant radiotherapy. The treatment start date was taken as the date of surgery or the first day of radiotherapy. A recurrence was defined as local (within 2cm of the primary lesion), regional (first echelon lymph node metastases) or metastatic (beyond the first echelon lymph node region).

Overall survival (OS), disease specific survival (DSS) and progression free survival (PFS) were calculated from the date of treatment, and the survival curves were reported using Kaplan-Meier methods. Log rank test was used to assess the impact of risk factors on OS and PFS for univariate analysis while Cox proportional hazard models were used for multivariate analysis. All statistical analyses were performed in R (version 3.0.1; R Development Core Team 2009).

Results

Patient characteristics

Data was collected for 235 patients. The majority of patients (88%) were male and the median age at diagnosis was 79 years (range 53-98). Immunosuppression was present in 29% (Table 1).

Primary lesion characteristics

The primary lesions characteristics are shown in Table 1. Despite the majority of lesions being less than 20mm (63%), the proportion of stage T2 lesions was 52% due to 78% of lesions graded as G2 and G3. Depth of invasion and presence or absence of in-situ disease was rarely recorded in pathology reports or notes and therefore not included in the analysis. No patients were found to have had nodal disease at the time of first presentation.

Treatment

Of the 235 patients analyzed, 45% had definitive surgery, 28% had definitive radiotherapy and 26% had surgery followed by adjuvant radiotherapy. In patients who had surgery as primary therapy, margin status was difficult to assess, as this information was not documented in 29% of reports. Of the cases in which margin status was available, 24% were noted to be positive and the majority of these (78%) had been referred directly for adjuvant radiotherapy following surgery performed outside of our institution. Re-excision was performed by our surgeons in 9 patients and clear margins achieved in 4. All patients that did not have a re-excision received adjuvant radiotherapy.

Radiotherapy was delivered with adjuvant intent to the primary tumour bed in 26% with a range of dose from 32Gy to 66Gy. Prophylactic radiotherapy was delivered to draining lymph node basins in only 3 cases relapsed cases receiving salvage treatment, with doses ranging from 55Gy to 60Gy. Definitive radiotherapy was delivered in 28% of cases with a range of dose from 32Gy to 70Gy.

Survival

The median follow up time from date of first treatment was 4.5 years. The estimated 5 year overall survival (OS), disease specific survival (DSS) and progression free survival (PFS) was 59%, 94% and 51% respectively (see Figure 1, 2, and 3).

First site of relapse

Recurrence overall was documented in 35 (14.9%) patients following treatment, with 21 local and 14 regional relapses. The estimated cumulative incidence of local and regional relapse at 5yrs was 11.1% and 6.9% respectively. The majority of recurrences occurred in the first year (local 7.3% and regional 4.5%), and the incidence of recurrence reached a plateau at 3 years.

Local relapse

The characteristics of the 21 cases where local relapse was the initial site of failure are presented in Table 2. Most were stage T2 and did not receive adjuvant radiotherapy. Of the patients who recurred locally, 14% were immunosuppressed.

Regional relapse

The characteristics of cases where regional nodal relapse was the initial site of failure are presented in Table 2. These were similar to those associated with local relapse, apart from immunosuppression which was present in 50% of patients with regional relapse versus 29% with local relapse. The majority of these cases (9/14) had received adjuvant radiotherapy to the primary site, but none had received prophylactic treatment to draining lymph node basins.

Salvage and second relapse

Curative treatment was attempted in all 35 patients after an initial relapse. Of the 21 patients that developed a local recurrence and received salvage treatment, 4 relapsed again (3 adjacent lymph nodes, 1 distant). Of the 14 patients that developed a regional recurrence and received salvage treatment, 5 relapsed again (2 in regional lymph nodes, 3 distant).

Distant relapse

There were no cases of distant recurrence as the initial site of relapse. All 4 patients who developed distant metastases following initial or local relapse, died of their SCC scalp.

Prognostic factors

On univariate analysis the factors significant for poorer outcome for OS were immunosuppresion, T stage, size and type of treatment (Table 3), and these same factors in addition to positive margins and presence of LVI were signifcant for poorer outcome for PFS (Table 4). On multi-variatine only immunosuppression and T stage remained significant for both.

For OS the hazard ratio (HR) for immunosuppression in the multi factor model was 3.4 [95% CI (2.2 – 5.1)] and the HR for T stage in the multifactor model was 1.7 [95% CI (1.1 – 2.5)]. For PFS the HR for immunosuppression in the multifactor model was 3.3 [95% CI (2.3 – 4.9)] and the HR for T stage in the multifactor model was 2.1 [95% CI (1.4 – 3.1)].

The 5yr DSS for Stage T1 versus T2 was 100% and 88% respectively (Figure 4). The 5yr DSS for immune competent patients versus immune compromised patients was 96% and 87% respectively (Figure 4).

The 5yr PFS for Stage T1 versus T2 was 67% and 36% respectively (Figure 5). The 5yr PFS for immune competent patients versus immunocompromised patients was 62% and 27% respectively (Figure 5).

Discussion

To our knowledge this is the largest reported cohort of patients (n=235) with primary scalp SCC treated with curative intent. The majority of our patients were elderly men, and were managed with surgery, radiotherapy or a combination of both modalities, consistent with other reports. No patients had nodal disease at presentation, and the role of staging was not assessed. We had a large representation of patients with high risk disease with 52% of tumours being T2 and 78% being moderately or poorly

differentiated, and almost a third of patients (29%) being immunosuppressed. This may reflect the referral patterns and nature of our unit, which is within the context of a large 'cancer only' hospital.

On reviewing the literature we have found only 3 other small studies addressing scalp specific populations, and another 2 addressing general skin cancer populations which included scalp patients. A comparison of these studies and ours are provided in Table 5. Mohs et al reported on a cohort of 83 scalp patients with good outcomes following Mohs surgery (12). Lang et al reported on a series of 11 scalp cases treated with Mohs microsurgery, which then progressed in an aggressive fashion. They noted a higher than expected rate of death due to SCC (5/11 patients) but prognostic factors were poorly reported (4). Howle et al reported on the outcomes and prognostic factors for 27 patients who developed metastatic nodal disease from a scalp SCC primary. The 5yr DSS was 59% reflecting the impact of nodal relapse on survival outcomes (13). Schumults et al (14) assessed 985 patients with 1832 treated invasive SCC's from all sites, with a median follow up of 50 months. The OS, loco- regional DFS and DSS at 5 years were 68%, 96% and 97% respectively. Overall local recurrence was 4.6%, nodal recurrence was 3.7% and 2.1% of patients died as a result of their SCC. Brantsch et al (15) reported on a prospective trial of 615 patients, documenting local and regional recurrence rates of 3% and a 4%.

The survival outcomes were slightly worse for our cohort of scalp SCC patients in comparison to those previously published. The 5yr OS of 59% and DSS of 94% suggest only a small proportion of patients died from their SCC scalp specifically, with the majority succumbing to age related co-morbidities. However, overall recurrence was 15% in our cohort, compared to 4-5% noted in series assessing SCC from all sites (14, 15). PFS at 5yrs was 51% indicating that the likelihood patients would relapse following initial treatment was high, but in most cases this was successfully salvaged. Our poorer control and survival outcomes are most likely a reflection of selection bias, as we demonstrated a statistically significant reduction in PFS and OS in the setting of increased stage of the primary lesion above T2 (HR 2.1), and in the presence of host immunosuppression (HR 3.3). We had high proportions of both these prognostic factors in our group.

Our finding that T2 primary lesions are associated with a worse OS and PFS indicates that accurate T staging of primary lesions is important for prognostication and treatment planning. Despite this, a third of pathology reports in our cohort did not document prognostic factors for accurate T staging of SCC with depth of invasion, status of PNI and LVI and margin status often omitted. Synoptic reporting is currently recommended for melanoma, and there may be a role for a similar type of report in for SCC, to ensure that the small percentage of 'high-risk' lesions are easily identified and managed appropriately at diagnosis.

Following accurate staging, adequate surgical management of the primary lesion is the gold standard of treatment. The impact of margin status on outcomes remains unclear, and the heterogeneity and poor documentation of the margin status in our cohort makes the results difficult to interpret. Of the 41 patients with documented positive margins, the majority of cases were positive at the deep margin (32/41), which is not un-expected for scalp lesions. In the group identified by Howle et al (7), a high proportion of patients with nodal spread had close or positive margins (51%) following treatment of the primary lesion. In the absence of clear evidence, basic oncological principles indicate clear margins should be the surgical goal. This approach is supported by surgical series suggesting that clear margins are associated with very low rates of recurrence, particularly if margins of >2 -4mm can be achieved (16, 17, 18, 19). In order to achieve this in the scalp, it may be necessary to consider re-excision, removal of periosteum or even removal of the outer table of the skull.

Host immunosuppression is now accepted as an important risk factor for adverse outcomes following management of SCC, and our results have further confirmed this. Immunosuppression is associated with an increased risk of nodal metastases, distant metastases and death from SCC as shown by multiple studies (20, 21, 22, 23). In our series, the 5yr PFS for immune-competent versus immune-compromised patients was 62 vs. 27%, with half of the patients who developed regional recurrence being

immuno-compromised. Although deaths from SCC are rare, in our and other cohorts most patients who died from their disease did so in the setting of nodal metastases (7, 24, 25).

Although not statistically significant, patients in our study who developed recurrent disease had poorer survival outcomes following salvage treatment with high rates of regional (14.3%) and distant relapse (11.4%). Lebovitch et al demonstrated a statistically significant increased risk of recurrence of 6.9% vs. 2.6% in patients treated for recurrent versus primary SCC (26). Mohs et al demonstrated a 5year cure rate of SCC of the scalp was 98.8% following Mohs microsurgery. However the presence of recurrent disease reduced the chance of cure to 90% (12). This suggests that prevention of local and regional relapse following the first presentation may be of significant value. The role of prophylactic surgery or radiotherapy of the clinically node negative neck remains unclear in this setting due to a lack of high quality clinical data. Only 3 of our patients received prophylactic nodal radiotherapy to draining lymph nodes at relapse, and none at first presentation, so we are unable to comment on its efficacy in this setting. However, elective nodal irradiation has been addressed in other series of SCC patients, showing it can reduce the risk of regional lymph-node recurrence in patients with high risk primary disease (27, 28, 29). Therefore, it could be considered in high-risk cases, but patients must be selected following an individualized risk: benefit analysis, acknowledging that enlarging treatment fields can have a significant impact on toxicity and quality of life, which may not be appropriate in some patients. More accurate nodal staging may aid in better patient selection for aggressive treatment. Sentinel lymph node biopsy (SLNB) in the staging of SCC has been investigated in small series and may be feasible, identifying occult nodal metastases in 20% of cases (30). Where available this could be useful in the setting of scalp SCC where lymphatic drainage is unpredictable, and could aid patient selection for elective nodal treatment versus observation.

In summary, we have presented a large cohort of scalp SCC cases and found that, although the majority of patients do well, there is a group who may have significantly

poorer outcomes. Patients with T2 primary lesions and immunosuppression have a lower OS and PFS, and although there is no evidence at this point that more aggressive management of these patients will result in improved survival outcomes, it is reasonable to offer treatments aimed at maximizing loco-regional control. SCC's of the scalp will become a more common problem with an aging population, and future research into the utility of staging and prophylactic nodal treatment of the clinically negative neck is warranted.

References

1. Australian Institute of Health and Welfare & Cancer Australia (2008). Non-melanoma skin cancer. General practice consultations, hospitalisation and mortality *Cancer Series* 2008: No 43

2. Staples, M. P., M. Elwood, R. C. Burtonete al.. Non-melanoma skin cancer in Australia: the 2002 national survey and trends since 1985. *Med J Aust***.** 2006: 184(1): 6-10.

3. Czarnecki, D., M. Staples, A. Mar et al. Metastases from squamous cell carcinoma of the skin in southern Australia. *Dermatology*. 1994; 189(1): 52-54.

4. Lang, P. G., M. A. Braun and R. Kwatra. Aggressive squamous carcinomas of the scalp. *Dermatol Surg* 2006; 32(9): 1163-1170.

5. Karjalainen, S., H. Salo and L. Teppo. Basal cell and squamous cell carcinoma of the skin in Finland. Site distribution and patient survival. *Int J Dermatol* 1989; **28**(7): 445-450.

6. Nolan, R. C., M. T. Chan and P. J. Heenan. A clinicopathologic review of lethal nonmelanoma skin cancers in Western Australia. *J Am Acad Dermatol*. 2005; 52(1): 101-108.

7. Edge, S. B. and C. C. Compton.The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. 2010; 17(6): 1471-1474.

8. Dinehart SM, Peteron S. Evaluation of the American Joint Committee on Cancer Staging System for cutaneous squamous cell carcinoma and proposal of a new staging system. *Dermatol Surg*. 2005;31(11):1379-84.

9. Veness, M. J. High-risk cutaneous squamous cell carcinoma of the head and neck. *J Biomed Biotechnol* 2007; (3): 80572.

10. Warner CL, Cockerell CJ. The new seventh edition American Joint Committee on Cancer Staging of Cutaneous Non-Melanoma Skin Cancer. *Am J Clin Dermato.* 2011; 12 (3):147-154.

11. Miller SJ, Alam M, Anderson J et al. NCCN practice guidelines in oncology: basal cell and squamous cell skin cancers. Version 1, 2009 (http://www.nccn.org)

12. Mohs, F. E. and J. A. Zitelli. Microscopically controlled surgery in the treatment of carcinoma of the scalp. *Arch Dermatol* 1981; 117(12): 764-769.

13. Howle, J. R., G. J. Morgan, I. Kalnins et al. Metastatic cutaneous squamous cell carcinoma of the scalp. *ANZ J Surg.* 2008; 78(6): 449-453.

14. Schmults, C. D., P. S. Karia, J. B. Carter et al. Factors predictive of recurrence and death from cutaneous squamous cell carcinoma: a 10-year, single-institution cohort study. *JAMA Dermatol* 2013; 149(5): 541-547.

15. Brantsch, K. D., C. Meisner, B. Schönfisch et al.Analysis of risk factors determining prognosis of cutaneous squamous-cell carcinoma: a prospective study. 2008; 9(8): 713-720.

16. Jambusaria-Pahlajani, A., Miller, CJ., Quon, H. et al. Surgical monotheraoy versus surgery plus adjuvant radiotherapy in high-risk cutaneous squamous cell carcinoma: a systematic review of outcomes. *Dermatol Surg* 2009; 35(4):574-585.

17. Brodland DG,. Zitelli, JA.Surgical margins for excision of primary cutaneous squamous cell carcinoma. *J Am Acad Dermatol* 1992; 27:241-248.

18. Tan, PY., Ek, E., Giorlando F. Incomplete excision of squamous cell carcinoma of the skin: a prospective observational study. *Plast Reconstr Surg* 2007; 120(4):910-916.

19. Broadland, DG., Zitelli, JA. Surgical margins for excision of primary cutaneous squamous cell carcinoma. *JAAD* 1992; 27: 241-248.

20. Cooper, J. Z. and M. D. Brown. Special concern about squamous cell carcinoma of the scalp in organ transplant recipients. *Arch Dermatol* 2006; 142(6): 755-758.

21. Rowe, D. E., R. J. Carroll and C. L. Day.Prognostic factors for local recurrence, metastasis, and survival rates in squamous cell carcinoma of the skin, ear, and lip. Implications for treatment modality selection. *J Am Acad Dermatol* 1992; 26(6): 976-990.

22. Tomaszewski, J. M., H. Gavriel, E. Link, S. et al. Aggressive behavior of cutaneous squamous cell carcinoma in patients with chronic lymphocytic leukemia. *Laryngoscope* 2014; 124(9): 2043-2048.

23. Frierson, H. F., B. D. Deutsch and P. A. Levine.Clinicopathologic features of cutaneous squamous cell carcinomas of the head and neck in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma. *Hum Pathol* 1988; 19(12): 1397-1402.

24. Clayman, G. L., J. J. Lee, F. C. Holsinger et al. Mortality risk from squamous cell skin cancer. *J Clin Oncol* 2005; 23(4): 759-765.

25. http://www.cancer.org.au/about-cancer/types-of-cancer/skin-cancer.html

26. Leibovitch, I., S. C. Huilgol, D. Selva et al. Cutaneous squamous cell carcinoma treated with Mohs micrographic surgery in Australia I. Experience over 10 years. 2005; 53(2): 253-260.

27. Khan, L., D. Breen, L. Zhang et al. Predictors of recurrence after radiotherapy for non-melanoma skin cancer. *Curr Oncol* 2014; 21(2): e326-329.

28. O'Brien, C. J. The parotid gland as a metastatic basin for cutaneous cancer. *Arch Otolaryngol Head Neck Surg***.** 2005; 131(7): 551-555.

29. Veness, M. J., C. E. Palme and G. J. Morgan. High-risk cutaneous squamous cell carcinoma of the head and neck: results from 266 treated patients with metastatic lymph node disease. 2006; 106(11): 2389-2396

30. Ross AS, Schmults CD.Sentinal lymph node biopsy in cutaneous squamous cell carcinoma: a systematic review of the English literature. *Am Soc Derm Surg.* 2006; 32 :1309-1321.

Figures

Figure 1 Overall survival (OS) for primary SCC of the scalp

Figure 2 Disease specific survival (DFS) for primary SCC of the scalp

Figure 3 Progression free survival (PFS) for primary SCC of the scalp

Figure 4 Disease specific survival (DSS) according to T stage and immunosuppression status

411 Figure 5 Progression free survival (PFS) according to T stage and
412 immunosuppression status

Table 1. Characteristics of 235 patients and primary cSCC scalp lesions.

Characteristic		**Number**	**Percentage**
Gender	Male	207	88%
	Female	28	12%
Immunosuppression	Yes	67	29%
	Co-existing malignancy*	49/67	73%
	Chronic immunosuppressant's	16/67	24%
	End stage renal failure	2/67	3%
Size	20mm or less	149	63%
	>20mm	86	37%
Grade	G1	38	22%
	G2	77	46%
	G3	54	32%
Margin status	Positive	41	24%
	Negative	128	76%
Positive margin type	Deep	32	78%
	Radial	9	22%
Perineural invasion	Positive	29	12%
	Negative or not reported	206	88%
Lymphovascular invasion	Positive	15	6%
	Negative or not reported	220	96%
T stage	T1	111	48%
	T2	122	52%

	T4	2	<1%
Treatment modality	Surgery alone	105	45%
	Radiotherapy alone	66	28%
	Surgery and adjuvant radiotherapy	62	27%

*35/49 (72.5%) patients with co-existing malignancy had hematological malignancy

Table 2. Characteristics of local and regional relapse as the first site of recurrence following definitive surgery of the primary lesion

	Local	Regional
Variable	Count	Count
Size: median (range)	22 (7 - 80mm)	8 (5 - 12mm)
Grade		
1	5	1
2	11	4
3	5	7
Margin		
Positive	4	6[£]
Negative	7	8
PNI[¥]		
Positive	4	3
Negative	6	10
LVI[¥]		
Positive	3	5
Negative	7	8
T stage		
I	7	0
II	14	14
Adjuvant RT (primary only)		
Yes	5	9
No	16	5
Immunosuppression		
Yes	6	7
No	15	7

[£] 4 of the 6 positive margins were deep

Table 3. Unifactor analysis of possible risk factors for overall survival.

Variable	Category	Count	%	HR (95% CI)	p-value
Immunosuppression	No	168	71	1	<0.001
	Yes	67	29	3.3 (2.2 - 5.0)	
T Stage[1]	Stage 1	111	48	1	0.013
	Stage 2	122	52	1.7 (1.1 - 2.6)	
Grade[2]	Grade 1	38	22	0.9 (0.7 - 1.3)	0.608
	Grade 2	77	46		
	Grade 3	54	32		
Size	20mm or less	149	63	1	0.013
	More than 20mm	86	37	1.7 (1.1 -2.6)	
Margins positive[3]	No	128	76	1	0.399
	Yes	41	24	1.3 (0.7 - 2.1)	
Margin type[4]	Deep	32	78	1	0.737
	Radial	9	22	0.8 (0.3 - 2.4)	
Closest deep margin[5]	<1mm	27	71	1	0.660
	1mm or more	11	29	0.8 (0.3 - 2.4)	
PNI	No	206	88	1	0.247
	Yes	29	12	1.4 (0.8 - 2.4)	

LVI	No	220	94	1	0.899
	Yes	15	6	0.9 (0.4 - 2.2)	
Treatment	RT	66	28	1	0.031
	Surgery	105	45	0.6 (0.3 - 0.9)	
	Surgery + RT	62	27	0.9 (0.5 - 1.7)	

Table 4: Unifactor analysis of possible risk factors for progression free survival.

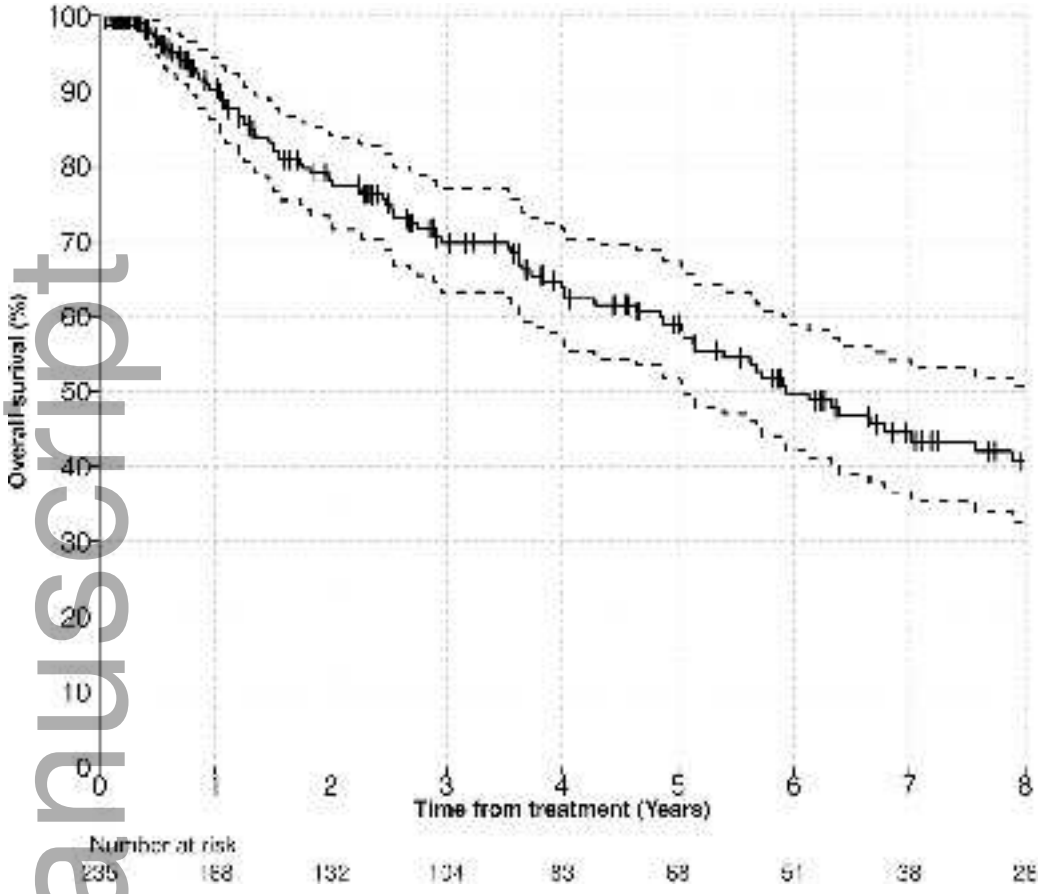
Table 5: Comparison of series data

Prognostic factors	Moh et al 1981	Lang et al 2006	Howle et al	Brantsch et al 2008	Schmults et al 2013	Estall et al 2014
Total number	83	11	27	653	1832	235
Scalp specific	Yes	Yes	Yes	ND	ND	100%
H&N specific	NA	NA	NA	ND	28.7%	NA
Male		55%	96%	63%	52.7%	88%
Size >20mm		ND **	50%	31%	12.9%	37%
MD/PD		36%	71%	47%	33.6%	78%
PNI		ND	ND	8%	4.3%	12%
LVI		ND	ND	ND	ND	6%
+margin		ND	51%	0	ND	24%
Immunosuppressed		ND	3%	5%	14.5%	29%
Excision/Mohs alone	100%	100%	77%	100% (with clear margins)	89%	45%
Radiotherapy alone		0		0	0	28%
Excision/Mohs + adjuvant RT		0	23%	0	1.2%	27%
Other/not documented		0	0	0	8.8%	0
5yr OS					69%	59%
5yr PFS	98.8%			97%	83%	51%
5yr DSS		54%	59%		97.5%	94%

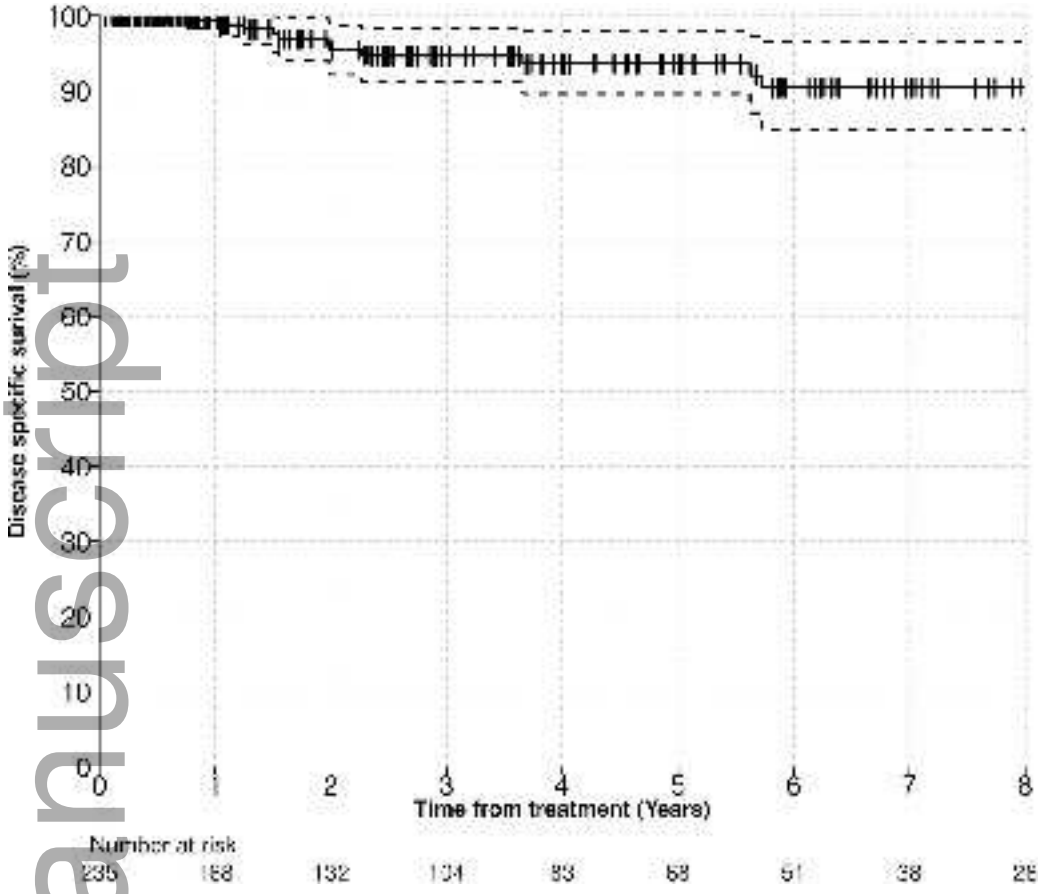
Local recurrence		73%		3%	4.6%	10.3%
Nodal recurrence		27%*	100%	4%	3.7%	6.9%

*8/11 patients developed satellite lesions and dermal spread, 3/11 developed nodal disease

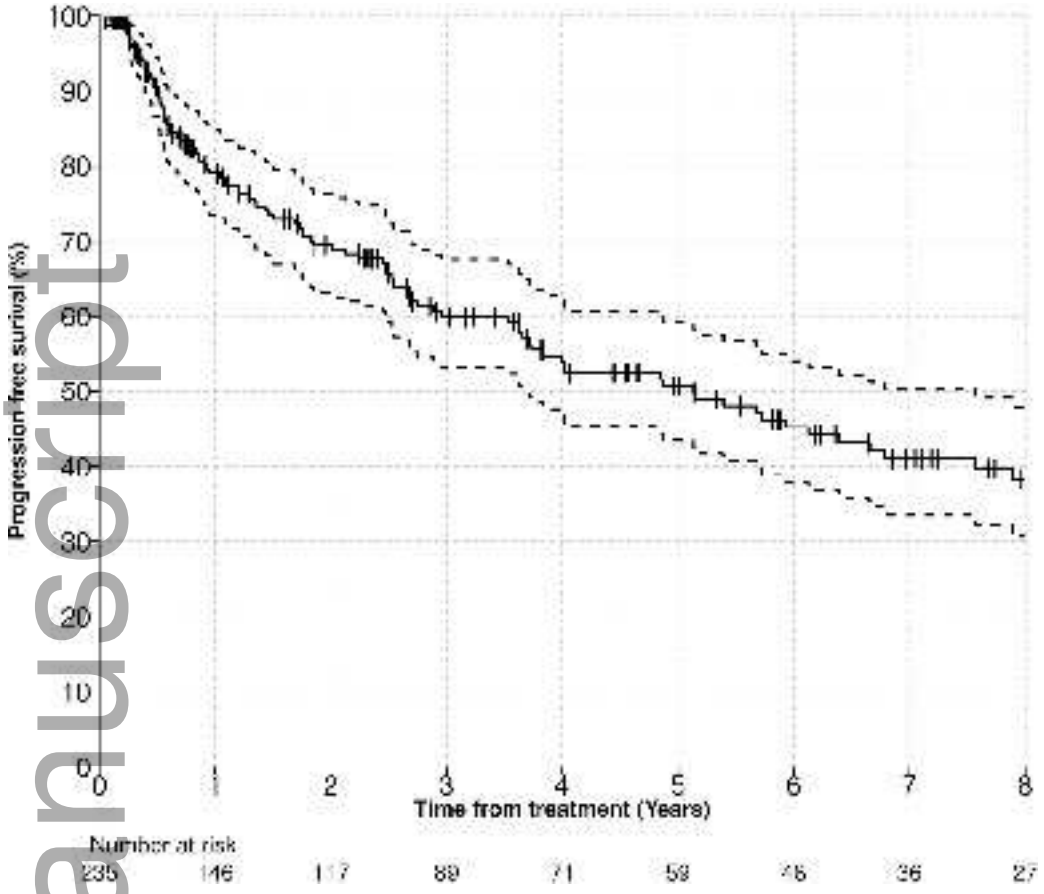
**not documented



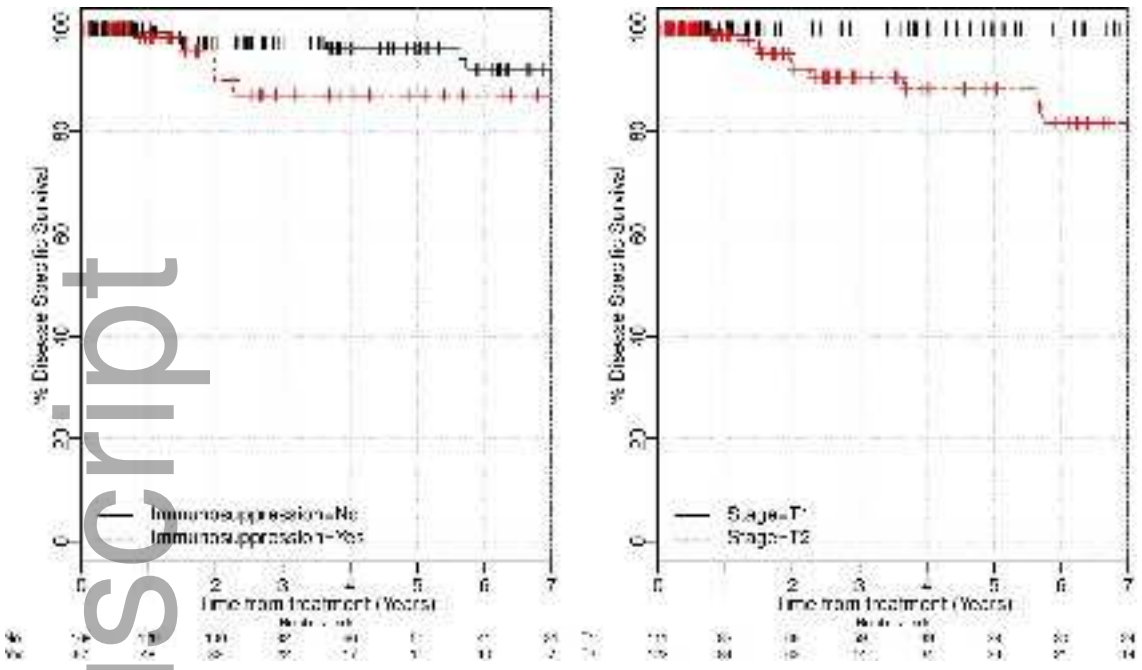
ajd_12520_f1.jpg



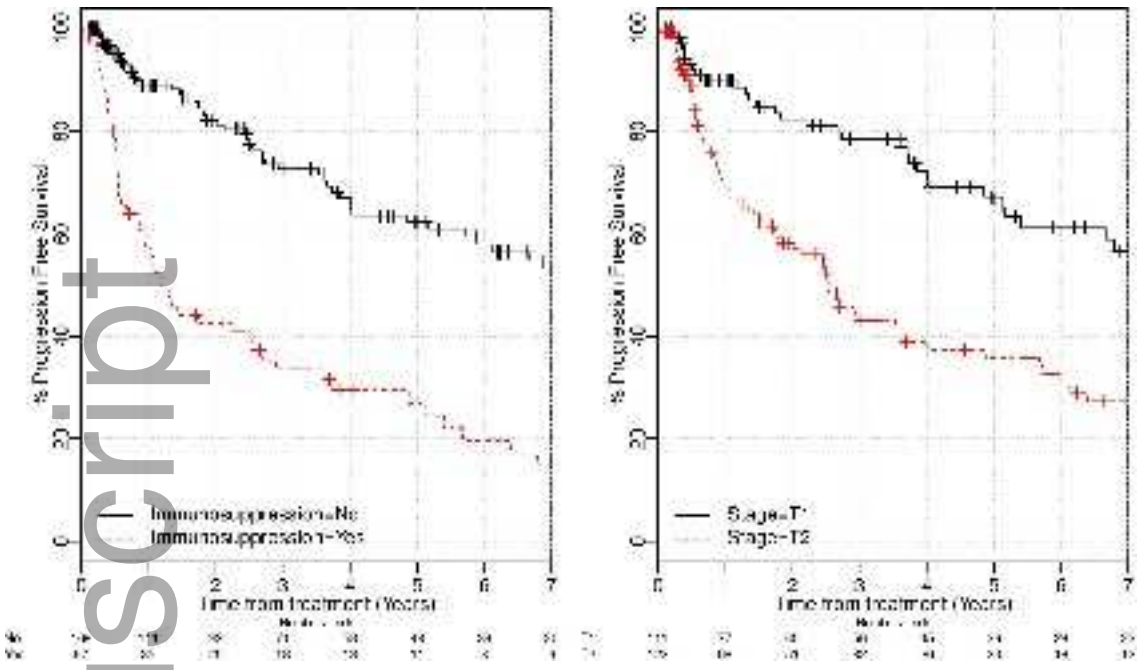
ajd_12520_f2.jpg



ajd_12520_f3.jpg



ajd_12520_f4.jpg



ajd_12520_f5.jpg