Follow up after conservative treatment of UM
H. B. Stallard

$^{60}\text{Co}$ Applicators (1950)
$^{106}$ Ru $^{106}$ Rh Applicators

Prof. P. Lommatzsch 1968

Beta irradiation

2.4 – 3.5 MeV
125 I Applicators

1975 Memorial Sloan Kettering Cancer center
1975 Rotman et al
Proton beam irradiation of intraocular tumors

- Boston –
  E. Gragoudas et al. 1975

- San Francisco
  D. Char et al. 1977

- Soviet Union
  A. Brovkina 1975

- Lausanne + PSI
  1984

- Present >10 major units

- Worldwide 25 – 30000 c.

- Optis > 6900 cases
Evaluation of risk factors with multimodal imaging techniques
ICG + FA 150° / OCT-A

Vitreoretinal surgery
IV Anti-VEGF medication
Periodic observation following conservative management of uveal melanomas

• Periodic general check up examination
• Observation of local tumor control
• Management of ocular surface and anterior segment complications
• Prevention and treatment of major complications
  Neovascular glaucoma
  Vitreous hemorrhage
  Toxic tumor syndrom
• Investigation and management of irradiation induced optic neuropathy and maculopathy
Periodic general check up examination

Liver US or Liver CT-Scan
Liver enzymes
• SGOT
• SGPT
• Gamma GT
• Alkaline phosphatase

<table>
<thead>
<tr>
<th>Time span</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 years</td>
<td>2x / year</td>
</tr>
<tr>
<td>15 years</td>
<td>1x / year</td>
</tr>
</tbody>
</table>
Observation of local tumor control

Proton beam irradiation

3 years 2x / year
7 years 1x / year
7-15 years 1x / 2 years
Observation of local tumor control

$^{106}\text{Ru} \quad ^{106}\text{Rh}$ Brachytherapy
Centered / Eccentric
Recurrent uveal melanoma 1 year following excentric $^{106}$Ru/$^{106}$Rh Brachytherapy
Observation of local tumor control

Obs. per. 6 m.

Obs. per. 3 y.

Proton beam irradiation
Observation of local tumor control

Obs. per. 1 y.

Obs. per. 6 y.
F. 66 ans
Choroidal melanoma
Proton beam irradiation

Obs period 9 years
Vis ac 0.1
Irradiation induce maculopathy
Peripheral retinal ischemia
Obs per 17 years
Vis ac 0.03
Extraocular extension

Enucleation and irradiation of the orbit
Periodic observation following conservative management of uveal melanomas

- Periodic general check up examination
- Observation of local tumor control
- Management and treatment of ocular surface and anterior segment complications
- Prevention of major complications
  - Neovascular glaucoma
  - Vitreous hemorrhage
  - Toxic tumor syndrom
- Investigation and management of irradiation induced optic neuropathy and maculopathy
Eyelid lesions

Madarosis
Skin atrophy
Telangiectasia
Lesions of the conjunctiva

Telangiectasia
Laser coagulation
Corneal lesions

1. Dry eye syndrome
   • Keratitis sicca
   • Scarring of the cornea

Risk factors
   • Bilateral chronic dry eye
   • Meibomian gland dysfonction
2. Corneal stem cell deficiency

Risk factors

• Global irradiation of the ant. Segment
• Corneal hypoesthesia
Conjunctival and scleral necrosis

Free scleral graft + Conjunctival large rotation flap
Invasion of the ciliary body

Advanced cortical and nuclear cataract
Ciliary body melanoma proton beam irradiation

H=5.1mm

Obs. p. 3y. H=3.1mm
Obs. p. 8y. H=2.51mm
Advanced cortical and nuclear cataract
Advanced cortical and nuclear cataract

1y. after cataract surgery
IOL dislocation
Cataract surgery following irradiation of posterior uveal melanoma

Phimosis of anterior capsula
Cataract surgery following irradiation of posterior uveal melanoma

Phimosis of anterior capsula
Phimosis of anterior capsula

Complementary capsulorexis
Periodic observation following conservative management of uveal melanomas

- Periodic general check up examination
- Observation of local tumor control
- Management and treatment of ocular surface and anterior segment complications
- Prevention of major complications
  - Neovascular glaucoma
  - Vitreous hemorrhage
  - Toxic tumor syndrom
- Investigation and management of irradiation induced optic neuropathy and maculopathy
Iris neovascularisation and neovascular glaucoma

Anti-VEGF treatment
Laser coagulation
IOP <20mm Hg  84%
150° F. Angiography
Disruption of the inner B/R barrier

Hypofluorescent SRD
Diffusion of the dye
Retinal ischemia
Retinal ischemia

Retinal detachment

< 1 quadr.  
1 quadr.  10%
2 quadr.  21%
≥ 3 quadr.  52%
Retinal ischemia

Height

≤ 5mm  9%
5,1-8mm  15%
≥ 8,1mm  33%
Therapeutic protocol

Retinal ischemia 91c.


[ + ] Anti-VEGF 29c

Anti-VEGF treatment
6 months 1 inj/2 m.

---------- 1 inj/3 m.

Laser coagulation of ischemic retina
Prophylactic use of anti-VEGFs to avoid anterior segment neovascularization following proton beam for uveal melanoma

Rubeosis rate

Control

Bevacizumab

AJO 2014 in press
Prevention of neovascular glaucoma and vitreous hemorrhage

Panoramic FA (150°)
Laser photocoagulation + Anti-VEGFs
Prevention of neovascular glaucoma and vitreous hemorrhage

Panoramic FA (150°)
Obs. per. 24 months
Toxic tumor syndrome

Proton beam irradiation + Transvitreal tumor excision
Irradiation induced maculopathy

Disruption of inner B/R barrier
Disruption of outer B/R barrier
Vaso-occlusif microangiopathy
Irradiation induced maculopathy

Superficial CP

Deep CP
Irradiation induced maculopathy
Obs. period 6 m.

Surface 0.661mm² - 1.038mm²
Density 40% - 32%
Irradiation induced maculopathy

7.2015 – 3.2019 N. of cases 221

Factors influencing best corrected Vis. Ac. Multivariate analysis N. of cases 93

- Age
- Hypertension / Diabetes
- Macular detachment at presentation
- Total macular irradiation

- Degree of vascular damage in FA
- OCT-b macular thickness
- OCT-A Foveal avascular zone area
- OCT-A SCP and DCP grading
- OCT-A Vascular density / fractal dimension
Radiation Maculopathy After Proton Beam Therapy for Uveal Melanoma: Optical Coherence Tomography Angiography Alterations Influencing Visual Acuity

Alexandre Matet, Alejandra Daruich, and Leonidas Zografos
Department of Ophthalmology, University of Lausanne, Jules-Gonin Eye Hospital, Fondation Asile des Aveugles, Lausanne, Switzerland

Disruption deep capillary plexus
Foveal avascular zone area

\( p < 0.0001 \)

\( p < 0.0001 \)
CME and SSPIM
Small Suspended Particles In Motion
Uveal melanoma
Proton beam irradiation

Deep vasc. network
minimally damaged
Vis. Ac. ≥ 0.6  72%
Uveal melanoma
Proton beam irradiation

Deep vascular network
desorganized
Vis. Ac. ≤ 0.1  74%
Uveal melanoma
Proton beam irradiation

Deep vascular network interrupted
Vis. Ac. 0.16 – 0.6  80%
Deep capillary plexus interrupted
Observation period > 6 months
Absence of previous IV anti-VEGF

<table>
<thead>
<tr>
<th></th>
<th>Anti-VEGF 1inj./2months</th>
<th>Various protocols</th>
</tr>
</thead>
<tbody>
<tr>
<td>N. of cases</td>
<td>48c.</td>
<td>32c.</td>
</tr>
<tr>
<td>Non flow area</td>
<td>0.482mm²</td>
<td>0.473mm²</td>
</tr>
<tr>
<td>Mean flow density</td>
<td>39.5%</td>
<td>40.6%</td>
</tr>
</tbody>
</table>

CME on OCT en face

- Abs/minimale: 59% 35%
- Limited: 24% 45%
- Extended: 17% 20%

Anti-VEGF: 1injection every 2 months

Various protocols: Various

Observation period > 6 months

Absence of previous IV anti-VEGF

1 injection every 2 months
**IV Anti-VEGF  Obs. period = 6 months**

<table>
<thead>
<tr>
<th></th>
<th>Vis. Ac. Increased</th>
<th>Vis. Ac. Stable</th>
<th>Vis. Ac. Decreased</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1IV / 2 months</strong></td>
<td>17c. / 48c.</td>
<td>26c. / 48c.</td>
<td>5c. / 48c.</td>
</tr>
<tr>
<td></td>
<td>30%</td>
<td>54%</td>
<td>10%</td>
</tr>
</tbody>
</table>

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</tr>
<tr>
<td>Vis. Ac. Increased</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vis. Ac. Stable</td>
<td>6c. / 32c.</td>
<td>19%</td>
</tr>
<tr>
<td>Vis. Ac. Decreased</td>
<td>26c. / 32c.</td>
<td>81%</td>
</tr>
</tbody>
</table>
IV Anti-VEGF  Obs. period = 6 months

Anti-VEGF 1IV/2m.  Variation non flow area 28%

Various regiments.  Variation non flow area 104%
### OCT-A guided anti-VEGF treatment

<table>
<thead>
<tr>
<th></th>
<th>Treatment protocol</th>
<th>Variable intervals</th>
<th>No treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N. of cases</strong></td>
<td>19</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td><strong>Capillary Density / %</strong></td>
<td>42%</td>
<td>43%</td>
<td>41%</td>
</tr>
<tr>
<td><strong>Loos in Log MAR BCVA</strong></td>
<td>p=0.004</td>
<td>+0.18</td>
<td>+0.17</td>
</tr>
<tr>
<td><strong>FAZ area changes</strong></td>
<td>0.08</td>
<td>0.63</td>
<td>0.69</td>
</tr>
</tbody>
</table>

A. Daruich et al., Retina 2018
CME and SSPIM  Small Suspended Particules In Motion

Obs. period 6 months

Decrease of vis ac ≥ 0.1

SSPIM + 80%

SSPIM - 20%
<table>
<thead>
<tr>
<th></th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vis. Ac. + or stable</td>
<td>93% of cases</td>
<td>89% of cases</td>
</tr>
<tr>
<td>Variation non flow area</td>
<td>26%</td>
<td>34%</td>
</tr>
<tr>
<td>Time Period</td>
<td>Vis. Ac. + or stable</td>
<td>Non-Flow Area Variation</td>
</tr>
<tr>
<td>-------------</td>
<td>----------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>6 months</td>
<td>31% of cases</td>
<td>84%</td>
</tr>
<tr>
<td>12 months</td>
<td>19% of cases</td>
<td>232%</td>
</tr>
</tbody>
</table>

**IV Anti-VEGF various regiments**

![Images of angiograms showing flow area and non-flow area variation]
6 months: IV / 2 months / 6 months: various régiments

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Vis. Ac. + or stable</th>
<th>Variation non flow area</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td>87% of cases</td>
<td>13%</td>
</tr>
<tr>
<td>12 months</td>
<td>37% of cases</td>
<td>51%</td>
</tr>
</tbody>
</table>

0.909
0.428
0.828
OCT-A guided anti-VEGF treatment of irradiation induced maculopathy

Evolution of visual acuity

![Graph showing the evolution of visual acuity over time (M0, M6, M12, M18) for different protocols (Protocol +, Protocol -, Protocol 6M+ / 6M-).]
## Therapeutic protocol  Bevacizumab / Ranibizumab

<table>
<thead>
<tr>
<th>Interval</th>
<th>Treatment</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 m.</td>
<td>1iv inj.</td>
<td>2 m.</td>
</tr>
<tr>
<td>6 m.</td>
<td>1iv inj.</td>
<td>2 m.</td>
</tr>
<tr>
<td>6 m.</td>
<td>1iv inj.</td>
<td>3 m.</td>
</tr>
<tr>
<td>6 m.</td>
<td>1iv inj.</td>
<td>3 m.</td>
</tr>
<tr>
<td>12 m.</td>
<td>1iv inj.</td>
<td>4 m.</td>
</tr>
</tbody>
</table>

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### Modifications of the therapeutic protocol (2nd year)

- Variation of non flow area > 35% / year  
  1iv / 2 months
- Increase of CME  
  Afibercept