Are there predictors of successful biopsy tests in patients treated with Ruthenium-106 Plaque Brachytherapy for Choroidal Melanoma?

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Background

- Metastasis of choroidal melanoma (CM) develops almost exclusively in patients with monosomy 3[(1)].
- For patients undergoing ruthenium-106 plaque brachytherapy (RPB), prognostic biopsy is typically undertaken during plaque insertion but may be taken prior to RPB or months later.

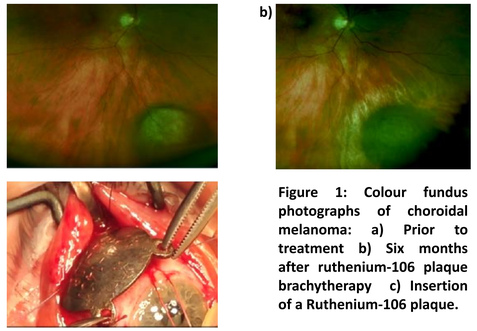


Figure 1: Colour fundus photographs of choroidal melanoma: a) Prior to treatment b) Six months after ruthenium-106 plaque brachytherapy c) Insertion of a Ruthenium-106 plaque.

Purpose

- To determine if there is a temporal association between the failure of cytogenetic tests and the time from RPB to biopsy and establish if there are other risk factors associated with cytogenetic test failures.

Methods

- Patients with CM who underwent RPB and cytogenetic tests at the Liverpool Ocular Oncology Centre (LOOC) between 1st July 2012 and 10th November 2023 were identified.
- Patients were grouped by biopsy prior to RPB (pre-RPB) and biopsy after RPB (post-RPB).
- Descriptive statistics, binary logistic regression and cox hazard modelling were performed using SPSS v.28.

Results and Discussion

Demographics

Table 1: Characteristics of the study population

		Overall n = 328 (% total)	Pre-RPB n = 172 (% group)	Post-RPB n = 157 (% group)	p-value
Sex (male)		160 (48.8)	79 (45.9)	81 (51.9)	0.278*
Age median (range)		68 (25 – 99) years	69 (25 – 99)	66 (28 – 94)	0.176§
Eye (right)		159 (48.5)	83 (48.3)	76 (48.7)	0.933*
Tumour thickness mean (SD) in mm		3.3 mm (1.4)	3.5 mm (2.4)	3.0 mm (1.3)	0.002†
LBD mean (SD) in mm		11.0 mm (2.6)	11.5 mm (2.4)	10.4 mm (2.57)	<0.001§
Tumour location	Pre-equator	148/272 (54.4)	110/158 (69.6)	38/144 (26.4)	<0.001*
	Post-equator	124/272 (45.6)	48/158 (30.4)	76/144 (66.7)	
TNM Staging	T1	151 (46.0)	63 (36.6)	88 (56.4)	<0.001*
	T2	153 (46.6)	92 (53.5)	61 (39.1)	
	T3	21 (6.4)	16 (9.3)	5 (3.2)	
	T4	3 (0.9)	1 (0.6)	2 (1.3)	
Number of days between biopsy and plaque		$\bar{X}$ = 58.9 days (Range: -49 to 4151) Median: 0 days	$\bar{X}$ = -2.45 days (Range: -49 to 0) Median: 0 days	$\bar{X}$ = 126.6 days (Range: 1 – 4151) Median: 35 days	0.585ǂ
Biopsy technique	Transretinal	160 (48.8)	26 (15.1)	134 (85.9)	<0.001*
	Trans-scleral	161 (49.1)	141 (82.0)	20 (12.8)	
	Other	7 (2.1)	5 (2.9)	2 (1.3)	

LBD, longest basal diameter. Statistical comparisons were made between Pre-RPB and Post-RPB: * Chi-squared test; § Independent t-test; † Mann-Whitney U test; ǂ Fisher's Exact test.

- Pre-RPB group had thicker and wider CMs (p = 0.002 and <0.001) which was reflected by more T2 and T3 staged CMs (Post-hoc p < 0.05) than post-RPB.
- Number of days between biopsy and RPB ranged from 49 days prior to 4151 days post-RPB; the most common time was at RPB insertion (45.7 %).
- Trans-scleral biopsies were performed more in pre-RPB group (p < 0.001), owing to the preference for performing this technique when the area of interest is exposed and the tissue less friable. (Figure 2).

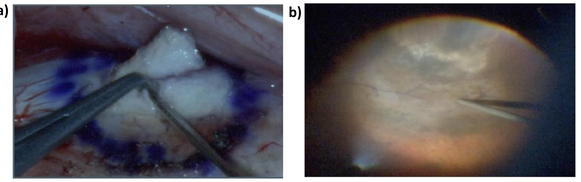


Figure 2: Choroidal melanoma biopsy approaches: a) Trans-scleral method using forceps for sample acquisition b) Transretinal method using a 25g vitrector.

Cytomorphological and genetic outcomes

- Success rate of cytomorphology was 93.6 % with no difference between pre- and post-RPB (p = 0.499).
- Although not statistically significant, it was noted that the success rate of cytomorphological and genetic tests reduced after six months to 71.4 % and 85.7 %, respectively (Table 2).

Table 2: Success rate of cytological and genetic testing

	Cytomorphology test success % (n)		Genetic test success % (n)	
	93.6 (307/328)		93.6 (307/328)	
	Pre-RPB	Post-RPB	Pre-RPB	Post-RPB
	92.4 (159/172)	94.9 (148/157)	91.9 (158/172)	95.5 (149/157)
Prior to RPB	100 (22/22)	-	90.9 (20/22)	-
Day of RPB insertion	91.3 (137/150)	-	92.0 (138/150)	-
≤ 1 month	-	92.6 (63/68)	-	97.1 (66/68)
2 – 3 months	-	98.7 (74/75)	-	94.7 (71/75)
3 – 6 months	-	100 (6/6)	-	100 (6/6)
> 6 months	-	71.4 (5/7)	-	85.7 (6/7)
Fisher's Exact p-value	0.499		0.259	

Binary logistic regression

- No significant relationship was demonstrated between the failure of cytomorphological tests and the timing of biopsy, age, sex, tumour thickness or biopsy technique (Nagelkerke R^2 = 0.224, Hosmer and Lemeshow test p = 0.899).
- Although not statistically significant, it was noted that thinner tumours had an increased risk of returning a failed test.
- Of note, 85.7 % (18/21) of the failed genetic tests were documented as having an 'insufficient' sample.

Cox proportional hazard modelling

- At closure, 29 (8.8 %) patients had died; six (20.7 %) from metastases.
- Cox proportional hazard modelling showed no evidence that a biopsy taken before or after RPB, accounting for chromosome 3 status, affects the risk of death from metastatic melanoma ($\chi 2$ = 3.58, p = 0.829).

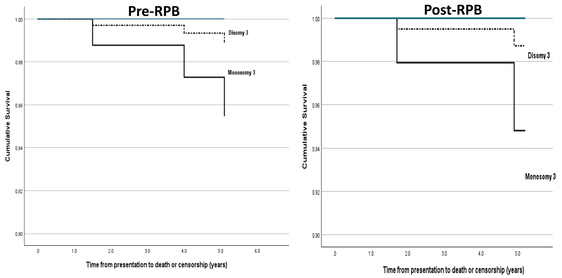


Figure 3: Cox regression cumulative survival graphs of the association between metastatic death and chromosome status where comparable when stratified by pre- and post-RPB: a) Pre-RPB and b) Post-RPB.

Conclusions

- Successful and reliable cytogenetical results can be gained from pre- and post-RPB biopsies, particularly when assessed by MLPA and/or MSA.
- Our findings suggest that ideally biopsies should be taken within six months of RPB but perhaps even earlier in smaller tumours where post-RPB tumour regression may make the surgical acquisition more difficult.

References

1. Damato et al. *Prog. Retin. Eye. Res.* 2011;30:285–295.

Acknowledgements and declarations

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