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Uveal Melanoma in Ireland

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Keywords
Choroid · Melanoma · Brachytherapy · Epidemiology · Survival · Incidence

Abstract
Purpose: To report the clinical features and epidemiology of uveal melanoma in Ireland. ***Methods:*** This was an observational study of 253 patients with a new diagnosis of uveal melanoma between June 2010 and December 2015. Main outcome measures included demographics, clinical features, age-adjusted incidence, relative survival, overall survival, and distant metastases-free survival. ***Results:*** The mean patient age was 61.7 years. Tumour location was choroidal in 82%, ciliochoroidal in 9%, iridociliary in 2%, and iris in 7%. Treatment modalities included brachytherapy (ruthenium-106 and iodine-125 [64%]), enucleation (27%), and proton beam radiation (8%). The mean age-adjusted incidence of uveal melanoma in Ireland from 2010 to 2015 was 9.5 per million of the population (95% confidence interval [CI]: 8.4–10.7). Four-year relative survival was 81.3% (95% CI: 72.8–87.3). Four-year overall survival was 84% (95% CI: 78–90) and 4-year distant metastases-free survival was 79% (95% CI: 73–86). ***Conclusion:*** Based on this data, the incidence of uveal melanoma in Ireland is high when compared with other reported incidence rates in Europe and worldwide. Relative and observed survival were in keeping with other reported European survival rates.

Introduction

Uveal melanoma is the most common primary intraocular malignancy in adults, albeit still a rare form of cancer [1]. Treatment of uveal melanoma has evolved over the past 3 decades with eye-conserving treatment options such as proton beam radiotherapy and brachytherapy for treatment of smaller tumours [1]. Despite this therapeutic shift, enucleation is still undertaken for larger tumours not amenable to radiation treatment [1].

The incidence of uveal melanoma across Europe has been shown to range from 2 per million in Spain and southern Italy [2] to over 8 per million in Scotland and the Nordic countries [2]. This geographic variability relating to a decrease in incidence going from a north-to-

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Table 1. Baseline clinical demographics and primary treatment of uveal melanoma in Ireland from 2010 to 2015 (n = 253)

Sex, *n* (%)	
Female	106 (42)
Male	147 (58)
Age (mean ± SD), years	61.7±13.9
Female, *n*	
0–15 years	1
15–44 years	15
45–54 years	25
55–64 years	27
65–74 years	26
>75 years	25
Male, *n*	
0–15 years	0
15–44 years	16
45–54 years	26
55–64 years	41
65–74 years	41
>75 years	24
Country of birth, *n* (%)	
Republic of Ireland	242 (96)
Lithuania	2
United Kingdom	3
Poland	3
France	2
Georgia	1
Eye, *n* (%)	
Left	115 (45)
Right	138 (55)
Location, *n* (%)	
Choroidal	207 (82)
Ciliochoroidal	23 (9)
Iridociliary	5 (2)
Iris	18 (7)
Presentation, *n* (%)	
Ophthalmologist	187 (74)
Optician	32 (13)
Emergency Department	22 (9)
Other	12 (5)
Stage, *n* (%)	
I	72 (28)
IIA	61 (24)
IIB	73 (29)
IIIA	30 (12)
IIIB	8 (3)
IIIC	1 (0)
IV	2 (1)
Unable to stage	6 (2)
Extrascleral extension, *n* (%)	
No	244 (96)
Yes	9 (4)
Basal diameter (mean ± SD), mm	12.6 (3.6)
Median (range)	12.6 (1.6 –21)
Thickness, mm	
Mean ± SD	6.3±3.8
Median (range)	5.0 (1.2–22)
Primary treatment, *n* (%)	
Brachytherapy	163 (64)
Enucleation	69 (27)
Proton beam radiation	21 (8)
Plaque type, *n* (%)	
I-125	57 (35)
Ru-106	106 (65)
Plaque diameter size, *n*	
Ruthenium	
15 mm CCA	16
18 mm CCD	19
20 mm CCB	24
20 mm notched COB	33
25 mm notched COC	13
Iodine	
14 mm	6
16 mm	1
18 mm	14
20 mm	37

south gradient suggests a protective role of ocular pigmentation [2]. The incidence in the United States has been reported as 5.1 per million [3]. It is lower in Asia with a reported incidence of 0.60 per million in South Korea [4]. The reported overall relative 5-year survival for uveal melanoma ranges from 68.9 to 81.6% [3, 5].

A dedicated Ocular Oncology Service was established in the Republic of Ireland in 2010. Prior to this, all patients were referred to the United Kingdom for management of uveal melanoma with the exclusion of those treated by primary enucleation. There are no previously published papers reporting the clinical demographics and epidemiology of uveal melanoma in Ireland since the establishment of this dedicated service.

Materials and Methods

All data was retrieved by retrospective analysis of case notes of 253 patients included in this study. Patients were included in the study if they were diagnosed with uveal melanoma between June 2010 and December 2015. All patients in the study were Irish residents at the time of diagnosis. Population estimates were calculated using data from the national Central Statistics Office. This study was approved by the ethics committee of the Royal Victoria Eye and Ear Hospital, Dublin.

Ocular Oncology Service

New cases of uveal melanoma are referred to this service from anywhere in the Republic of Ireland. Diagnosis, initial treatment plan and follow-up are completed in a single department, therefore capture of all cases is robust. Patients are referred to our affiliated oncology service for medical oncology treatment and follow-up.

Notification of death is given either directly to our service or via the medical oncology team.

Clinical Examination and Diagnostic Methods

The diagnosis of uveal melanoma was based on clinical and ultrasonographic findings. Clinical evaluation and ultrasound examination were carried out by one specialist in ocular oncology (N.H.). At the time of diagnosis, age, gender, ethnicity, Snellen visual acuity, tumour thickness, largest basal diameter of the tumour, and location of the tumour margins were documented. Tumour biopsy was carried out if there was any uncertainty regarding the diagnosis or at the patient's request. Staging was performed using the American Joint Committee on Cancer (AJCC) staging criteria [6–8]. All patients were referred for medical oncology follow-up.

Treatment Methods

Treatment modalities available in Dublin include brachytherapy, enucleation and resection in selected iridociliary tumours. There is no proton beam facility on the island of Ireland, so patients requiring proton beam therapy were referred to the Royal Liverpool University Hospital and Clatterbridge Cancer Centre in the United Kingdom. Transpupillary thermotherapy was used as an adjunctive treatment in selected cases. Treatment recommendations were based on tumour size, tumour location, visual potential as well as the patient's needs and preferences.

Proton Beam Radiation

Proton beam radiation was utilised, in general, for uveal melanomas located in the peripapillary or juxtapapillary region. "Juxtapapillary" was defined as any lesion with a posterior margin within 1 disc diameter of the optic nerve [9]. Tumours were categorised as "peripapillary" when the lesion edge was contiguous with the optic disc margin.

Brachytherapy

Brachytherapy was utilised for uveal melanomas measuring up to 10 mm in thickness. In general ruthenium-106 plaques were used to treat tumours up to 5 mm in thickness and iodine-125 was used to treat tumours between 5 and 10 mm in thickness. In some cases, brachytherapy was used to treat tumours greater than 10 mm thickness; e.g., in the case of an "only" eye, or where the patient refused enucleation and accepted the additional risks associated with treating a larger tumour with radiation.

Enucleation

In general, enucleation was reserved for uveal melanomas measuring greater than 10 mm in thickness.

Histology

Histological analysis was performed on all enucleated eyes and cytology was carried out in those cases that underwent fine needle biopsy. Tumours were categorised as spindle, epitheloid or mixed cell type. All histology specimens were analysed for molecular genetic abnormalities. Fluorescence in situ hybridisation studies were carried out on touch prints using the Vysis (Abbott Laboratories Ltd., Dublin, Ireland) CEP 3 probes (specific for the centromeric region of chromosome 3), the Vysis CEP 8 probe (specific for the centromeric region of chromosome 8) and the Vysis MYC (8q24) probe. Extrascleral extension was confirmed on pathological examination.

Table 2. Histology of uveal melanoma patients in Ireland from 2010 to 2015

Patients (n = 79)	n (%)
Histology	
Epitheloid	12 (15)
Spindle	33 (42)
Mixed	34 (43)
Monosomy 3/chromosome 8	
+ Monosomy 3 + chromosome 8 abnormality	25 (32)
+ Monosomy 3 – chromosome 8 abnormality	13 (16)
– Monosomy 3 + chromosome 8 abnormality	19 (24)
– Monosomy 3 – chromosome 8 abnormality	15 (19)
Data not available	7 (9)

+, presence of monosomy 3/chromosome 8 abnormality; –, absence of monosomy 3/chromosome 8 abnormality. Note: it was not routine practice to perform cytology on patients undergoing brachytherapy treatment, hence, the vast majority of histology samples were from patients who underwent enucleation.

Incidence

The National Cancer Registry (NCR) in Ireland was used to calculate age-adjusted incidence. All patient data was cross-checked with the Ocular Oncology Service to ensure it was a consistent patient cohort; however, NCR data included all cases diagnosed between 2010 and 2015 nationally (total 269 cases, including those diagnosed between January and May 2010, those who declined referral, and those who were retrospectively diagnosed on death). Age-standardised incidence rates (cases per million per year) for a population aged 0+ years were calculated using age-specific incidence rates weighted by the 1976 European population standard and presented as an annual average for the given time period. International Classification of Disease for Oncology codes (ICD-0–3) for both morphology (8720–8790) and site (C69.2 [retina], C69.3 [choroid], C69.4 [ciliary body] or C69.9 [eye, not further specified]) were used to identify cases. Ocular melanoma cases coded as "retina" (1 case) were included in the analysis if they were confirmed as a miscoding of uveal melanoma by cross-checking clinical details. Those coded as "eye, not further specified" (8 cases) were excluded from the analysis.

Survival

Relative survival of uveal melanoma patients in Ireland was calculated using NCR data covering the follow-up period from 2010 to 2014. This was estimated by comparing observed survival of patients with survival expected in the general population of the same age and sex (based on life tables published by the Central Statistics Office). The Strs algorithm with "Pohar Perme" option (generating what is sometimes termed "net survival") was used, in Stata 13. Follow-up was until the end of 2014, by matching against death certificates.

All other survival parameters were calculated using patient information taken from the Ocular Oncology Service database.

Overall survival (OS) times were calculated from the date of primary treatment until the date of death (from any cause) or the date of the last follow-up. Cancer-specific survival times were cal-

Table 3. Incidence of uveal melanoma in Ireland (cases of uveal melanoma per million of the population)

2010–2015	Males	Females	Total
2010	20	14	34
2011	21	15	36
2012	34	27	61
2013	36	18	54
2014	18	21	39
2015	20	25	45
Annual average	25	20	45
Age-standardised rate (95% CI)	11.1 (9.3–12.9)	8.2 (6.7–9.7)	9.5 (8.4–10.7)
Male:female directly standardised rate ratio	1.35 (1.06–1.73)		

Table 4. Metastases following enucleation as a primary treatment for uveal melanoma in Ireland from 2011 to 2015 (n = 69) by histology and chromosomal alteration

	Enucleated, n (%)[a]	Developed metastatic disease, n (%)[b]	Median time free from metastatic disease, months[c]
Histology			
Epitheloid	10 (14)	5 (50)	8.3
Spindle	30 (43)	4 (13)	27.5
Mixed	29 (42)	10 (34)	13.0
Chromosomal alterations			
+ Monosomy 3 + chromosome 8	25 (36)	13 (52)	15.4
+ Monosomy 3 – chromosome 8	10 (14)	3 (30)	16.2
– Monosomy 3 + chromosome 8	17 (25)	2 (12)	41.5
– Monosomy 3 – chromosome 8	11 (16)	0	26.2
Data not available	6 (9)	1 (17)	

+, presence of monosomy 3/chromosome 8 abnormality; –, absence of monosomy 3/chromosome 8 abnormality. Monosomy 3 data not available for 6 patients. Chromosome 8 data not available for 5 patients. [a] Percent of enucleated cases. [b] Percent of those enucleated who developed metastases. [c] Months from enucleation to either metastatic disease, death, or last contact.

culated from the date of primary treatment until the date of death from uveal melanoma or the date of the last follow-up. Recurrence-free survival times were calculated from the date of primary treatment until the date of local or distant metastases or the date of death or the date of the last follow-up. Distant metastases-free survival (DMFS) times were calculated from the date of primary treatment until the date of metastases or the date of death or the date of the last follow-up. Enucleation-free survival times were calculated from the date of primary treatment until the date of enucleation or the date of death or the date of the last follow-up. For cancer-specific survival, local recurrence, distant metastases and secondary cancers were not treated as events. Death from uveal melanoma was treated as an event but death from other cancers and non-cancer-related deaths were censored. For recurrence-free survival, local recurrence and distant metastases were treated as events while secondary cancers were not treated as events. All deaths were treated as events.

Statistical Analysis

Categorical variables were analysed using χ^2 tests and continuous variables were analysed using the Kruskal-Wallis and Mann-Whitney tests. The Kaplan-Meier method was used to estimate survival times and the log-rank test was used to compare differences in survival. All statistical tests were two-sided and assessed for significance at the 0.05 level. Statistical analyses were carried out using IBM® SPSS® statistical software version 21.

Results

Baseline clinical demographics and treatment are outlined in Table 1. Histology, chromosome 3 and chromosome 8 abnormalities are outlined in Table 2.

Table 5. Five-year relative survival of patients diagnosed with uveal melanoma from 2010 to 2014, based on National Cancer Registry data, by sex and age-group

	5-year relative survival (95% CI)	*n*
Total	77.3% (68.3–83.9)	192
Sex		
Male	79.3% (67.0–87.4)	105
Female	74.4% (60.5–83.9)	87
Age group		
15–44	85.7% (61.4–95.2)	24
45–54	65.9% (46.9–79.4)	44
55–64	80.2% (64.1–89.5)	52
65–74	81.8% (62.4–91.8)	43
75+	62.4% (31.6–82.3)	29

Median ophthalmologic follow-up for patients treated with brachytherapy was 28.5 months (28.9 months for iodine-125 [range 0.2–58.3] and 26.6 months for ruthenium-106 [range 0.1–63.2]), 23.3 months (range 1.4–64.2) for those treated with proton beam radiotherapy, and 24.8 months (range 0.2–66.0) for enucleation (p = 0.19).

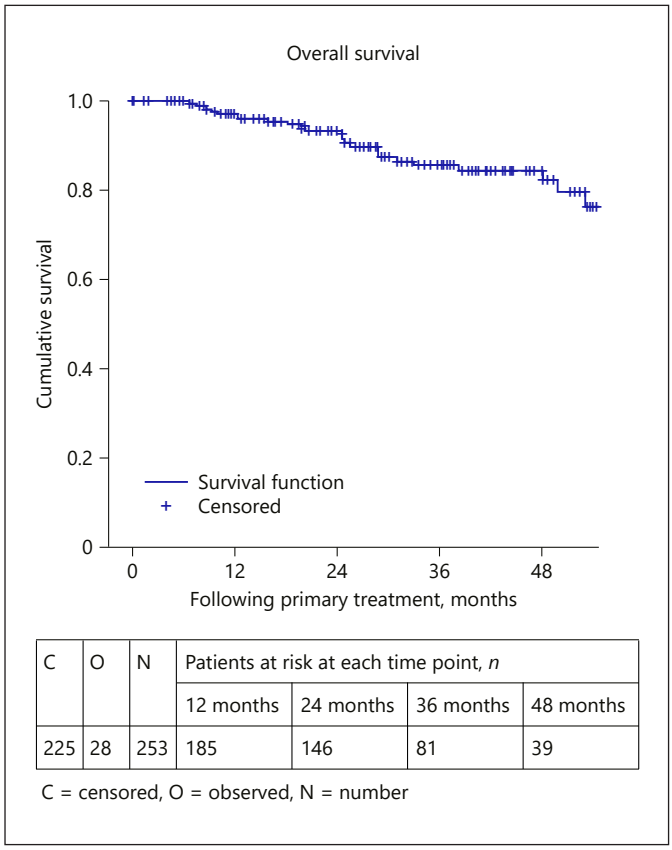
The mean tumour thickness in males (n = 143) was 6.5 ± 3.8 mm, compared with 6.1 ± 3.7 mm in females (n = 105, p = 0.95). The mean tumour basal diameter was 12.8 ± 3.6 mm in males (n = 142), compared with 12.5 ± 3.6 mm in females (n = 103, p = 0.55).

Almost two thirds of the patients were treated with brachytherapy. The majority were treated with ruthenium-106 plaques (65%; tumour basal diameter 3.0–18.2 mm) while 35% had iodine-125 plaques (tumour basal diameter 6.5–20 mm). Plaque diameters are outlined in Table 1. Thirty-one (19%) of the brachytherapy patients had transpupillary thermotherapy laser as an adjunctive treatment.

The incidence of uveal melanoma is outlined in Table 3.

Disease Control

During the course of the study, 6 brachytherapy patients had subsequent enucleations; 4 due to local recurrence and 2 due to complications of radiation retinopathy. One patient had a subsequent exenteration due to local orbital recurrence 39 months following primary enucleation. Of note, in that case, there was scleral vascular channel invasion but no evidence of macroscopic or microscopic extrascleral extension at the time of primary enucleation. Two of those who had subsequent enucleations for local recurrence later developed metastatic disease.



C	O	N	Patients at risk at each time point, *n*			
			12 months	24 months	36 months	48 months
225	28	253	185	146	81	39

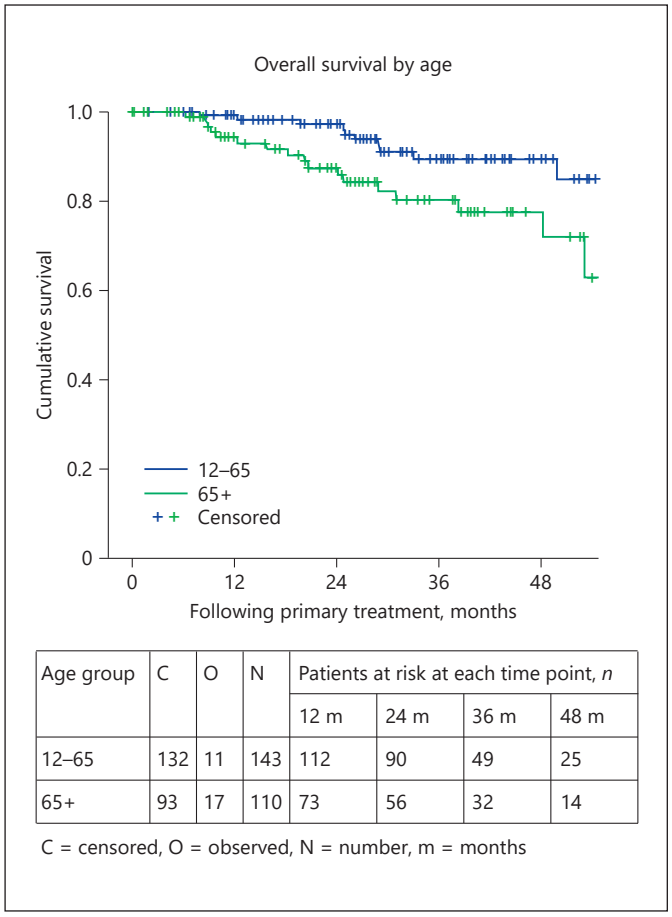
C = censored, O = observed, N = number

Fig. 1. Overall survival.

Table 4 outlines the number of patients with enucleation as a primary treatment who developed metastases, according to histological and chromosomal alteration groups. It is important to note that it was not routine practice during this time to perform biopsy for cytology or cytogenetics on patients undergoing brachytherapy treatment, hence, the vast majority of histology samples were from patients who underwent primary enucleation.

The mean tumour thickness at presentation in patients who did not have metastatic disease at the last follow-up was 5.9 mm as compared to 8.9 mm in those who did have metastatic disease (p < 0.0005). Similarly, the mean basal diameter was 12.3 mm in those who did not have metastatic disease as compared to 14.9 mm in those who did develop metastatic disease (p < 0.001).

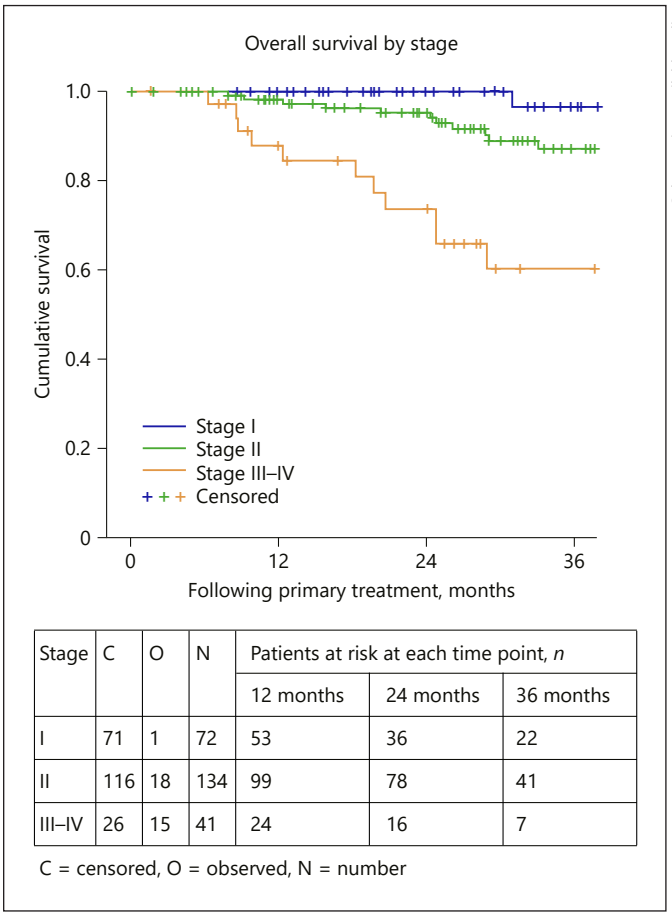
Relative survival is outlined in Table 5. The OS and DMFS curves are shown in Figures 1–6. The OS curves were curtailed at 52 months when the cumulative probability of survival was 80 and 77%, respectively, and when 29 and 24 cases, respectively, were remaining. The 3- and 4-year OS rates were 86% (95% confidence interval [CI]:



Age group	C	O	N	Patients at risk at each time point, *n*			
				12 m	24 m	36 m	48 m
12–65	132	11	143	112	90	49	25
65+	93	17	110	73	56	32	14

C = censored, O = observed, N = number, m = months

Fig. 2. Overall survival by age.



Stage	C	O	N	Patients at risk at each time point, *n*		
				12 months	24 months	36 months
I	71	1	72	53	36	22
II	116	18	134	99	78	41
III–IV	26	15	41	24	16	7

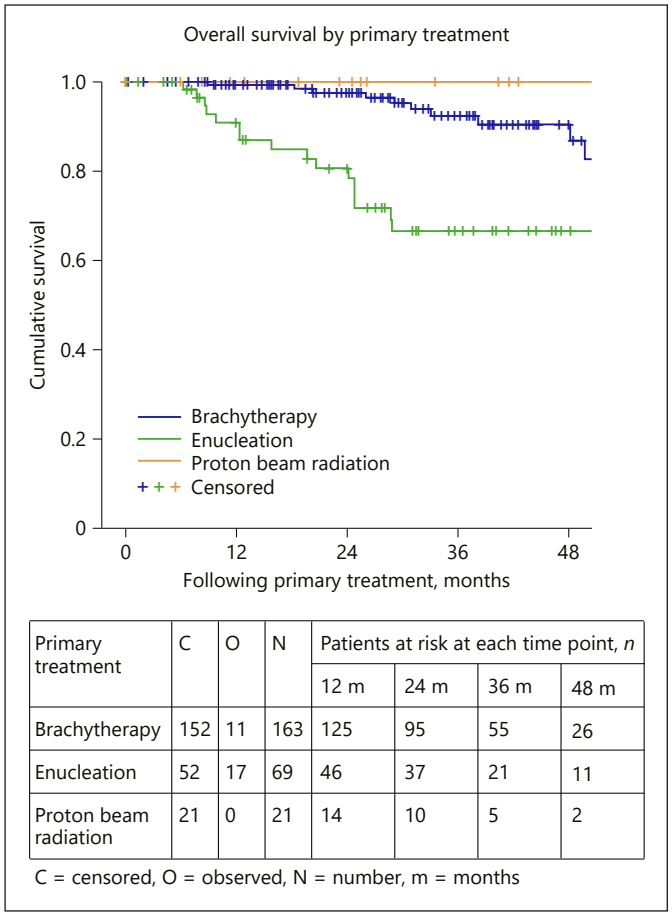
C = censored, O = observed, N = number

Fig. 3. Overall survival by stage.

80–91) and 84% (95% CI: 78–90), respectively (Fig. 1). OS was statistically significantly different depending on age group ($p = 0.017$), AJCC stage ($p < 0.0005$), tumour thickness ($p = 0.013$), and the primary treatment received ($p < 0.0005$). The 3-year OS rates were 85% (95% CI: 78–93%) and 72% (95% CI: 60–83%), for those aged 12–65 and 65+ years, respectively (Fig. 2). The 3-year OS rates were 97% (95% CI: 90–103), 87% (95% CI: 80–94), and 60% (95% CI: 41–79), for those with stage I, stage II, and stage III–IV disease, respectively (Fig. 3). The 3-year OS rates were 89% (95% CI: 83–94) and 70% (95% CI: 53–87) for those with tumours measuring less than or equal to 10 mm and those measuring 10 mm or more, respectively. The 3-year OS rates were 92% (95% CI: 87–98), 66% (95% CI: 53–80), and 100% for those treated with brachytherapy, enucleation, and proton beam radiation, respectively (Fig. 4). OS did not differ significantly by sex ($p = 0.803$). The 3-year OS rates were 86% (95% CI: 72–101), 57% (95% CI: 25–89), and 58% (95% CI: 37–80) for spindle, epithelioid and mixed histology, respectively. The 3-year OS rates were 66% (95% CI: 50–82) and 79% (95% CI: 60–98) for the presence and absence of chromosomal abnormality, respectively.

The 4-year cancer-specific survival was 88% (95% CI: 82–93) at 4 years. The median recurrence-free survival was 15.4 months (95% CI: 7.4–23.4); 7.7 months (95% CI: 0–15.6) for those with local recurrence and 15.4 months (95% CI: 6.8–24) for those with distant metastatic disease. The recurrence-free survival rates at 3 and 4 years were 76% (95% CI: 69–82) and 74% (95% CI: 67–82), respectively. The median enucleation-free survival was 62 months. The enucleation-free survival at 3 and 4 years following eye-conserving treatment was 97% (95% CI: 94–100) and 96% (95% CI: 91–100), respectively.

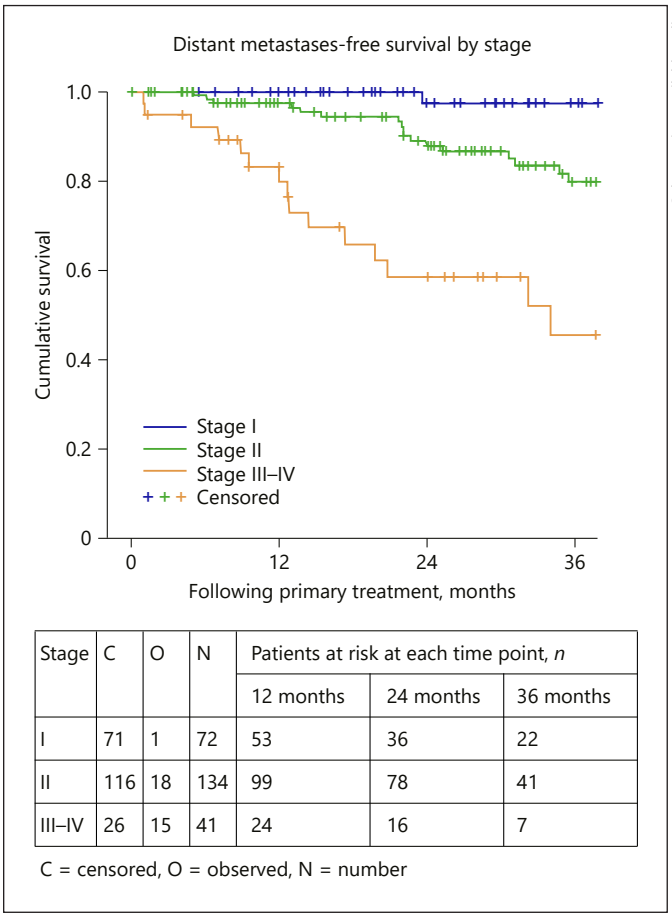
The 3- and 4-year DMFS rates were 79% (95% CI: 73–86) in each case. DMFS was statistically significantly different depending on AJCC stage ($p < 0.0005$), extrascleral extension ($p = 0.018$), tumour thickness ($p = 0.002$), and



Primary treatment	C	O	N	Patients at risk at each time point, *n*			
				12 m	24 m	36 m	48 m
Brachytherapy	152	11	163	125	95	55	26
Enucleation	52	17	69	46	37	21	11
Proton beam radiation	21	0	21	14	10	5	2

C = censored, O = observed, N = number, m = months

Fig. 4. Overall survival by primary treatment.



Stage	C	O	N	Patients at risk at each time point, *n*		
				12 months	24 months	36 months
I	71	1	72	53	36	22
II	116	18	134	99	78	41
III–IV	26	15	41	24	16	7

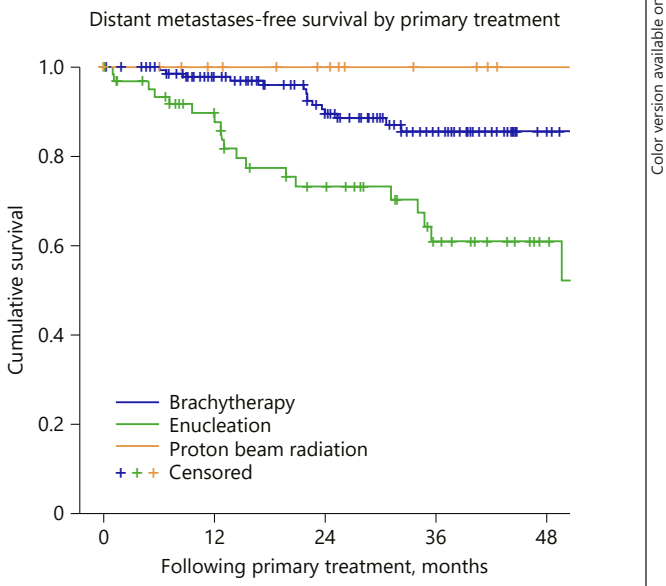
C = censored, O = observed, N = number

Fig. 5. Distant metastases-free survival by stage.

the primary treatment received ($p < 0.0005$). The 3-year DMFS was 97% (95% CI: 90–100), 87% (95% CI: 80–94) and 60% (95% CI: 41–79) for those with stage I, stage II, and stage III–IV disease, respectively (Fig. 5). The 3-year DMFS was 83% (95% CI: 76–90) and 60% (95% CI: 41–79) for those with tumours measuring less than or equal to 10 mm and for those with tumours measuring greater than 10 mm, respectively. The 3-year DMFS was 86% (95% CI: 79–93), 61% (95% CI: 46–76), and 100% for those treated with brachytherapy, enucleation, and proton beam radiation, respectively (Fig. 6). DMFS did not differ significantly by age group ($p = 0.067$) or sex ($p = 0.435$).

Discussion

The age-adjusted incidence of uveal melanoma in our study was 11.1 per million in males, 8.2 per million in females, and 9.5 per million overall. The largest published series looking at incidence rates of uveal melanoma in Europe from 1983 to 1994 found an incidence of uveal melanoma of between 2 and 8 per million for a population aged ≥0 years [2]. The study by Virgili et al. [2] also described a geographic variability that was related to a north-to-south gradient. They did, however, comment that there was no gradient noted within the Nordic, eastern European or United Kingdom when considered alone. They described how the geographic variability related to latitude may be attributable to increased light exposure functioning as a positive risk factor or darker skin pigmentation and increased ocular pigmentation functioning as a protective factor [2, 10–16]. Singh and Topham [17] tabulated a summary of 22 published reports on incidence of uveal melanoma worldwide from 1961 to 2001. The incidence rates ranged from 0.3 per million in Japan to between 9 and 10.4 per million in Norway, Connecticut (USA), Sweden, East Germany, and Ohio (USA) [17–24]. A more recent large series looking



Primary treatment	C	O	N	Patients at risk at each time point, *n*			
				12 m	24 m	36 m	48 m
Brachytherapy	148	15	163	122	92	51	23
Enucleation	50	19	69	44	32	18	8
Proton beam radiation	21	0	21	14	10	5	2

C = censored, O = observed, N = number, m = months

Fig. 6. Distant metastases-free survival by primary treatment.

at the incidence of uveal melanoma in the United States over a 36-year period from 1973 to 2008, predominantly occurring in Caucasian adults, demonstrated a figure of 5.1 per million [3]. The incidence in Ireland, when compared with these studies, appears to be remarkably high. It is important to note that many of these studies examined data from more than 10 years. Despite these considerations, the higher incidence rate of uveal melanoma in Ireland appears significant and would be in keeping with the recognised predisposing factors to uveal melanoma of pale skin colour, light eye colour and inability to tan, which are stereotypical traits in the native Irish population [13]. It is also worth considering the theory of solar ultraviolet light, via its role in vitamin D photosynthesis, having a protective effect against the development of uveal melanoma [25].

The mean age at diagnosis in this study was 61 years, which is in keeping with other studies that recognise uveal melanoma as increasing in incidence with age [17, 26]. In relation to other published series, there is increasing evidence to support a higher incidence of uveal melanoma in men [17, 26]. Damato and Coupland [27] described gender differences in relation to tumour location with a trend towards thicker, posterior tumours in men and involvement of the ciliary body and iris occurring more frequently in females. Zloto et al. [28] found similarly that men had more posterior tumours and had an increased rate of metastasis and an increased melanoma-related mortality. In this study, 58% of subjects were male. However, we found no statistical difference in the site of the tumour, basal diameter or tumour thickness between men and women.

Despite the availability of multiple treatment options, OS for uveal melanoma patients has not changed in the past 3 decades. Approximately, 50% of uveal melanoma patients will develop metastatic disease within 3 decades of diagnosis [29], with median survival following diagnosis of metastases ranging from 6–12 months [3, 5, 29–33] to 12–24 months [34–37] in studies that reported retrospective analyses of specific treatments. Many of the patients in the latter studies were under surveillance for early detection, hence, lead time bias may be somewhat contributing to their longer survival times. Historically, uveal melanoma size at diagnosis was believed to be the most important clinical prognostic factor related to prognosis and survival [30, 31]. However, recent studies have clearly underscored the importance of cytogenetics (aberrations in chromosome 1, 3, 6, and 8 and mutations in BRCA1-associated protein 1, BAP1, or the splicing factor SF3B1dd) [38–42] and gene expression profile (class 2) [43–46] in determining prognosis in uveal melanoma. Additionally, other recognised clinical and histopathological negative predictive factors include ciliary body location, diffuse tumour configuration, extraocular extension, epitheloid cell type, and advanced staging [47–56]. In keeping with some of these recognised negative predictive factors, patients in our study with large tumours treated with enucleation, epitheloid histology, and chromosome 3 abnormalities had a worse prognosis (Table 4). Additionally, those with advanced staging and extrascleral extension also had a worse outcome. It is also worth noting that the survival difference noted due to primary treatment received was not as a result of superior efficacy of radiation over enucleation but rather due to patient selection according to tumour size at presentation.

This is the first study to describe the epidemiology of uveal melanoma in Ireland since the establishment of a dedicated ocular oncology service in 2010. It is important

to note that due to the limited follow-up in our 5-year group, we did not report on 5-year survival, hence this is a limitation of this paper. Despite this, our data offers considerable insight into the incidence and survival in this cohort of patients.

Despite the numerous advances in treatment of uveal melanoma, survival will ultimately not be improved without significant advances in systemic treatments. Fortunately, systemic treatments continue to evolve and hopefully in time will effectively improve OS for uveal melanoma patients in Ireland and worldwide.

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Statement of Ethics

Ethical approval was granted for this study from the Ethics and Medical Research Committee of the Royal Victoria Eye and Ear Hospital, Dublin.

Disclosure Statement

None of the authors have any proprietary interests or conflicts of interest related to this submission. This submission has not been published anywhere previously and is not simultaneously being considered for any other publication.

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