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Management of Head and Neck Melanoma

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1. Introduction

The incidence of melanoma in New Zealand (NZ) is one of the highest in the world: The rate in Caucasians is approximately 50 per 100,000, while the incidence in the NZ Maori population and the NZ Polynesian population is much lower contributing 15% and 7% of the total number of melanoma reported annually (Shaw, 2008). The primary author has twenty-six years' Consultant Surgical experience with melanoma surgery. Our database goes back to 1984 and includes 3,500 patients, of which 550 patients have been managed for head and neck melanoma. We have included all patients with either head and neck primary melanoma or regional melanoma involving cervical regional nodes or parotid nodes managed in the Auckland area 1984-2005. No patients have been excluded. These Head & Neck melanoma (H&NMM) data have never been published in the world literature. We reviewed our head and neck melanoma data base and this constitutes the basis of this study.

2. Background & methods

The head and neck area is a preferred site for melanoma; 9% of the body's surface area but 15% of the total melanoma distribution (Douglas & Shaw, 1987)

The outcome is probably less favourable in the head and neck area than in limbs or trunk (Douglas & Shaw, 1987) (Fisher & O'Brien, 2002). In addition, some head and neck sites are less favourable than others for example scalp, mucosal lesions tend to be less favourable than facial lesions (Douglas & Shaw, 1987; Fisher & O'Brien, 2002), further it is unclear whether melanomas from the trunk metastasising to cervical lymph nodes are more or less favourable than melanomas spreading to regional nodes with a head and neck primary.

Over the past 20 plus years for lesions < 1 mm in thickness we have used a 1 cm margin for lesions, > 2 mm thickness a 2 cm margin and for lesions between 1 and 2 mm thickness a margin of between 1 and 2 cm. The approach for thin lesions has been based on the work of Umberto Veronessi and colleagues (Veronessi et al, 1998), while our approach for thicker lesions has been validated in a prospective study by Merion Thomas and colleagues (Thomas et al, 2004).

Prior to the advent of sentinel node biopsy regional disease was treated with a therapeutic node dissection after positive fine needle aspirate cytology (FNA). Most commonly this was a selective neck dissection. Since the advent of sentinel node biopsy patients with a positive sentinel node have all been treated with either a selective or modified neck dissection depending upon the site of the primary lesion. After neck dissection virtually all patients

were offered radiotherapy and this was accepted by around half the patients. Nodal disease was classified N0 if no nodes were involved, N1 if one node was positive, N2 if 2-3 nodes were involved, and N3 if 4 or more nodes involved.

Survival was calculated using Kaplan Myer analysis while comparison between patient groups was performed using Chi squared analysis.

Questions asked of our data-base included assessment of :

- a. Anatomical-site, sex, and primary thickness on outcome
- b. Significance of local and regional recurrence on outcome
- c. Determine extent of neck dissection required as a function of primary anatomical site
- d. Determine effect of adjuvant radiation following neck-dissection on regional re-recurrence and survival
- e. Assess the outcome for patients with primary site that is:
 - i. outside head and neck area
 - ii. desmoplastic subtype and
 - iii. mucosal subtype

3. Results

3.1 Anatomical distribution and thickness of primary lesions

The commonest H&N primary anatomical site was face (52%), followed by scalp (19%), neck (17%), ear (9%), and mucosal lesions (3 %).

37% of primary lesions were < 0.75 mm thick, 14% were 0.76-1.5 mm thick, 27% were 1.5 – 4.0 mm thick, and 23% were > 4.0 mm thick.

Predictably, as in other parts of the body, the thickness of the primary lesion governed outcome see Figure 1.

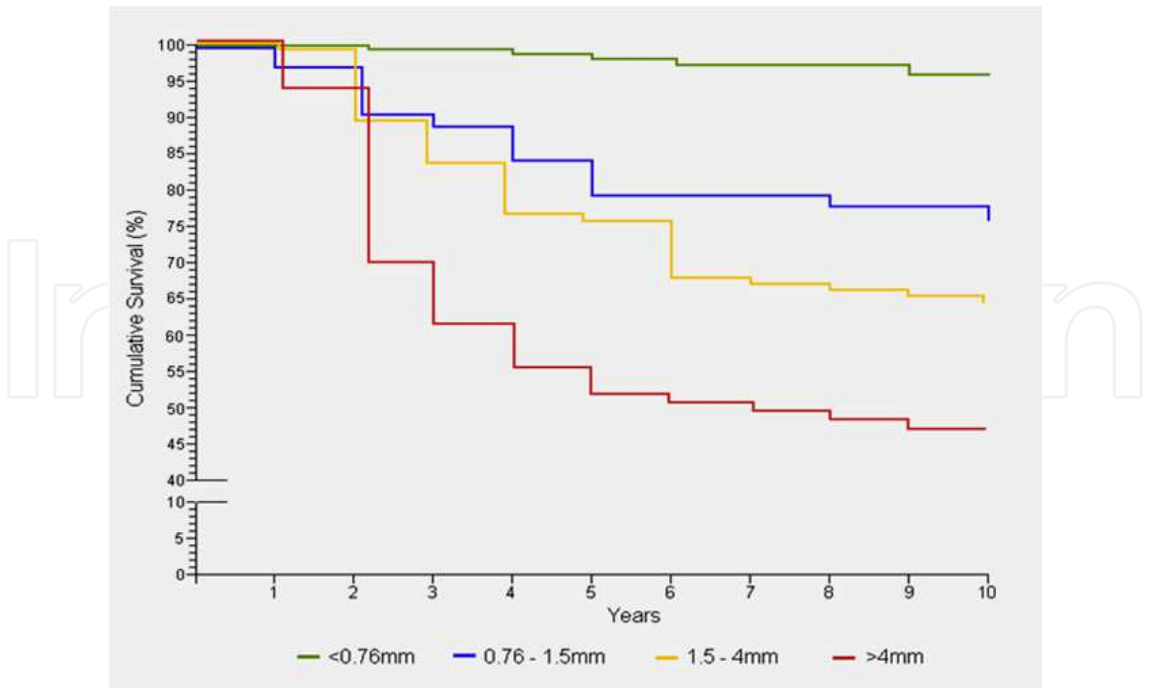


Fig. 1. Effect of Primary Thicknesses on Survival – Auckland

The sex incidence was higher in males than females and is summarised in Table 1:

Trunk primary lesions metastasising to cervical nodes, and scalp lesions, were significantly more common in males ($p<0.05$, and $p<0.03$ respectively). Ear lesions were almost twice as common in males as in females.

	Male	Female	Ratio
Face	140	126	1.1
Neck	49	40	1.2
Ear	28	15	1.9
Trunk	15	4	3.8*
Scalp	75	10	7.5 **
Total	307	195	1.6

Table 1. Sex Incidence Head & Neck Melanoma - Auckland

The effect of anatomical site on survival is shown in fig 2. Survival for facial lesions is significantly better than for neck lesions ($p<0.05$) and for Scalp & ear lesions ($p<.01$).

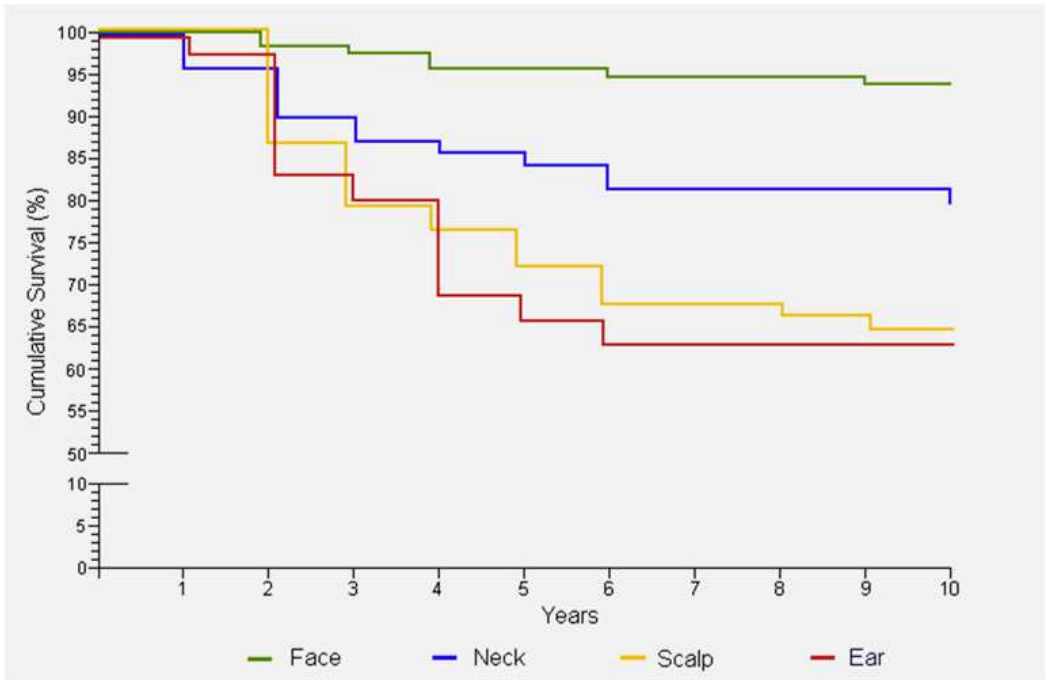


Fig. 2. Effect of Anatomical Site on Survival - Auckland

Local recurrence (LR) occurred in 5% for patients with facial, neck and ear lesions versus 13% for scalp lesions ($p < 0.05$) and 50% for mucosal lesions ($p < 0.01$). Local recurrence became progressively more common with increasing thickness of the primary lesion: see Table 2.

Thickness mm	% Local Recurrence	Fraction
< 0.76	5%	8/168
0.76 - 1.5	11%	7/62
1.5 - 4.0	10%	11/112
> 4	20%	20/99
Overall	10%	46/441

Table 2. Effect of Thickness on Local Recurrence – Auckland

The pie graph (Fig 3) outlines the most likely reasons for local recurrence and their relative frequencies.

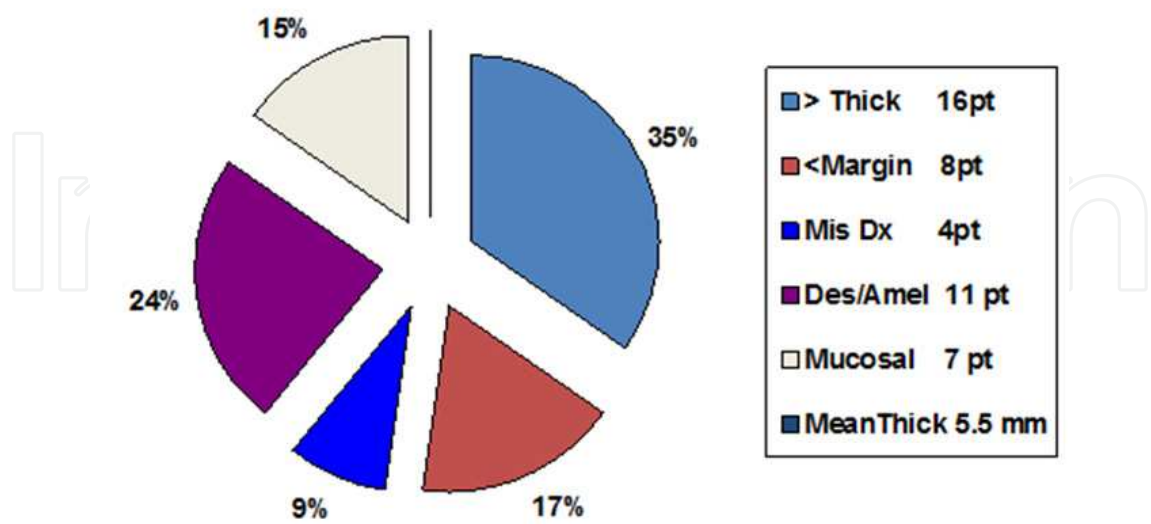


Fig. 3. Factors Associated with 46 Local Recurrences - Auckland

Local recurrence had a major impact on outcome in particular there was a significant increase in both the development of regional disease and also death from disease in those patients who developed LR compared with those who did not develop LR. see Table 3

No Local Recurrence		Local Recurrence	
Regional Nodes	26% (97/425)	Regional Nodes	46%*21/46***
Dead of Disease	25% (99/425)	Dead of Disease	72%*** (33/46)****

Table 3. Local Recurrent & Outcome - Auckland

The impact on survival of either local recurrence or regional recurrence was almost identical: see Figure 3.

Regional disease was a function of thickness of the primary with 5% of patients developing regional disease with primary lesions < 0.75 mm. 25% of patients with primary lesions 0.76 – 1.5 mm thickness developed regional disease and 35% of patients with melanomas over 1.5 mm thickness developed regional disease.

The timing of regional disease was a function of the thickness of the primary melanoma. Patients who had regional disease at initial presentation had a mean primary thickness of over 6 mm, while patients who presented with progressively thinner primary lesions developed regional disease progressively later. see Table 4.

Timing of Nodes	10 Thickness	No of Nodes
@ Diagnosis	6.2 +/- 1.2 mm	2.1
@ 1-12 mths	2.8 +/- 0.4 mm	3.1
@ 12-48 mths	1.9 +/- 0.3 mm	2.8
@ 48 mths +	1.3 +/- 0.5 mm	2.2

Table 4. Timing of Nodal Disease v 10 Thickness - Auckland

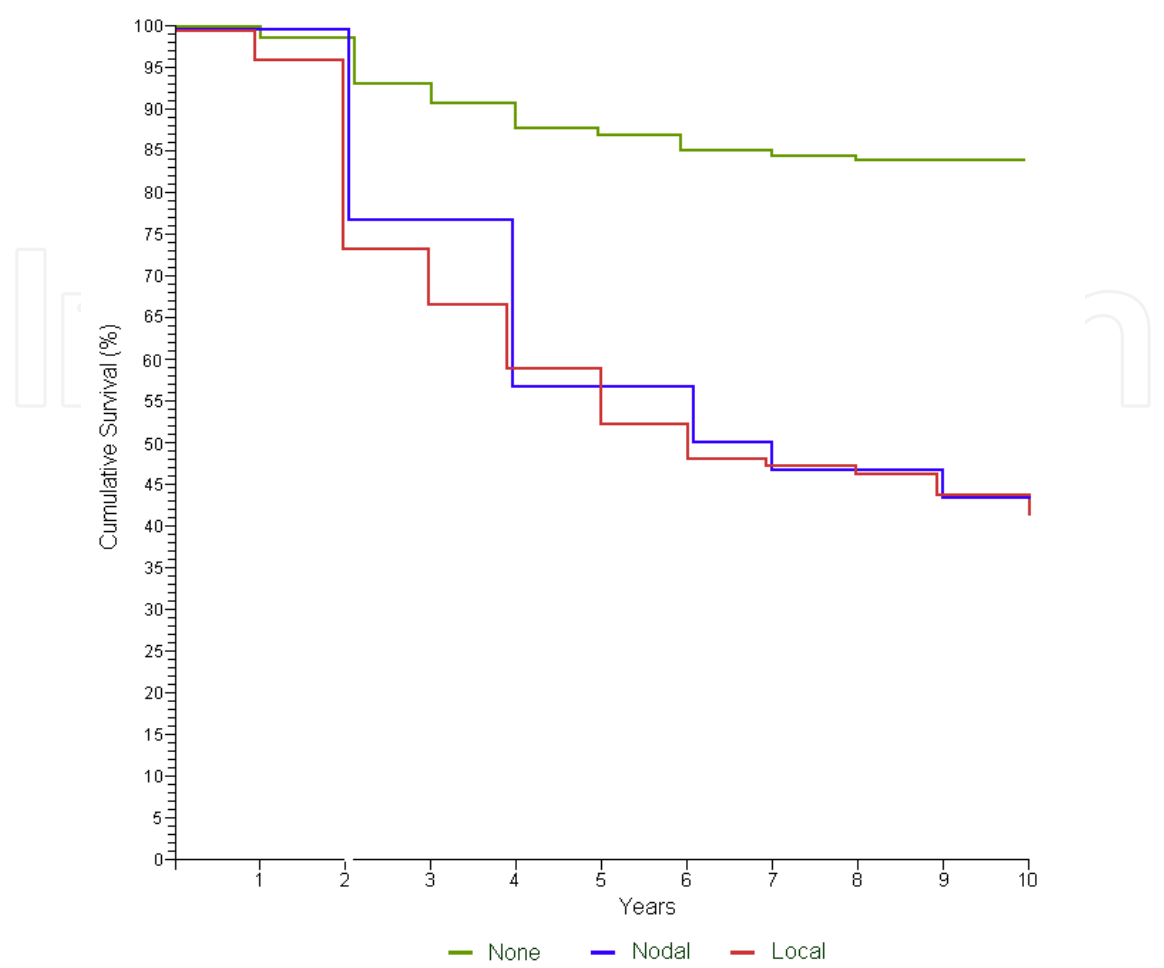


Fig. 3. Influence Local or Regional Recurrence on Survival - Auckland

Survival following the diagnosis of regional disease was not influenced by disease free interval. Although patients who had longer disease free intervals between initial diagnosis and the development of regional disease lived longer overall, once regional disease occurred the survival curves were not significantly different. See fig 4.

The sites of Regional Disease as a Function of anatomical site of the primary lesion are summarised in Table 5. The commonest sites of regional disease were level 2 nodes and parotid nodes.

	Ear n=14	Face n=41	Scalp n=39	Neck n=29	Total n=123
Parotid	64%	46%	31%	10%	38%
Level 1	-	11%	7%	21%	9%
Level 2	50%	29%	30%	90%	50%
Level ¾	7%	5%	20%	67%	25%
Level 5	-	5%	28%	67%	25%
Sub-occipital	-	-	8%	7%	4%
Post-auricular	-	-	18%	7%	6%

Table 5. Regional Disease v Anatomical Site of Melanoma – Auckland

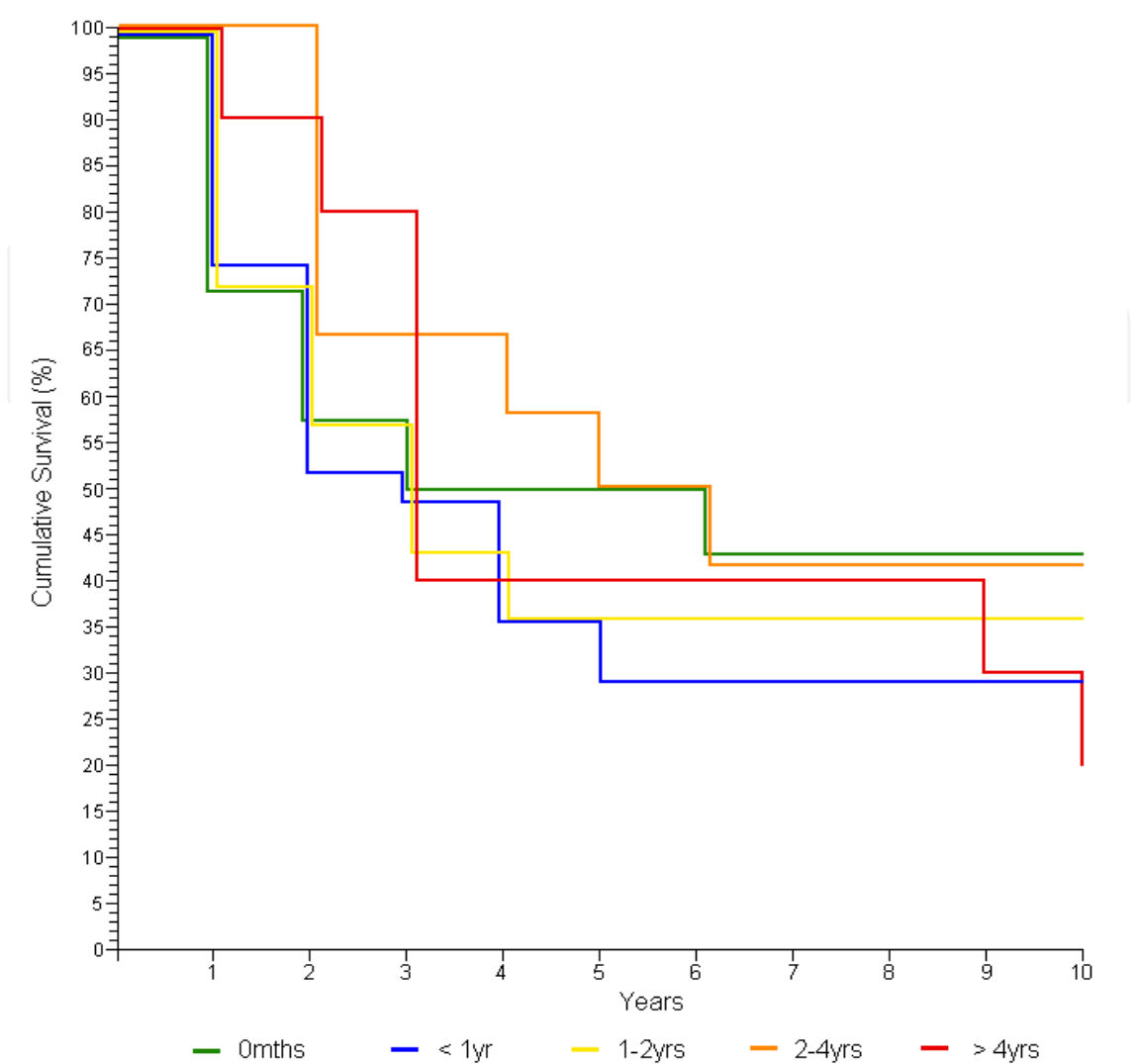


Fig. 4. Survival Node +ve Patients from Onset of Regional Disease - Auckland

3.2 Sentinel node studies

Our Sentinel node data were in general accord with the above data regarding site of regional disease as a function of anatomical site of the primary melanoma with Level 2 and Parotid being the commonest sites of involvement. The unusual findings from these studies were:

- 1. Bilateral or contralateral sentinel nodes in patients with lesion near the midline.
- 2. The frequent incidence of multiple sentinel nodes (up to 5)
- 3. The unpredictability of upper trunk lesions, for example spreading to contralateral Level 1.

See Discussion for detailed analysis of sentinel data with world literature.

3.3 Survival as a function of regional disease

Patients without regional disease (stage No) had 90% 5 year survival. Patients with only one node involved (stage N1), had 70% 5 yr survival, patients with stage N2 disease (2-3 nodes involved) had 57% 5 yr survival, while N3 patients with 4 or more nodes involved had 37% 5 yr survival. See Fig 5

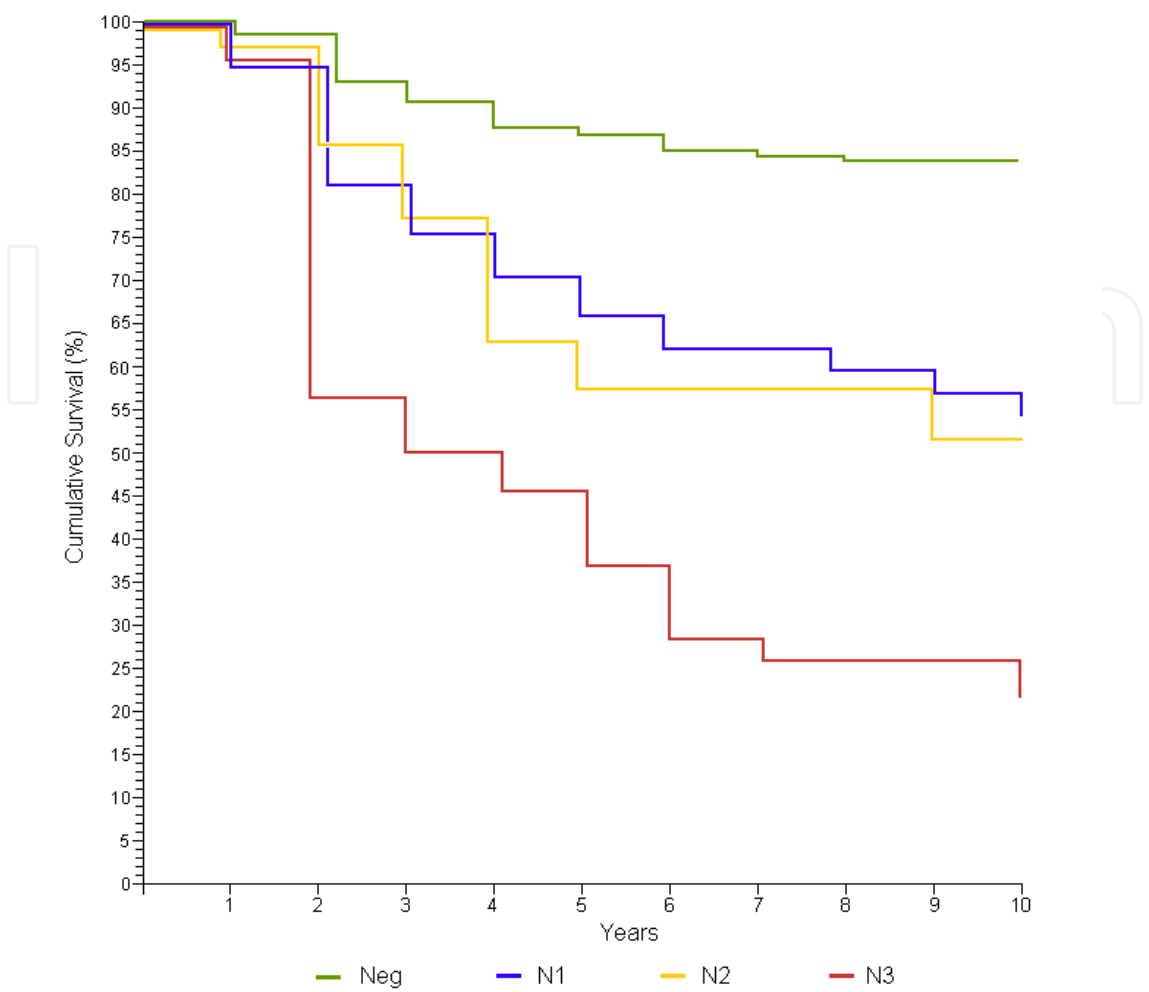


Fig. 5. Stage of Regional Disease & Survival – Auckland

3.4 Regional failure after neck dissection and the impact of radiation

Regional failure was dependent on the N status of the neck. The rate of failure in patients with N1 disease was 5%, N2 disease 17% and N3 disease 22%. These rates of regional failure were all decreased with radiation and these reached statistical significance for patients with N3 disease and for regional disease overall. See Table 6.

	% Failure no RT		% Failure with RT	
N1	11%	1/19	3%	1/31
N2	25%	4/16	9%	2/22
N3	38%	8/21	10%*	2/20 p < .04
Overall	28%	13/46	7%***	5/71 p < .002

Table 6. Influence of RT on Recurrence after Neck Dissection

Although adjuvant radiation significantly decreased regional recurrence after neck dissection adjuvant radiation had no impact on survival: The Kaplan Meyer curves for survival after neck dissection alone versus neck dissection with radiation the curves were virtually super-imposed. See Fig 6

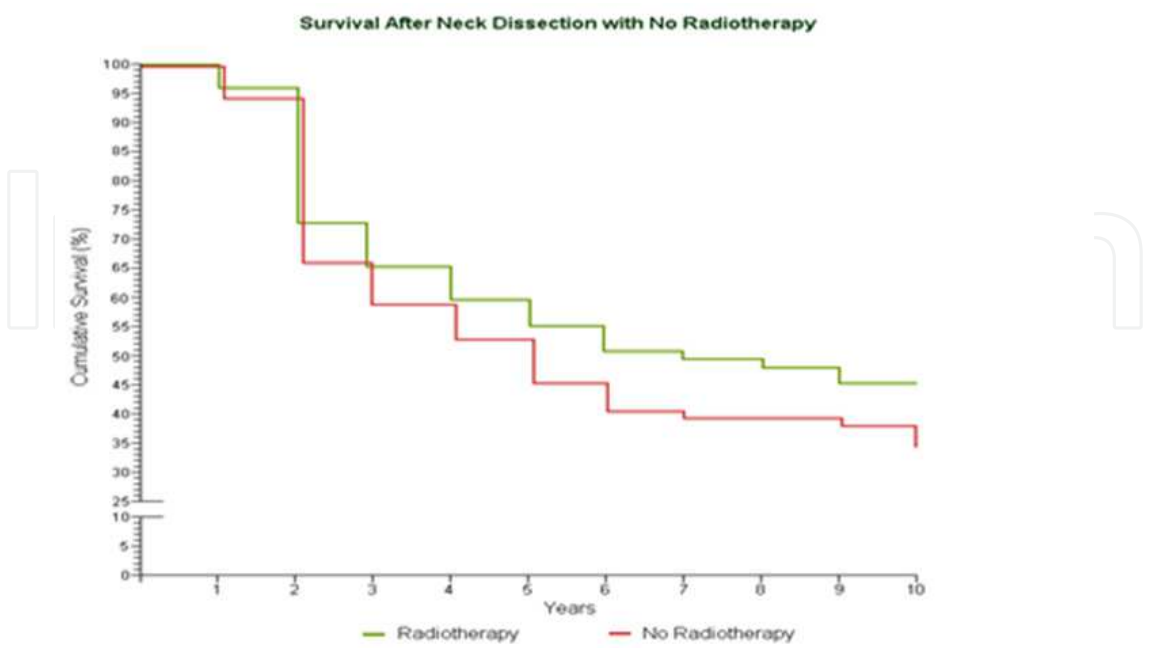


Fig. 6. Survival after neck dissection with and without Adjuvant radiation

3.5 Less common situations

3.5.1 Primary site unknown

There were nine patients in this group all with stage N2 or N3 disease with a 35% 5 year survival which was virtually identical when compared with the 5 year survival for the group of patients with N2 and N3 disease who had a known primary.

3.5.2 Cervical regional disease from primary site on trunk

There were 19 patients in this group, 14 had axillary and neck disease, 5 had neck disease alone. The mean number of nodes involved was 11 (range 3-48). Neck Levels most commonly involved were:

Level 5: 14 patients

Level 4: 6 patients

Level 3: 4 patients

Level 1 or 2: 4 patients (including 1 patient with contralateral Level 1 disease)

The outcome was very poor with 15/19 patients dead of disease at five years. See Fig 7

3.5.3 Desmoplastic neurotropic melanoma

There were 19 patients in this group. The lesions were thick with a mean thickness of 3.5 mm. When the desmoplastic patient group were compared with patients with equivalent thickness lesions that were not desmoplastic: the local recurrence rate was higher in the desmoplastic group at 26% versus 7% ($p < 0.04$), while regional recurrence was lower in the desmoplastic group at 22% versus 47%. Death from disease was virtually identical in the two groups See Table 7.

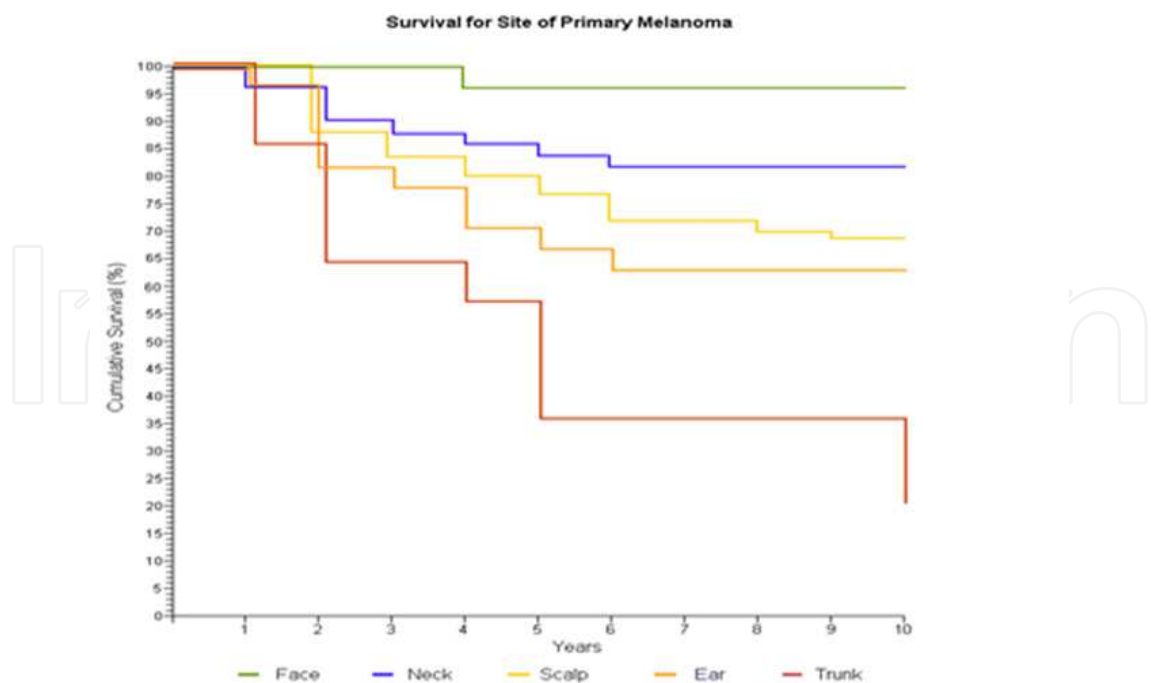


Fig. 7. Survival of Patients with Trunk Primary versus primary lesion in the Head and Neck

	Non Desmoplastic	Desmoplastic
Median Thickness	3.5 mm	4.1 mm
Local Recurrence	7% (20/261)	26%*** (9/19)
Regional Nodes	47%* 107/261)	22%* p.06 (4/19)
Dead of Disease	41% (8/19)	42% (95/261)

Table 7. Desmoplastic v Non-Desmoplastic Melanoma – Auckland - Stratified for Equivalent Thickness

3.5.4 Mucosal melanoma

There were 14 patients in this group. The commonest sites were conjunctival, oral and nasal. There were poor outcomes here even for very thin lesions. Seven of the 14 patients developed local recurrence and 5/14 were dead of disease at 5 years despite a mean thickness of only .3 mm.

4. Discussion

Our study is one of the largest studies of Head & Neck melanoma reported from a single centre. The single greatest experience is however from the Sydney Melanoma Unit (De Wilt et al, 2004; Fisher & O'Brien, 2002; Thompson et al, 2005), and we have compared and contrasted our experience with theirs along with various centres worldwide. The data from Fisher S.R & O'Brien, C.J., 2002 are similar to ours with respect to anatomical site, sex-incidence. In addition outcome versus anatomical site were similar to reports of others with face and neck lesions having a more favourable outcome than scalp and ear. In addition the reason for these differences is largely explained on the basis of the face & neck lesions being thinner and therefore having a better outcome. Further, although H&NMM

was more common in males the two sites where the incidence was almost the same for males and females (Face and Neck) the outcome was better. We have previously shown that for melanoma overall when all sites are pooled the incidence in males and females is similar (Jones et al, 1999) and that overall males tend to have poorer outcomes than females especially older males (Jones et al, 1999; Shaw, 2008). Trunk and scalp lesions were significantly more common in males in our study: we have previously shown the highest incidence of melanoma in males is on the back (Jones et al, 1999), Scalp melanoma is most common in bald patients and there are more bald men than women (Douglas & Shaw, 1987; Jones et al, 1999).

The outcome for patients with desmoplastic melanoma (DM) is similar to that reported by Quinn and colleagues from the Sydney Melanoma Unit (Quinn et al, 1998). In particular DM is associated with a relatively high incidence of LR coupled with a relatively low incidence of regional disease and when compared to non DM melanoma patients a similar risk of death. The relatively low rate of regional disease has some implications when considering the performance of sentinel node studies in patients with DM. Our data indicating that the outcome of patients with regional disease and primary site unknown is similar to patients with regional disease and primary site known when stratified for similar stage of regional disease are in general agreement with the literature (Santini et al, 1985).

Local recurrence (LR) in H&NMM has been reported to be more common than for limb melanomas (Douglas & Shaw, 1987; Jones et al, 1999; Ng et al, 2001). Our current findings are in agreement with this in a general sense, with the pie chart summarising the individual main causative factors, namely thickness of the primary, inadequate margin, unfavourable histological sub-type. We have previously documented the effect of tumour thickness and inadequate margin on local recurrence (Ng et al, 2001). In addition the studies by Balch and colleagues (Balch et al, 2001) have highlighted that tumour thickness is very reliable and an independent predictor of both recurrence and survival.

One sub-group where this rule of thickness being a reliable predictor of outcome is not useful is in patients with mucosal melanoma; the highest incidence of which is in the head and neck region (Tomicic & Wanebo, 2003). In our patients despite the medial thickness being only 1.3 mm the rates of recurrence and death from disease were markedly higher than for non- mucosal lesions of similar thickness. A variety of authors have underlined the poor prognosis associated with mucosal melanoma irrespective of either conservative or radical treatment involving surgery alone or combined with radiation (Tomicic & Wanebo, 2003), but the fact that even very thin lesions tend to recur appears to be relatively under-reported.

The implications of LR are substantial with approximately double the incidence of regional disease and approximately a three- fold risk of dying of melanoma. Further, the impact of LR and regional recurrence on survival were virtually identical. These findings are similar to those reported by O'Brien and colleagues (Fisher & O'Brien, 2002)

The regional nodes of significance when managing H&NMM are outlined in Fig 8. See below: In particular the nodes as classified by Memorial Sloan Kettering Cancer Centre (Shah et al, 1991) involving levels 1-5, along with intra-parotid nodes coupled with the post-auricular nodes and the Sub-occipital nodes highlighted by the SMU (De Wilt et al, 2004). In addition the axillary nodes are important especially for upper trunk lesions and lower neck lesions. The importance of primary lesions from trunk regional to the neck, and neck lesions regional to the axilla(e) has been relatively understudied but following the widespread use of sentinel node studies a far better understanding of H&N regional

lymphatics has been developed, especially by Morton and colleagues at the John Wayne Cancer Centre (Morton et al, 2006) and Thomson and colleagues in Sydney Australia (De Wilt et al., 2004; Thompson et al., 2005).

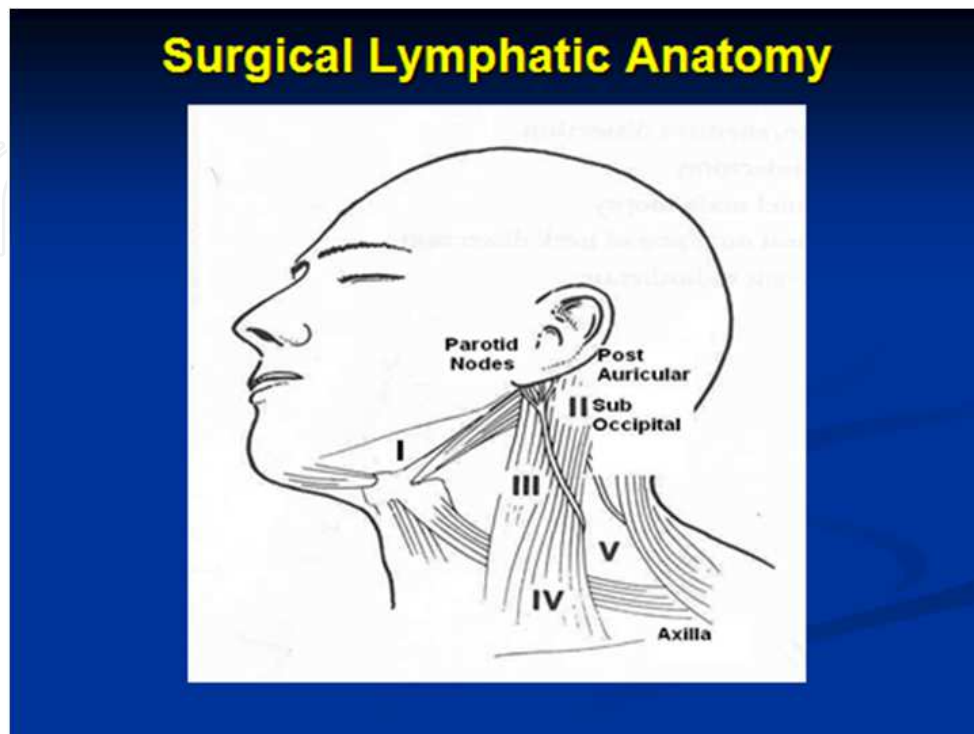


Fig. 8. Surgical Lymphatic Anatomy

Timing of regional failure in our study was a function of primary tumour thickness with patients who had regional disease at initial presentation had a mean primary thickness of over 6 mm, while progressively thinner primary lesions went on to be associated with region disease of several years: 3 mm lesions tending to recur regionally inside 1 yr, 2mm lesions recurring regionally most commonly in 1-4 yrs, and lesions 1-2 mm thick recurring most commonly later than 4 yrs. These findings are similar to those reported by O'Brien and Fischer (Fisher & O'Brien, 2002) and underline the capacity of even relatively thin melanomas to recur many years after initial diagnosis (Thompson et al., 2005). These finding also fit well with the findings of Balch and colleagues in 2001 (Balch et al., 1985). After analysing 10 yr survival data for over 15,000 melanoma patients with lesions in all anatomical sites, the 10 yr mortality increased steadily as a smooth curve as a function of primary thickness from approximately 20% for 1 mm lesions through to 70% mortality for lesions 10 mm thick. See Fig 9 below

For some malignancies disease free interval is an important prognostic factor (Fisher Fisher & O'Brien, 1998), however for melanoma the situation is less clear (Thompson et al., 2005). In our study although patients who developed regional progressively further along the course of their disease had a relative long absolute survival, once regional disease occurred the survival data curves from that time on were not significantly different between the various groups.

One very important but contentious issue in the surgical management of H&NMM patients is the extent of neck dissection which should be performed for regional disease as a function

of the anatomical site of the primary melanoma. Shah and colleagues in 1991 (Shah et al., 1991) concluded that virtually all neck nodal levels along with the parotid nodes should be dissected in virtually all patients with H&NMM. Their data were based on therapeutic neck dissections for FNA diagnosed palpable regional disease. Their data are presented in modified format in Table 8

Site of Nodal Involvement v Anatomical Site						
Shah et al., Amer J Surg, 1991						
	Face	Ant Scalp	Ant Neck	Post Neck	Post Scalp	Ear
Parotid	44%	100%	33%	-	29%	83%
L1	48%	57%	13%	-	47%	27%
L2	48%	65%	50%	50%	60%	73%
L3,4	12%	50%	28%	25%	27%	41%
L5	20%	57%	-	30%	20%	27%

Table 8. Regional H& N Melanoma v Anatomical Site, Shah et al., Amer J Surg 1991

From the Shah data (Shah et al., 1991) one would conclude that virtually all patients with regional H&NMM require a Level 1-5 neck dissection and resection of parotid nodes. The exceptions being that posterior neck does not require parotidectomy (P) or dissection of Level 1, while anterior neck primary while requiring parotidectomy does not require dissection of Level 5 nodes, and only occasionally will level 1 nodes be involved. Another major study addressing sites of regional disease as a function of anatomical primary melanoma site is that from the Sydney Melanoma Unit (SMU) (De Wilt et al., 2004). Their approach was a different one whereby 918 sentinel nodes were mapped in 362 patients with H&NMM. A modified assessment of their data is presented in Table 9 below. The conclusions from the Sydney data are in general agreement with those of Shah and colleagues (Shah et al., 1991) whereby:

1. Ear primary requires P, and Levels 2-5 neck dissection, but in contrast to Shah (Shah et al., 1991) level 1 would not require dissection
2. Face primary requires P and Levels 1-4 , but in contrast to Shah (Shah et al., 1991) who found 20% of facial lesions involved L5
3. Anterior scalp requires P and Levels 1-4 and possibly L5 also as 10% chance of involvement at SMU versus 57% involvement at MSKCC.
4. Anterior neck requires Levels 1-5 but not P while Shah (Shah et al., 1991) found 33% had parotid involvement but no L5 disease

918 Sentinel nodes in 362 Melanoma Patients								
SMU Ann Surg 2004								
	Parotid	L1	L2	L3 / 4	L5	S O	P A	Axilla
Ear	36%	-	90%	12%	27%	-	21%	-
Face	57%	48%	70%	20%	-	-	-	-
P Scalp	14%	-	47%	18%	59%	39%	32%	-
C Scalp	50%	-	70%	10%	30%	20%	50%	-
C Neck	17%	20%	80%	24%	40%	-	-	-
A Scalp	80%	-	90%	-	10%	-	35%	-
A low Neck	-	-	28%	21%	77%	-	-	43%
A up Neck	-	13%	63%	38%	25%	-	-	-
P low Neck	-	-	14%	28%	100%	18%	-	23%
P up Neck	11%	-	72%	15%	56%	16%	-	-

Table 9. 918 Sentinel Nodes in 362 Melanoma Partients

- 5. Posterior neck requires Levels 2-5 neck dissection with P only rarely required, concurring with while Shah (Shah et al., 1991)
- 6. Posterior scalp requires levels 2-5 neck dissection with only 14% chance of P being required, while Shah (Shah et al., 1991) found level 1 involved in 47% & and Parotid in 29% of patients.

The SMU data (14) also highlight the importance of the post-auricular and the Sub-occipital nodes especially for patients with Ear, Scalp, and posterior neck lesions. These were not assessed in the Shah data (Shah et al., 1991).

Our own data agree with Shah (Shah et al., 1991) that: L1 does not usually require dissection for ear primary

Our data are in agreement with SMU 14(15) :

- 1. Face does not usually require dissection of L5
- 2. L1 only rarely involved aside from face and neck primary lesions

Our data are in agreement with both MSKCC and SMU that neck lesions require a L2-5 dissection and occasional inclusion for dissection of L1 and P depending on the site of the neck primary. Our data also highlight the importance of upper trunk lesions spreading to cervical nodes, and the fact that these lesions have an especially bad prognosis as most patients have N2 or N3 disease often with involvement of both cervical nodes and one or more axilla. The importance of trunk lesions involving neck nodes, and the associated bad prognosis has been relatively understudied in the literature. The principal levels involved by trunk primary melanoma are levels 5 followed by levels 4, but occasionally levels 3,2,and 1 are involved. In addition for mid line lesions especially contralateral disease in unexpected sites may occur. In our study the outcome for trunk lesions that metastasised to cervical nodes either alone or in combination with axillary disease is markedly worse than for acral lentigenous melanoma, a known poor prognosis subtype which we have reported on previously (Koea & Shaw, 1988)

In order to provide a guideline for management of the neck in H&NMM we have modified the figure from O'Brien and colleagues (O'Brien, 1999) to provide some general rules regarding extent of neck dissection as a function of primary anatomical site. See Fig 9

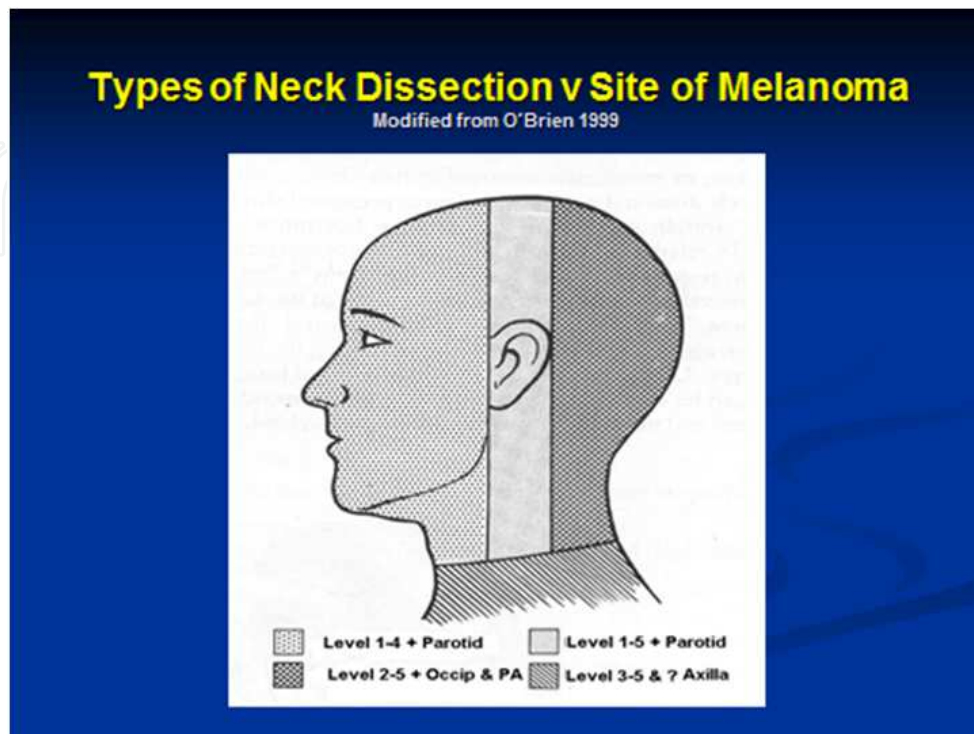


Fig. 9. Types of Neck Dissection v Site of Melanoma

There are a number of provisos to be incorporated with this figure based on our findings and those from SMU (15) and MSKCC (14). These include:

1. The risk of contralateral and bilateral regional disease with primary melanomas close to midline
2. Level 1 is not often involved but occasionally may be involved from as far away as posterior trunk and rarely bilateral
3. Trunk lesions may require dissection of more than levels 4 and 5, and involvement of one or both axillae must be excluded either by sentinel node study or imaging

Results predicting regional disease levels as a function of anatomical site of primary may be different when data from sentinel node studies are compared with studies from therapeutic neck dissection data. Also the extent of the neck dissection performed is also important for example; in our study selective dissection was frequently used in our patients whereas in the Shah (Shah et al., 1991) data many patients underwent either conservative or radical neck dissection. In addition spread of melanoma cells along involved lymphatic channels may be different compared to the distribution of tracer as part of a sentinel node study in a clinically uninvolved neck.

Survival as a function of extent of regional disease in our study is similar to what has been reported by others (Balch et al., 2001; Fisher & O'Brien, 2002; O'Brien, 1999). One common finding across centres is the dramatic drop-off in survival between N1 -N2 disease and N3 disease. The reason for this being that the maximum number of nodes involved in N2 patients is 3 while some patients with N3 disease may have 20 or more nodes involved. See Table 10

Regional Disease 5 yr Survival						
	NZ	UAB	SMU	Duke	MDA	Overall
N1	64%	53%	40%	-	39%	50%
N2	57%	48%	-	-	39%	49%
N3	36%	27%	12%		23%	25%
Overall	48%	43%	38%	45%	35%	42%

Table 10. Regional Disease 5y Survival

NZ: New Zealand
UAB: University of Alabama
Duke: Duke University
MDA: MD Anderson Cancer Clinic, Texas

In more detail the results of O’Brien and others (20) are summarised in Table 11 below:

Neck Dissection for Melanoma	
O'Brien et al W J Surg 16:222, 1992	
<ul style="list-style-type: none">■ 152 Therapeutic neck dissections■ 28% Re - recurrence in neck■ 34% 10 yr Survival■ 67% if node –ve■ Postoperative RT: multiple nodes or ECS	

Table 11. Neck Dissection for Melanoma – (O’Brien et al., 1992)

The role of adjuvant radiation to minimise recurrence after neck disease is debated in the literature. We offered the majority of patients adjuvant radiation while many clinicians offer radiation only for patients with multiple nodes or if extra-nodal spread is present (eg 20).

While the role of adjuvant radiation will only be totally resolved by a prospective randomised study some important findings emerge from our data. Firstly we were able to show a significant reduction in recurrence in patients who received adjuvant radiation, especially those with N3 disease. O'Brien (O'Brien et al., 1997) was also able to demonstrate a reduction in recurrence but this fell short of statistical significance (just). Our overall recurrence rate of 28% in patients who did not receive adjuvant radiation is similar to the figure reported by O'Brien et al (O'Brien et al., 1997) and lower than many reports (O'Brien et al., 1997). The dramatic decrease in recurrence in our patient both with N3 disease and regional disease overall is in agreement with the findings of Ang and colleagues (Ang et al., 1994) from the MD Anderson unit in Texas. Ang and colleagues (Ang et al., 1994) were able to demonstrate a dramatic reduction in recurrence when neck dissection was followed with adjuvant radiation compared with historic control data where surgery alone was used. Incidentally they were also able to demonstrate that adjuvant radiation also reduction in recurrence following excision of prognostically unfavourable primary melanomas. For many years melanoma was considered to not be a radio-responsive tumour but this is now largely refuted (Mendenhall et al., 2008). The fact that adjuvant radiation decreased regional recurrence in our study while not influencing survival makes good sense from the surgical oncology standpoint. Adjuvant radiation is well known to minimise recurrence following neck dissection for squamous cell carcinoma (Fisher & O'Brien, 1998), and adjuvant radiation has been shown to minimise recurrence following anterior resection for rectal cancer (Fisher & O'Brien, 1998), and also minimise recurrence in some patients following surgery for Breast cancer, but in most of these circumstance this decrease in recurrence does not translate into improved survival.

We have not presented data addressing complications in this present study. We have previously presented a comparison between our complications for node dissection in the neck, the axilla, and groin (Shaw & Rumball, 1990). In that study the complication rate following neck dissection and axillary dissection was similar and in both sites was markedly lower than following neck dissection. In addition the complications associated with the addition of adjuvant radiation was lower in the neck than in the two other sites.

5. Conclusions and recommendations

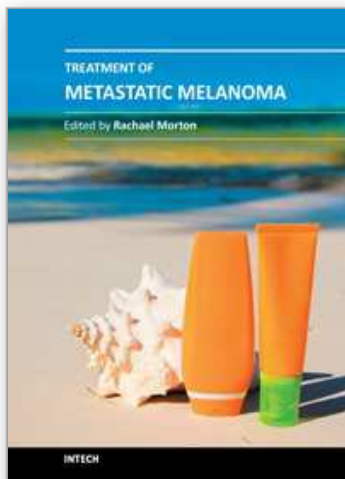
1. The head and neck area is a preferred site for melanoma and has an unfavourable outcome in comparison to the rest of the body with respect to local recurrence and death from disease.
2. There is a complex lymphatic system and both the performance of sentinel node studies in the head and neck area and their analysis is more complex than in the trunk or limbs. Unpredicted sites of sentinel nodes are more common in the head & neck region than in the rest of the body.
3. The timing of regional disease in H&NMM is important. Patients who had palpable regional disease at the time of initial presentation had an average primary thickness over 6 mm. Patients with progressively thinner primary lesions developed regional disease over subsequent years with the general rule being the thicker the primary the more quickly regional disease developed. Many of these patients were assessed prior to the use of sentinel node mapping and this will probably detect patients likely to recur especially in the first year after initial diagnosis of melanoma. Prolonged disease-free interval does not appear to be a favourable prognostic factor once regional disease has occurred.

4. Management of regional disease can often be accomplished using a selective neck dissection, the regional beds requiring resection can be assessed as a function of the primary site of the melanoma. In particular:
 - a. For anterior scalp and face parotidectomy plus levels I-IV neck dissection.
 - b. For coronal lesions including scalp and ear parotidectomy and levels I-V neck dissection.
 - c. For posterior scalp and posterior neck level II-V neck dissection.
 - d. For trunk lesions with cervical regional disease Level 4 & 5 neck dissection is appropriate, often in association with one or more axillary dissections.
 - e. Recommendations for sites of regional disease that should be resected for various primary melanoma sites are summarised in Fig 7. It is important to note that this is just a guideline as sites of regional disease are unpredictable. In particular upper back lesions involving cervical nodes can occasionally involve as far away as level 1, while primary lesions close to the midline (either head and neck or upper trunk primary) have a tendency to involve either contralateral nodes or bilateral nodes.
 - d. The post -auricular nodes and sub- occipital nodes have to be considered in for patients with posterior scalp, coronal scalp and ear lesions and to a lesser extent with patients with posterior neck lesions.
5. Desmoplastic melanoma, mucosal melanoma, and melanoma from trunk metastasising to neck have a relatively poor prognosis. Desmoplastic lesions tend to have relatively low rates of regional disease and relatively high rates of local recurrence resulting in survival similar to non-desmoplastic melanomas. Trunk melanomas metastasising to the neck usually represent N3 disease (occasionally N2) as a result of one or more axillary nodal beds also being involved. In addition trunk lesions, especially those close to the mid-line are one of the least predictable in terms of where they are likely to spread in the neck. Further, while outcome for most melanomas is a function of primary melanoma thickness the exception to this rule is mucosal melanoma where even thin lesions are often lethal.
6. Adjuvant radiation after neck dissection appears to minimise recurrence in the neck but does not appear to impact on survival. A prospective trial would be required to clarify this for certain.

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Treatment of Metastatic Melanoma

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Surgery continues to be the mainstay treatment for melanoma localized to the primary tumor and/or lymph nodes. Results from randomized controlled trials indicate that sentinel node biopsy for the treatment of cutaneous melanoma of intermediate thickness has a beneficial effect on recurrence rates, and adjuvant radiotherapy to regional lymph node fields following surgical resection reduces loco-regional recurrence in patients at high risk of relapse. Isolated limb perfusion, electrochemotherapy, and photodynamic therapy continue to be evaluated for treatment of stage IV disease. However, the greatest excitement in new treatment has been with targeted therapies for genetic mutations. In particular, the promising results of partial and complete tumor response in stage IV disease from early phase trials of the B-RAF kinase inhibitors. This book provides a contemporary insight into the therapeutic treatment options for patients with metastatic melanoma and is relevant to clinicians and researchers worldwide. In addition, an update on current clinical trials for melanoma treatment has been included, and two chapters have been reserved to discuss the treatment of oral and uveal melanoma.

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