

Table S1. Incidence and risk factors of cataracts after hematopoietic cell transplantation.

Author Study type Study year	Number of patients HCT type Disease type	Conditioning regimen (N)	Cataract N (%)	Duration of follow-up (years)	Notes
Adult studies					
Tichelli et al ¹ Single center 1979- 1991	197 Allo 174, Syngeneic 5, Auto 18	S-TBI (74) F-TBI (90) Chemotherapy (33)	70 (36%) S-TBI (100%) F-TBI (20%) Chemotherapy (3%)	0.2- 5.2	- Risk factors: Use of irradiation, mode of irradiation, steroid use > 3 months
Bray et al ² Single center 1983- 1989	41 Allo 17, Auto 24	F-TBI (30) Chemotherapy (11)	20 (49%) F-TBI (63%) Chemotherapy (9%)	Allo 0.6- 7 Auto 0.5- 5.2	- Incidence by HCT type: Allo (71%), Auto (33%) - Risk factors: Dose of TBI, rate of TBI administration
Belkacemi et al ³ Multicenter (EBMT) Up to 1996	1063 Allo 688, Auto 375 AML, ALL, AUL	S-TBI (495) F-TBI (568)	257 (24%) S-TBI (35%) F-TBI (14%) Incidence at 10 years: 50%	1- 17.1	- 10 year estimated cataract incidence by HCT type: Allo (65%) vs Auto (46%) (p=0.0018) - Risk factors: Age > 23, higher dose rate of TBI (>0.04 Gy/ min), Allo HCT, steroids >100 days, - Protective factors: F-TBI, Heparin in S-TBI
Baker et al ⁴ Multicenter (BMTSS) 1974- 1998	248 Allo 220, Auto 28 CML	TBI (233) Chemotherapy (14)	95 (38%)	2- 27	- Cataract odds ratio 15.3 (95% CI 2.4- 6.4) compared to siblings (p<0.001) - Incidence by cGVHD: Yes (61%) vs No (41%), - Incidence by HCT type: Allo (40%) vs Auto (21%) (p= 0.01) - 15-year cumulative incidence: 53% (Auto), 63% (related donor), 67% (unrelated donor)
Benyunes et al ⁵ Single center 1969-1981	492 Allo 480, Auto12 AML, ALL, CML, Lymphoma, SAA, Others	S-TBI (74) F-TBI (333) Chemotherapy (85)	159 (32%) Incidence at 11 years: S-TBI (85%) >12 Gy F-TBI (50%) 12 Gy F-TBI (34%) No TBI (19%)	2-18	- Incidence by steroids exposure: Yes (45%) vs No (38%) (P <0.001) - Risk factor: S-TBI - Protective factor: No TBI
Deeg et al ⁶ Single center 1969- 1981	277 Allo SAA, ALL, AML, CML, NHL, others	S-TBI (105) F-TBI (76) Chemotherapy (96)	86 (31%) S-TBI (55%) F-TBI (16%) Chemotherapy (17%)	1-12	- Risk factors: S-TBI [4.7-fold higher risk than F-TBI or Chemotherapy (p <0.001)], chronic steroid use, diagnosis of ALL, CML
Zierhut et al ⁷ Single center 1982-1994	85 Auto AML, ALL, lymphoma	F-TBI	28 (33%) Incidence at 13 years: 54%	1.7-13	

Bieri et al ⁸ Single center 1984- 2004	142 Allo AML, ALL, CML, MDS, MM, MPS	TBI (121) Chemotherapy (21)	31 (22%) Incidence at 10 years: 34%	> 2	
Dunn et al ⁹ Single center 1978-1991	366 Allo 293, Auto 73 AML, ALL, CML, Lymphoma, Other, SAA	TBI (185) Chemotherapy (181)	40 (11%)	0-12.5	- Risk factors: total dose and duration of corticosteroids
Pediatric studies					
Suh et al ¹⁰ Single center 1981-1996	104 Allo 95, Auto 9 AML, SAA, ALL, others	F-TBI	24 (23%)	0-15	- Incidence by HCT type: Allo- 24%, Auto- 11% - Risk factor: chronic GVHD
Levy et al ¹¹ Single center 1994-2010	15 Allo ALL, AML, NHL	F-TBI	9 (69%)	1.4-13	
Frisk et al ¹² Single center 1985-1994	29 Auto 28, syngeneic 1 ALL, AML, Lymphoma	S-TBI (20) F-TBI (1) Chemotherapy (8)	22 (76%) TBI (100%) Chemotherapy (12%)	4-10	- Risk factor: TBI
Ricardi et al ¹³ Single center	51 Allo 32, Auto 19 AML, ALL, CML, NHL	F-TBI	36 (72%)	5.1-17.9	- Incidence by HCT type: Allo (84%) vs Auto (53%) ($p=0.02$) - Risk factor: AlloHCT
Fahnehjelm et al ¹⁴ Single center 1986-2004	79 Allo ALL, AML, CML, MDS, JMML, SAA, Non-malignant	S-TBI (17) F-TBI (18) Chemotherapy (44)	46 (58%) S-TBI (100%) F-TBI (83%) Chemotherapy only (34%)	2-18	- Risk factor: S-TBI
Fahnehjelm et al ¹⁵ Single center 1986-2012	131 Allo Leukemia, MDS, non-malignant	S-TBI (17) F-TBI (36) Chemotherapy (86)	65 (50%)	1-19.4	Risk factors: TBI (HR 25.9, 95% CI 8.29-81.26, $p < 0.001$), malignancy (HR 5.38, 95% CI 3.02-9.56, $p < 0.001$)
Kinori et al ¹⁶ Single center 2001-2008	23 Allo AML, MDS, CML, non-malignant	Chemotherapy	1 (4%)	0.3-9.7	40% had <2 years follow-up
Ng et al ¹⁷ Single center 1991-1995	57 Allo 47, Auto 10 ALL, Beta thalassemia major, CML	F-TBI (56)	4 (14%)	0.2-4.5	
Holmstrom et al ¹⁸ Single center 1987-1994	45 Allo 42, Auto 3 AML, ALL, CML, HLH, MDS, SAA	F-TBI (21) Chemotherapy (24)	25 (56%) F-TBI: 20 (95%) Chemotherapy: 5 (21%)	F-TBI: 2-9 Chemotherapy: 3-10	- Risk factors: TBI, busulfan
Callissendorff et al ¹⁹ Single center 1978-1989	61 Allo Leukemia, SAA, others	F-TBI (43) Chemotherapy (18)	44 (72%) F-TBI (100%) Chemotherapy (0)	1-10	- Risk factor: TBI

S-TBI, single dose TBI; F-TBI, fractionated TBI.

Table S2. Treatment of cataracts after hematopoietic cell transplantation

Author Study type Study year	Number of Patients Patient age at HCT	Cataract N (%)	Duration of follow-up (years)	Treatment of Cataracts
Najima et al ²⁰ Single center 1986-2006	622 (ADULTS) Median age 36 y Allo 622	45/561 (8.02%)	Median 836 days (0-7316)	- 13 of 45 (29%) underwent phacoemulsification and intraocular lens implantation - Mean interval from HCT to surgery 1028 days - Median age at surgery 42 y - Complication of posterior capsule opacification in 6/13
Fahnehjelm et al ¹⁵ Single center 1986-2012	139 (PEDIATRICS) Median age 6.6 y	50% developed cataracts at 10.2 years after HCT	Median 8 y (1.0-19.4)	- 19/131 had surgery - Median age at surgery 20.4 years (range 14.7-24.5) - Mean 11.6 y, median 11.4 y (range 3.3-21) after HCT - Of 35 operated eyes, 13 (37%) required further treatment with laser or re-operation due to secondary cataract.
De Melo et al ²¹ Single Center 2006 - 2011	261 (ADULT) Mean age 56 y	41/261 (15.7%)	Mean 55 weeks (40-201)	- Posterior subcapsular cataracts seen only in patients less than 45 years. - Mean interval from HCT to surgery 14 weeks (34-299) - All patients underwent cataract extraction with phacoemulsification using temporal clear corneal, suture less incisions. - Cystoid macular edema was most common post-operative complication seen in 4 (5.6%) eyes.
Vaidya et al ²² Single Center 1984 - 1996	31 (PEDIATRICS) Median age 8 y (5-20)	12/31(38.7%)	Median 7.64 y (0.56-14.2)	- 12 who developed cataracts needed surgery
Aristei et al ²³ Single center 1985 - 1998	193 (ADULT) Median age 33 y (2-59)	S-TBI 18/86 (21%) F-TBI 14/107 (13%)	Median S-TBI 3.02 y (1.13-7.28) F-TBI 7.56 y (1.14-14.9)	- Median time to cataract S-TBI 2.52 y after HCT, 11 (61.1%) had surgery F-TBI 7.6 y after HCT, 2 (14.3%) had surgery
Horowitz et al ²⁴ Multi-center 2004 - 2010	308 (PEDIATRICS) Mean age 8.7 y	113/308 (41.7%)	Mean 10.3 y	- Median time to cataract 5.3 y after HCT - 9/113 (8.1%) had cataract surgery at a median of 3.8 years after cataract diagnosis (IQR 2.2-4.7).

S-TBI, single dose TBI; F-TBI, fractionated TBI.

Table S3. Ocular complications of the posterior segment after hematopoietic cell transplantation

Author	Year	N	Study	Ophthalmological evaluation	Findings	Risk factors
Hirst et al ²⁵	1983	45	Children/adults Prospective	All patients underwent visual acuity tests, slit-lamp and fundus.	No patients with microvasculopathy were reported	
Bernauer et al ²⁶	1991	127	Adults Prospective Allo/auto HCT	All patients underwent visual acuity tests, slit-lamp examination and fundus.	13 patients (10%) microcirculation changes	TBI, cyclosporine
Coskuncan et al ²⁷	1994	397	Retrospective Allo HCT	Ophthalmological evaluation	17 patients (4.3%) cotton-wool spots, 11 patients (2.8%) optic disc edema, 14 patients (3.5%) hemorrhagic complications	TBI, chronic GVHD, cyclosporine
Johnson et al ²⁸	1999	140	Adults Prospective Auto HCT	All included patients underwent visual acuity test, and fundus.	10 patients (7%) cotton wool spots / optic disc edema	Carmustine
Bylsma et al ²⁹	2001	399	Adults Retrospective Allo HCT	Ophthalmological evaluation on demand Fundus Angiography	4 patients (1%) late retinal microvasculopathy (mean 50 months after HCT)	Busulfan + Cyclophosphamide, Cyclophosphamide + TBI
Tabbara et al ³⁰	2009	620	Children/adults Retrospective Allo HCT	Ophthalmological evaluation on demand	No patients with microvasculopathy were reported	
Westeneng et al ³¹	2010	101	Prospective Allo HCT	All included patients underwent ophthalmological evaluation	1 patient unilateral visual loss due IMR	GVHD
Ivanir et al ³²	2013	111	Prospective Allo HCT	All included patients underwent visual acuity tests. Slit-lamp examination, fundus	No patients with microvasculopathy	

References

1. Tichelli A, Gratwohl A, Egger T, et al. Cataract formation after bone marrow transplantation. *Ann Intern Med.* 1993;119:1175-1180.
2. Bray LC, Carey PJ, Proctor SJ, Evans RG, Hamilton PJ. Ocular complications of bone marrow transplantation. *Br J Ophthalmol.* 1991;75:611-614.
3. Belkacemi Y, Labopin M, Vernant JP, et al. Cataracts after total body irradiation and bone marrow transplantation in patients with acute leukemia in complete remission: a study of the European Group for Blood and Marrow Transplantation. *Int J Radiat Oncol Biol Phys.* 1998;41:659-668.
4. Baker KS, Gurney JG, Ness KK, et al. Late effects in survivors of chronic myeloid leukemia treated with hematopoietic cell transplantation: results from the Bone Marrow Transplant Survivor Study. *Blood.* 2004;104:1898-1906.
5. Benyunes MC, Sullivan KM, Deeg HJ, et al. Cataracts after bone marrow transplantation: long-term follow-up of adults treated with fractionated total body irradiation. *Int J Radiat Oncol Biol Phys.* 1995;32:661-670.
6. Deeg HJ, Flournoy N, Sullivan KM, et al. Cataracts after total body irradiation and marrow transplantation: a sparing effect of dose fractionation. *Int J Radiat Oncol Biol Phys.* 1984;10:957-964.
7. Zierhut D, Lohr F, Schraube P, et al. Cataract incidence after total-body irradiation. *Int J Radiat Oncol Biol Phys.* 2000;46:131-135.
8. Bieri S, Roosnek E, Ozsahin H, et al. Outcome and risk factors for late-onset complications 24 months beyond allogeneic hematopoietic stem cell transplantation. *Eur J Haematol.* 2011;87:138-147.
9. Dunn JP, Jabs DA, Wingard J, Enger C, Vogelsang G, Santos G. Bone marrow transplantation and cataract development. *Arch Ophthalmol.* 1993;111:1367-1373.
10. Suh DW, Ruttum MS, Stuckenschneider BJ, Mieler WF, Kivlin JD. Ocular findings after bone marrow transplantation in a pediatric population. *Ophthalmology.* 1999;106:1564-1570.
11. Mulcahy Levy JM, Tello T, Giller R, et al. Late effects of total body irradiation and hematopoietic stem cell transplant in children under 3 years of age. *Pediatr Blood Cancer.* 2013;60:700-704.
12. Frisk P, Hagberg H, Mandahl A, Soderberg P, Lonnerholm G. Cataracts after autologous bone marrow transplantation in children. *Acta Paediatr.* 2000;89:814-819.

13. Ricardi U, Filippi AR, Biasin E, et al. Late toxicity in children undergoing hematopoietic stem cell transplantation with TBI-containing conditioning regimens for hematological malignancies. *Strahlenther Onkol.* 2009;185 Suppl 2:17-20.
14. Fahnehjelm KT, Tornquist AL, Olsson M, Winiarski J. Visual outcome and cataract development after allogeneic stem-cell transplantation in children. *Acta Ophthalmol Scand.* 2007;85:724-733.
15. Tear Fahnehjelm K, Tornquist AL, Olsson M, Backstrom I, Andersson Gronlund M, Winiarski J. Cataract after allogeneic hematopoietic stem cell transplantation in childhood. *Acta Paediatr.* 2016;105:82-89.
16. Kinori M, Bielorai B, Souroujon D, Hutt D, Ben-Bassat Mizrachi I, Huna-Baron R. Ocular complications in children after hematopoietic stem cell transplantation without total body irradiation. *Graefes Arch Clin Exp Ophthalmol.* 2015;253:1397-1402.
17. Ng JS, Lam DS, Li CK, et al. Ocular complications of pediatric bone marrow transplantation. *Ophthalmology.* 1999;106:160-164.
18. Holmstrom G, Borgstrom B, Calissendorff B. Cataract in children after bone marrow transplantation: relation to conditioning regimen. *Acta Ophthalmol Scand.* 2002;80:211-215.
19. Calissendorff BM, Bolme P. Cataract development and outcome of surgery in bone marrow transplanted children. *Br J Ophthalmol.* 1993;77:36-38.
20. Najima Y, Kakihana K, Ohashi K, et al. Incidence, risk factors, and clinical outcomes of cataracts following hematopoietic stem cell transplantation. *Am J Hematol.* 2011;86:508-510.
21. de Melo Franco R, Kron-Gray MM, De la Parra-Colin P, et al. Outcomes of cataract surgery in graft-versus-host disease. *Cornea.* 2015;34:506-511.
22. Vaidya SJ, Atra A, Bahl S, et al. Autologous bone marrow transplantation for childhood acute lymphoblastic leukaemia in second remission - long-term follow-up. *Bone Marrow Transplant.* 2000;25:599-603.
23. Aristei C, Alessandro M, Santucci A, et al. Cataracts in patients receiving stem cell transplantation after conditioning with total body irradiation. *Bone Marrow Transplant.* 2002;29:503-507.
24. Horowitz M. The role of registries in facilitating clinical research in BMT: examples from the Center for International Blood and Marrow Transplant Research. *Bone marrow transplantation.* 2008;42 Suppl 1:S1-S2.

CIBMTR/EBMT Non-GVHD Ocular Complications Supplement

25. Hirst LW, Jabs DA, Tutschka PJ, Green WR, Santos GW. The eye in bone marrow transplantation. I. Clinical study. *Arch Ophthalmol.* 1983;101:580-584.
26. Bernauer W, Gratwohl A, Keller A, Daicker B. Microvasculopathy in the ocular fundus after bone marrow transplantation. *Ann Intern Med.* 1991;115:925-930.
27. Coskuncan NM, Jabs DA, Dunn JP, et al. The eye in bone marrow transplantation. VI. Retinal complications. *Arch Ophthalmol.* 1994;112:372-379.
28. Johnson DW, Cagnoni PJ, Schossau TM, et al. Optic disc and retinal microvasculopathy after high-dose chemotherapy and autologous hematopoietic progenitor cell support. *Bone Marrow Transplant.* 1999;24:785-792.
29. Bylsma GW, Hall AJ, Szer J, West R. Atypical retinal microvasculopathy after bone marrow transplantation. *Clin Exp Ophthalmol.* 2001;29:225-229.
30. Tabbara KF, Al-Ghamdi A, Al-Mohareb F, et al. Ocular findings after allogeneic hematopoietic stem cell transplantation. *Ophthalmology.* 2009;116:1624-1629.
31. Westeneng AC, Hettinga Y, Lokhorst H, Verdonck L, van Dorp S, Rothova A. Ocular graft-versus-host disease after allogeneic stem cell transplantation. *Cornea.* 2010;29:758-763.
32. Ivanir Y, Shimon A, Ezra-Nimni O, Barequet IS. Prevalence of dry eye syndrome after allogeneic hematopoietic stem cell transplantation. *Cornea.* 2013;32:e97-101.