NATIONAL GUIDELINES FOR THE MANAGEMENT OF UVEAL MELANOMA

Sponsored by Melanoma Focus
GDG MEMBERS

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• Stephen Fenwick (Liver Surgeon Liverpool)
• Jonathan Evans (Radiologist Liverpool)
• Christian Ottensmeier (Oncologist Southampton)
• Neil Pearce (Liver surgeon Southampton)
• Brian Stedman (Radiologist Southampton)
MEETINGS

27th April 2012
8th October 2012
28th January 2013
1st May 2013
10th July 2013
18th October 2013
Today 14th March 2014

- **Primary management**
  Victoria Cohen and Salvin Sachi

- **Surveillance and prognosis**
  Sarah Coupland and Christian Ottensmeier

- **Metastatic disease**
  Johnathon Evans and Stephen Fenwick
**LEVELS OF EVIDENCE**

1++ High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+ Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1- Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++ High quality systematic reviews of case control or cohort or studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+ Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2- Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3 Non-analytic studies, e.g. case reports, case series
4 Expert opinion

**GRADES OF RECOMMENDATIONS**

(A) At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

(B) A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+

(C) A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++

(D) Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+

(GPP) Recommended best practice based on the clinical experience of the guideline development group
MANAGEMENT OF PRIMARY UVEAL MELANOMA
TREATMENT

4,000 papers up until October 2013
`sifted down to 100 on treatment which are referenced
excluded animal studies, case reports, outdated or novel treatments,
publications before 1990, emphasis on meta-analysis and RCTs
1. The COMS "Small" study: 204 patients with small choroidal melanomas (height 1 - 3 mm, diameter more than 5mm) were prospectively observed. This study showed that with prospective follow-up, overall survival is comparable to the general population (COMS report number 4 and 5) (Hawkins et al 1997; Melia et al. 1997)

2. The COMS "Medium" randomized trial: 1317 patients with medium tumours (height 2.5 - 10.0 mm and diameter <=16 mm) were randomized to either treatment with I-125 plaque brachytherapy (85 Gy) or enucleation. The overall survival and risk of death from metastatic disease were comparable between the two groups, thus establishing plaque brachytherapy as a reasonable primary treatment for choroidal melanomas. At 5, 10, and 12 years, the mortality rate for patients treated with brachytherapy was 10%, 18% and 21% and for patients treated with enucleation was 11%, 17% and 17% respectively. (COMS report 16,17,18, 28) (Diener et al 2001, Melia et al 2001, Hawkins et al 2001 a & b, Hawkins et al 2006) (GRADE OF EVIDENCE A)

3. The COMS “Large” randomized trial: 1003 patients with large tumours (height >=10 mm or diameter >=16 -27 mm) were randomized to pre-enucleation external beam radiation therapy (EBRT) 20/5 or enucleation only without EBRT. This study showed that pre-enucleation radiotherapy does not provide any additional benefit. (COMS report 9, 10, 11, 15, 24) (Hawkins et al 1998, Schachat et al 1998, Wilson et al 2001, Hawkins et al 30 2004) (GRADE OF EVIDENCE A)
ADDITIONAL PAPERS
LAST 6 MONTHS

5 papers (3 relevant)
Proton, endoresection, brachytherapy versus endoresection, physics, palladium
Risk factors for neovascular glaucoma after proton beam therapy of uveal melanoma: a detailed analysis of tumor and dose-volume parameters.


• 704 patients, 1996-2010, The 5-year PBRT NVG rate was 12.7%. Multivariate analysis confirmed significant independent risk factors for NVG were increasing tumor height (P<.0001), age (P<.0001), %disc treated to ≥50% Dose (<100% vs 100%) (P=.0007), larger tumor diameter (P=.01), %lens treated to ≥90% Dose (0 vs >0%-30% vs >30%) (P=.01), and optic nerve length treated to ≥90% Dose (≤1 mm vs >1 mm) (P=.02). i.e higher rate of NVG for anterior and juxtapapillary UM
Long-term outcome of primary endoresection of choroidal melanoma.


- 71 patients, 1996-2010, small tumours (max base 9.5mm and height 4.1mm) recurrence in only 3%, retinal detachment in 22%, vision better than 6/30 in 31% eyes, metastatic death in 5 patients.
Brachytherapy and endoresection for choroidal melanoma: a cohort study.


- 48 brachytherapy and 22 endoresection patients. Rates of local recurrence (18.2% vs 14.9%, p=0.75) and metastases or death (18.2% vs 14.2%, p=0.75) were higher in the endoresection group. The likelihood of achieving a final visual acuity of better than 2/60 was 22% higher in the endoresection group (risk ratio 1.22, 95% CI 1.02 to 1.28, p=0.034). However the cases were not matched as endorection group had tumours further from the fovea