APPENDIX 1. Checklists for reporting standards

PRISMA Checklist

Section/topic	#	Checklist item	Reported
TITLE			
Title	1	Identification as a systematic review, meta-analysis, or both.	✓
ABSTRACT			
Structured summary	2	Structured abstract including background, objectives, data sources, study eligibility criteria, methodological assessment, synthesis method, results, conclusions and implications of key findings.	✓
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	✓
Objectives		Provide an explicit statement of questions being addressed with reference to participants, interventions, outcomes (PICO design).	✓
METHODS			
Protocol and registration	4	Indicate if a review protocol exists, and where it can be accessed.	✓
Eligibility criteria	5	Specify study characteristics and report characteristics (such as years considered, language, publication status) used as criteria for eligibility.	✓
Information sources	6	Describe all information sources (such as databases with dates of coverage, contact with study authors, experts) in the search, and the date of last search.	✓
Search	7	Present full electronic search strategy, including limits used, such that it could be repeated.	✓
Study selection	8	State the process for selecting studies (i.e., screening, eligibility) and make sure that this is done by 2 authors.	✓
Data collection	9	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	✓
Data items	10	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	✓
Risk of bias in individual studies	11	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	✓
Summary measures	12	State the principal summary measures (e.g., risk ratio, difference in means).	✓
Synthesis of results	13	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	✓
Risk of bias across studies	14	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	✓
Additional analyses	15	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	✓
RESULTS			
Study selection	16	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, illustrated with a flow diagram.	✓
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	✓
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	✓
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	✓
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	✓
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies.	✓
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression).	✓
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	✓
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	✓
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	✓
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	✓

APPENDIX 2. Search strategies

OVID Medline and Embase

1. Gamma knife surgery/
2. Gamma knife/
3. GKRS/
4. GKS/
5. GK/
6. Radiosurg*/
7. Stereotactic
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. Arteriovenous Malformation/
10. AVM
11. 9 or 10
12. 8 and 11
13. (brain* or cerebral or intracerebral or central nervous system or intracranial or cerebellar or intraventricular or supratentorial).tw.
14. 12 and 13 (English language only)

Number of references identified: 3402
Last date searched: October 17, 2021

Open Grey

1. arteriovenous malformation
2. AVM
3. radiosurgery

Number of references identified: 41
Last date searched: October 17, 2021

Cochrane

1. cerebral arteriovenous malformation or cerebral arteriovenous malformations or intracranial arteriovenous malformations or AVM
2. stereotactic or radiosurgery or gamma knife
3. 1 and 2

Number of references identified: 48
Last date searched: October 17, 2021

APPENDIX 3. Excluded studies, with the reasons for their exclusion

First author, year of publication	No access/Non-english/Not full paper	Study period pre- 1989	No original data or review	<20 patients / < 1 year FU	No reporting of demographic data (Age/ Nidus volume/ Dose)	No reporting of location/SM/ Presentation	No reporting of clinical outcomes of interest (Obliteration/ Haemorrhage/ RICs)	LINAC/ Cyberknife/ Repeat GK/ Multi-stage GKRS	Superseded by another study
Abecassis et al. 2017					*[1]				
Anderson et al. 2020								*	
Back et al. 2008					*	*			
Bowden et al 2014 “in/near Sylvian fissure”									*[2]
Bowden et al 2014 “near ventricles”									*[2]
Bowden et al. 2014 “cerebellum”									*[2]
Bowden et al. 2015									*[2]
Bowden et al. 2017									*[2]
Burrow et al. 2014									*[3]
Chen, C.J et al. 2018									*[4]
Chen, C.J et al. 2019 “seizures”									*[4]
Chen, C.J et al. 2019 “micro vs GK”									*[5]
Chen, C.J et al. 2020									*[4]
Cheng C.H et al 2012									*[5]
Coffey et al. 1995	*								
Cohen-inbar et al. 2015									*[5]
Cohen-Inbar O. et al. 2017 “cerebellar”									*[4]
Cohen-Inbar O. et al. 2017 “early vs late”									*[4]
Da Costa et al. 2009							*		
Ding et al 2013 “eloquent locations”									*[5]
Ding et al 2014 “cerebellar”									*[5]
Ding et al. 2014 “Ruptured AVMS”									*[5]
Ding et al. 2015 “effect of prior haemorrhage on GK outcomes…”									*[5]
Ding et al. 2015 “temporal Lobe”									*[5]
Ding et al. 2016 “ARUBA eligible AVMs.”									*[4]
Ding et al. 2016 “repeat GK”									*[7]
Ding et al. 2017 “ARUBA Grade 1/2 AVMs”									*[4]
Ding et al. 2017 “Grade 3 AVMs”									*[4]

First author, year of publication	No access/Non-english/Not full paper	Study period pre- 1989	No original data or review	<20 patients / < 1 year FU	No reporting of demographic data (Age/ Nidus volume/ Dose)	No reporting of location/SM/ Presentation	No reporting of clinical outcomes of interest (Obliteration/ Haemorrhage/ RICs)	LINAC/ Cyberknife/ Repeat GK/ Multi-stage GKRS	Superseded by another study
Ding et al. 2017 "Unruptured AVMS"									*4
Ding et al. 2019 "Risk of… Hemorrhage"									*4
Douglas et al. 2008						*			
Duma et al. 1993	*								
El-Shehaby et al. 2019								*	
Flickinger et al. 1992							*		
Flickinger et al. 1997							*		
Flickinger et al. 1998							*		
Flickinger et al. 1999		*							
Flickinger et al. 2000							*		
Flickinger et al. 2002							*		
Franzin et al. 2016								*	
Friedman et al. 2003								*	
Graffeo et al. 2020									*3
Hanakita et al. 2014									*6
Hanakita et al. 2016									*6
Hasegawa et al. 2017									*6
Hasegawa et al. 2018 "a comprehensive study"							*		*6
Hasegawa et al. 2018 adv age"									*6
Hasegawa et al. 2020									*6
Hou et al. 1998	*								
Hung et al. 2020									*5
Ilyas et al. 2017				*					
Inoue. 2006						*			
Izawa et al. 2009			*						
Jevalkar et al. 2009				*					
Jokura et al. 2009						*			
Kano et al. 2012 "Large"								*	
Kano et al. 2017 "Estimating risks of ARE"							*		
Kano et al. 2017 "Repeat -GK"								*	
Karlsson et al. 1997		*							
Karlsson et al. 1999		*							
Karlsson et al. 2019					*				

First author, year of publication	No access/Non-english/Not full paper	Study period pre- 1989	No original data or review	<20 patients / < 1 year FU	No reporting of demographic data (Age/ Nidus volume/ Dose)	No reporting of location/SM/ Presentation	No reporting of clinical outcomes of interest (Obliteration/ Haemorrhage/ RICs)	LINAC/ Cyberknife/ Repeat GK/ Multi-stage GKRS	Superseded by another study
Kasliwal et al. 2008							*		
Kawashima et al. 2020									*[6]
Kemeny et al. 1989				*					
Kemeny et al. 2007					*				
Kihlstrom et al. 1997				*					
Kim H et al. 2010								*	
Kim M.J. et al. 2020							*		
Koga et al. 2010									*[6]
Koga et al. 2012									*[6]
Koltz et al. 2013					*				
Kurita et al. 2000 “occipital”									*[6]
Kurita et al. 2000 “brainstem”									
Lang et al.2018									
Lenck et al. 2018								*	
Lunsford et al. 1989									*[2]
Lunsford et al. 1990	*								
Lunsford et al. 1992	*								
Marciscano A.E. et al. 2017			*						
Maruyama et al. 2004									*[2]
Maruyama et al. 2005									*[6]
Maruyama et al. 2005 “corpus Callosum”									*[6]
Nagy et al. 2012 “deep”		*							
Nagy et al. 2012 “large”		*							
Nagy et al. 2017								*	
Nerva et al. 2015					*				
Nicolato et al. 2006[i] Part 1							*[8]		
Nicolato et al. 2006[i] Part 2							*[8]		
Niranjan et al. 2018									*[2]
Park et al. 2016								*	
Patibandla M.R. et al. 2018									*[4]
Patibandla M.R. et al. 2019									*[4]
Paul et al. 2014							*		
Pollock et al. 1994	*								
Pollock et al. 1996 “factors that predict”							*		
Pollock et al. 1996 “haemorrhage risk”									*[2]

First author, year of publication	No access/Non-english/Not full paper	Study period pre- 1989	No original data or review	<20 patients / < 1 year FU	No reporting of demographic data (Age/ Nidus volume/ Dose)	No reporting of location/SM/ Presentation	No reporting of clinical outcomes of interest (Obliteration/ Haemorrhage/ RICs)	LINAC/ Cyberknife/ Repeat GK/ Multi-stage GKRS	Superseded by another study
Pollock et al. 1996 "post-geniculate"							*		
Pollock et al. 1998									*3
Pollock et al. 1999					*				
Pollock et al. 2003									*3
Pollock et al. 2004									*3
Pollock et al. 2013									*3
Pollock et al. 2017								*	
Pomeraniec et al. 2018									*5
Potts M.B. 2014							*		
Safain M.G. et al. 2014				*					
Sasaki et al. 1998		*							
Schwyzer et al. 2012									*5
Serizawa et al. 2012	*								
Seymour et al. 2020								*	
Shi et al. 2007	*								
Shin et al. 2004									*6
Sirin et al. 2006									*2
Starke et al. 2013									*5
Starke et al. 2017									*4
Steiner et al. 1992		*							
Sun et al. 2011						*			
Sung et al. 2009								*	
Tonetti et al. 2018					*				
Wegner et al. 2011						*			
Yamamoto et al. 1992		*							
Yamamoto et al. 1992		*							
Yamamoto et al. 1995									*3
Yamamoto et al. 1996		*							
Yamamoto et al. 1998		*							
Yamamoto et al. 2012								*	
Yamamoto et al. 2013		*							
Yang et al. 2012						*			
Yen C.P et al. 2010								*	
Yen C.P et al. 2013			*						
Yen C.P et al. 2014									*5
Total number of studies:	**8**	**12**	**3**	**5**	**8**	**7**	**16**	**15**	**57**

[1]This study reported on the outcomes following multimodal management for SM III AVMs. However, it was not possible to extract demographic data (Age/Margin dose/Median Nidus volume) specifically for those patients treated with Gamma Knife. [2] Superseded by Kano et al 2012 [41, 43-45] [3]Superseded by Pollock *et al,* 2016 [64] [4]Superseded by Chen, C.J et al, 2018 [7] [5]Superseded by Ding et al. 2014 [14-16] [6] Superseded by Hasegawa et al. 2018 [32] [7] Superseded by Yen C.P *et al* 2011 [73]. [8i]Nicolato et al. Part 1 and 2, 2006 were both excluded following senior discussion and review as both papers in combination do meet minimum outcomes dataset for inclusion, and it was not possible to assume that both studies were referring to the exact same patient set. The corresponding author was contacted via email for further data, however, a response is still pending at time of article submission.

APPENDIX 4. Overview of overlapping studies

Institution	First author and year of publication	Treatment Period	Number of patients	Median Follow-up (Months)	Included/ excluded with reason for exclusion
University of Virginia	Ding *et al* 2014 (SM 1/2)	1989-2012	502 patients SM1/2	Clinical: 61.6 (6.8–239.4)	Included.
	Ding *et al* 2014 (SM 3)	1989-2009	398 patients SM3	Clinical: 67.5 (6.2–239.2)	Included.
	Ding *et al* 2014 (SM 4/5)	1989-2009	110 patients SM4/5	Clinical: 97.4 (6.5– 312.9)	Included.
	Yen C.P *et al* 2009 Repeat GK cohort	1989-2007	140 patients	Mean Clinical: 84.2 (15-220)	Included.
	Ding *et al.* 2015 "effect of prior haemorrhage on GK outcomes…"	1989-2009	270 patients All Ruptured cohort	Mean Clinical: 85.7	Excluded. Reason: superseded by Ding et al. 2014 SM1-2/3/4-5
	Ding et al. 2016 "repeat GK"	1989-2013	84 patients Repeat GK cohort	Mean: 77.6 (±SD 47.6)	Excluded. Reason: Longer study time period 1989-2013 however fewer (case matched) patients at 84 compared to Yen C.P et al 2009:
	Starke *et al*. 2013 A practical grading…	1989-2009	1012 patients	Mean: 96 (24–240)	Excluded. Reason: superseded by Ding et al. 2014 SM1-2/3/4-5 which stratifies by SM grade
	Pomeraniec et al. 2018	1989-2015	1159 patients	Mean: 72.1	Excluded. Reason: Data split according to cyst formation and Ding et al. 2014 SM1-2/3/4-5 stratifies by SM grade
	Cohen-inbar *et al.* 2015 "A quantitative analysis of .."	1987-2012	105 patients	Mean Clinical: 53.8	Excluded. Reason: superseded by Ding et al. 2014 SM1-2/3/4-5
	Hung *et al.* 2020 "pre-embolisation vs GK-only"	1989-2012	35 patients GK alone cohort	Angiography: 65 (13–48)	Excluded. Reason: superseded by Ding et al. 2014 SM1-2/3/4-5
	Chen, C.J *et al.* 2019 Microsurgery vs GK	2001-2013	59 patients GK alone cohort	Mean Clinical: 92.1 (±SD 58.3)	Excluded. Reason: superseded by Ding et al. 2014 SM1-2/3/4-5
	Ding *et al.* 2014 Ruptured AVMS	1989-2009	465 patients All Ruptured cohort	Mean Clinical: 72.2 (6.2–312.9)	Excluded. Reason: superseded by Ding et al. 2014 SM1-2/3/4-5. Not possible to extract data for all patients.
	Yen C.P *et al* 2014	1989-2009	31 patients All Incidental findings	Clinical: 51(24-196)	Excluded. Reason: superseded by Ding et al. 2014 SM1-2/3/4-5
	Schwyzer *et al.* 2012	1989-2008	729 patients GK alone cohort	Mean Clinical: 79.2 (6-324)	Excluded. Reason: superseded by Ding et al. 2014 SM1-2/3/4-5
	Cheng C.H *et al* 2012 "BG and Thalamus"	1989-2007	182 patients Basal ganglia and thalamus	Clinical: 85.8 (24-266)	Excluded. Reason: Only Basal Ganglia and Thalamus located AVMs Superseded by Ding et al. 2014 SM1-2/3/4-5

Institution	First author and year of publication	Treatment Period	Number of patients	Median Follow-up (Months)	Included/ excluded with reason for exclusion
	Ding *et al.* 2015 "temporal Lobe"	1989-2012	175 patients Temporal lobe	Clinical 73.3 (6.2–230.4)	Excluded. Reason: Only Temporal located AVMs Superseded by Ding et al. 2014 SM1-2/3/4-5
	Ding *et al* 2014 "cerebellar"	1989-2010	60 patients Cerebellar	Clinical: 52.8months (6.8 to 195.4)	Excluded. Reason: Only Cerebellar located AVMs superseded by Ding et al. 2014 SM1-2/3/4-5
	Ding *et al* 2013 "eloquent locations"	1989-2009	134 patients Eloquent	79.8 (8.4 to 223.5)	Excluded. Reason: Only eloquent area located AVMs superseded by Ding et al. 2014 SM1-2/3/4-5
University of Pittsburgh	Kano *et al* 2012 (SM1/2)	1987-2006	217 patients SM1/2	64 (6–267)	Included.
	Kano *et al* 2014 (Grade 3)	1987-2009	474 patients SM3	89 (2–278)	Included.
	Kano *et al* 2012 Part 4 (BG and thalamus)	1987-2006	140 patients Basal Ganglia or Thalamus	Mean Clinical 81(2–265)	Included.
	Kano *et al* 2012 Part 5 (brainstem)	1987-2006	67 patients Brainstem	73.3 months (6–269)	Included.
	Kano *et al* 2012 Part 3 (repeat)	1987-2006	105 patients Repeat-GK	80 (6–205)	Included.
	Kano *et al* 2012 Part 6 (large multistage)	1987-2006	47 patients Large 10cm3+	87 (0.4–206)	Included.
	Bowden *et al* 2014 "in/near Sylvian fissure"	1987-2009	87 patients In/Near Sylvian fissure	59 (6–295)	Excluded. Reason: Only AVMs located in/near Sylvian fissure Superseded by Kano *et al. (include reference numbers)*
	Bowden *et al* 2015 "post-geniculate pathway"	1987-2009	171 patients Along course of optic radiation	74 (5–297)	Excluded. Reason: Only AVMs located along optic radiation Superseded by Kano *et al. (include reference numbers)*
	Bowden *et al*. 2014 "cerebellum"	1987-2007	64 patients Cerebellum	Radiological 73 (4–255)	Excluded. Reason: Only Cerebellar located AVMs Superseded by Kano *et al. (include reference numbers)*
	Bowden *et al* 2014 "near ventricles"	1987-2009	188 patients Within or in contact ventricles	Radiological 65 (2–265)	Excluded. Reason: Only AVMs located in/near ventricles Superseded by Kano *et al. (include reference numbers)*
	Maruyama *et al* 2004 "brainstem"	1987-2002	50 patients Brainstem	56 (5-176)	Excluded. Reason: Only Brainstem located AVMs Superseded by Kano *et al* 2012 Part 5 (brainstem)
	Niranjan *et al* 2018 "seizure presentation"	1987-2012	28 patients Large volume-staged	59 (6–295)	Excluded. Reason: Only AVMs with seizure presentation Superseded by Kano *et al. large (include reference numbers)*

Institution	First author and year of publication	Treatment Period	Number of patients	Median Follow-up (Months)	Included/ excluded with reason for exclusion
	Bowden *et al* 2017 "impact on headaches"	1995-2013	102 patients	89.7 (13-249)	Excluded. Reason: Only AVMs with headache presentation Superseded by Kano *et al. (include reference numbers)*
	Pollock *et al*. 1996 haemorrhage risk…	1987-1992	315 patients	Mean: 47	Excluded. Reason: Superseded by Kano *et al. (include reference numbers)*
	Sirin *et al* 2006 Large	1987-2004	28 patients Large volume-staged	50 (3–15)	Excluded. Reason: Superseded by Kano *et al* 2012 Part 6 (large multistage)
	Lunsford et al. 1989	1987-1989	113 AVM cohort	not stated "minimum 6 months"	Excluded. Reason: Superseded by Kano *et al. (include reference numbers)*
Mayo Clinic Rochester, USA	Pollock *et al* 2016 "The effect of treatment periods…"	1990-2009	371 patients (1990-1999 + 1999-2009 cohort)	93 (3-290)	Included
	Pollock *et al 2017* "volume staged" large	1997-2012	34 patients Large Volume-staged	98.4 (36-159.6)	Included
	Graffeo *et al*. 2020	1990-2011	173 patients SM1/2	68 (24-275)	Excluded. Reason: Fewer case numbers and so superseded by Pollock *et al* 2016 *(include reference numbers)*
	Pollock *et al* 2003 patient outcomes after…	1990-1997	144 patients	Mean: 86 (23–169)	Excluded. Reason: Superseded by Pollock *et al* 2016 *(include reference numbers)*
	Pollock *et al* 2013 risk of stroke…	1990-2005	174 patients	64 (IQR 36–120)	Excluded. Reason: Superseded by Pollock *et al* 2016 *(include reference numbers)*
	Pollock *et al* 2004 "BG thalamus, and BS"	1990-2000	56 patients Deep located AVMs	45 (12–121)	Excluded. Reason: Superseded by Pollock *et al* 2016 *(include reference numbers)*
	Pollock *et al.* 1998 "factors associated"	1987-1992	220 patients	mean: 47 (±SD 20)	Excluded. Reason: No overlap 1987-1990 however fewer patients (220) compared to Pollock et al. 2016 (371)
	Yamamoto *et al* 1995	1990-1993	121 patients	97 (54-205)	Excluded. Reason: Superseded by Pollock *et al* 2016 *(include reference numbers)*
	Burrow *et al* 2014	1990-2009	80 patients	Mean: 68 (12-133)	Excluded. Reason: Superseded by Pollock *et al* 2016 *(include reference numbers)*

Institution	First author and year of publication	Treatment Period	Number of patients	Median Follow-up (Months)	Included/ excluded with reason for exclusion
University of Tokyo Hospital	Hasegawa et al. 2018 "Comparison of the long term.."	1990-2014	592 Patients	92 (1–320)	Included.
	Hanakita *et al.* 2016 ARUBA eligible	1990-2010	292 Patients ARUBA-eligible	62 (IQR 36–106)	Excluded. Reason: Superseded by Hasegawa *et al.* 2018 which includes ARUBA eligible cohort.
	Hanakita *et al.* 2014	1998-2010	67 patients Large (10cm3+)	55 (7-178)	Excluded. Reason: Superseded by Hasegawa *et al.* 2018 which includes large AVMs
	Maruyama *et al.* 2005	1990-2003	500 patients	93.6 (IQR 115.2)	Excluded. Reason: Superseded by Hasegawa *et al.* 2018 (include reference number)
	Shin *et al.* 2004	1990-1999	408 patients	65 (1-135)	Excluded. Reason: Superseded by Hasegawa *et al.* 2018
	Kawashima *et al.* 2020 "Ruptured AVMs"	1990-2016	410 patients All Ruptured cohort	111 (1–351)	Excluded. Reason: Only ruptured AVMs Superseded by Hasegawa *et al.* 2018
	Kurita *et al* 2000 "occipital"	1990-1997	37 patients Occipital lobe	46 12-103	Excluded. Reason: Only Occipital lobe located AVMs Superseded by Hasegawa *et al.* 2018
	Kurita *et al* 2000 "brainstem"	1990-1997	30 patients Brainstem	Mean: 52.2 (±SD 31.3)	Excluded. Reason: Only brainstem located AVMs Superseded by Hasegawa *et al.* 2018
	Hasegawa *et al. 2017* "cerebellar"	1990-2010	45 patients Cerebellum	120 (5-291)	Excluded. Reason: Only cerebellar located AVMs Superseded by Hasegawa *et al.* 2018
	Hasegawa et al. 2020 "re-evaluating"	1990-2014	791 patients (Adults+Paediatrics)	83 (1-320)	Excluded. Reason: Superseded by Hasegawa *et al.* 2018 which excludes paediatric patients.
	Hasegawa et al. 2018 "a comprehensive study"	1990-2010	581 patients	121.2 (24-320.4)	Excluded. Reason: No data on RICs
	Hasegawa et al. 2018 adv age"	1990-2013	561 Patients Age 65 years + versus 65-	91	Excluded. Reason: Superseded by Hasegawa *et al.* 2018
	Maruyama *et al* 2005"corpus Callosum"	1990-2002	32 patients Corpus Callosum	108 (12-144)	Excluded. Reason: Only corpus callosum located AVMs Superseded by Hasegawa *et al.* 2018

Institution	First author and year of publication	Treatment Period	Number of patients	Median Follow-up (Months)	Included/ excluded with reason for exclusion
	Koga *et al* 2010 "SRS thalamus"	1990-2009	48 patients Thalamus	45 (6-198)	Excluded. Reason: Only Thalamus located AVMs Superseded by Hasegawa *et al.* 2018
	Koga et al. 2012 "tractography"	Not Stated ("from 2000")	52 patients Diffusion Tensor Tractography treatment planning cohort	48 (36-80)	Excluded. Reason: Superseded by Hasegawa *et al.* 2018 which includes DTT cohort
Multi-Center (International Gamma Knife Research Foundation): USA: University of Virginia, University of Pittsburgh, University of Louisville, Cleveland Clinic Foundation, New York University, Beaumont Health System, Michigan Canada: University of Sherbrooke, Quebec. Puerto Rico: University of Puerto Rico, San Juan.	Chen, C.J *et al. 2018* (paediatric vs adult AVM)	1987-2014	1845 patients Adults	Mean: 80.7 (±SD 62.5)	Included.
	Seymour *et al.* 2020 "volume staged GK IGKRF"	1991-2016	257 patients Two-stage+	69.5 (1.68-302.4)	Included.
	Starke *et al.* 2017	1988-2013	2236 patients Adult+Paediatrics	Mean: 84 (6-240)	Excluded. Reason: Unlike Chen *et al. 2018 does not split data (same) into adult:Paediatric*
	Ding *et al.* 2019 *"*Risk of… Hemorrhage"	1987-2014	2320 patients	Mean: 80.36 (±SD 62.4)	Excluded. Reason: No data on RICs which were included in Chen *et al. 2018*
	Patibandla *et al.* 2019 "—> "outcomes pre/post-2000"	2001–2014	664 patients	Mean: 45.0 ± 29.6	Excluded. Reason: Superseded by Chen *et al. 2018* which includes 1987-2000 data
	Chen, C.J *et al.* 2018 "Advanced age…"	1987-2014	1845 patients Adults	Mean: 80.7 (±SD 62.5)	Excluded. Reason: Same dataset as Chen C.J *et al. 2018 but splits data into age 65 +/-*
	Chen, C.J *et al.* 2020 "Basal ganglia and thalamus"	1987-2014	363 patients Basal Ganglia or Thalamus	Mean: 86.5	Excluded. Reason: Same data as Chen *et al. 2018 but only includes patients with Basal ganglia or Thalamus located AVMs*
	Chen, C.J *et al.* 2019 "seizures"	1987-2014	419 patients	Mean: 37.2 (±SD 16)	Excluded. Reason: Unlike Chen *et al. 2018 does not split data (same) into adult:Paediatric*
	Cohen-Inbar *et al.* 2017	1988-2014	1398 patients All obliterated		Excluded. Reason: Outcome data only on patients who had proven obliteration
	Ding *et al.* 2017 ARUBA-eligible Grade 1/2 AVMs	1987-2014.	232 patients SM1/2	Mean: 90.5 (12.0-324.7)	Excluded. Reason: Only SM1/2 ARUBA-eligible AVMs Superseded by Chen *et al. 2018*

Institution	First author and year of publication	Treatment Period	Number of patients	Median Follow-up (Months)	Included/ excluded with reason for exclusion
	Ding *et al.* 2017 Grade 3 AVMs	1987-2014	891 patients SM3	Mean: 88.6 (12.0 to 278.4)	Excluded. Reason: Only SM3 ARUBA-eligible AVMs Superseded by Chen *et al. 2018*
	Ding *et al.* 2016 ARUBA eligible AVMs.	1987-2014.	509 patients ARUBA-eligible	Mean: 86.2 (±SD 62.3)	Excluded. Reason: Only ARUBA-eligible AVMs Superseded by Chen *et al. 2018*
	Ding *et al.* 2017 Unruptured AVMS	Not stated	938 patients All Unruptured	70.9 (12.0-275.6)	Excluded. Reason: Only unruptured AVMs Superseded by Chen *et al. 2018*
	Patibandla M.R. *et al.* 2018 Grade 4/5	Not stated	233 patients (SM4/5)	84.5 (±SD 59.5)	Excluded. Reason: Only SM4/5 AVMs Superseded by Chen *et al. 2018*
	Cohen-Inbar O. *et al.* 2017	1988-2015	162 patients Cerebellar	Median 60 (7–325)	Excluded. Reason: Only Cerebellar AVMs Superseded by Chen *et al. 2018*

[a]Median clinical or radiological follow-up, whichever is longer. [b]ARUBA (A Randomised **trial** of Unruptured Brain Arteriovenous malformation.

APPENDIX 5. Risk of bias Summary ROBINS-I

First author, year of publication	Bias due to confounding	Bias in selection of participants into the study, selection bias	Bias in classification of interventions	Bias due to deviation from intended interventions, performance bias	Bias due to missing data, <80%, attrition bias	Bias in measurement of outcomes, detection bias	Bias in selection of the reported result, outcome reporting bias
Arslan *et al.* 2017 [2]							
Bir *et al.* 2015 [4]							
Bose *et al.* 2015 [5]							
Chang *et al.* 2000 [6]							
Chen *et al.* 2018 [7]							
Choe *et al.* 2008 [8]					[a]		
Ding *et al.* 2014 [14]							
Ding *et al.* 2014 [15]							
Ding *et al.* 2014 [16]							
Ditty *et al.* 2017 [18]							
Franzin *et al.* 2013 [24]							
Han *et al.* 2008 [31]							
Hasegawa *et al*. 2018 [32]							
Hirschmann *et al.* 2019 [35]							
Hu *et al.* 2020 [36]							
Izawa *et al.* 2005 [39]							
Kano *et al.* 2014 [41]							
Kano *et al.* 2012 [43]							
Kano *et al*. 2012 [44]							
Kano *et al.* 2012 [45]							
Kim BS *et al.* 2019 [46]							
Kiran *et al.* 2009 [47]							
Liscak *et al.* 2007 [49]							
Matsunaga et Shuto. 2014 [51]							
Missios *et al.* 2014 [52]							
Nicolato et al. 2002 [54]							
Orio *et al.* 2006 [56]							
Pan *et al.* 2000 [57]							
Parkhutik *et al.* 2013 [58]							
Pollock *et al.* 2016 [64]							
Raboud *et al.* 2018 [65]							
Tuleasca *et al.* 2020 [71]							
Zeiler *et al.* 2011 [74]							
Zhao *et al.* 2008 [75]							

Green indicates low risk of bias; yellow indicates moderate risk of bias; red indicates serious risk of bias; grey indicates no information on which to base a judgement about risk of bias for this domain [a]Choe et al. 2008 [8] has missing radiological follow-up data (MRI) for 24 patients (/100) affecting obliteration & RICs data which has been attributed to '*incomplete short term follow up*' and additionally, '*a signif[i]cant proportion of lost patients before reaching final outcome*'. [b] Raboud et al. 2018 [65] is the single prospective study of all included studies (which are retrospective).

APPENDIX 6. Detailed characteristics of included studies

Study, year of publication	Total number of patients	Female patients (%)	Median age (range/ SD)	Location[2] (%)	Eloquent Location (%)	SM grade (%)	Venous Drainage (%)	Median Maximum Nidus Diameter, cm (range)	Associated flow-related or intranidal aneurysm (%)	Median RBAS OR VRAS Score	Pre-GKRS intervention (%)	Presentation with Haemorrhage (%)	Presentation with seizure (%)	Asymptomatic presentation (%)	Median Nidus Volume cm^3 (range)	Median Prescription dose Gy (Range)	Median Duration of follow-up months(range)	Number of patients with follow-up	Complete Obliteration rate — Angiography-confirmed (%)	Complete Obliteration rate — Angiography or MRI confirmed (%)	Median Time to obliteration (months)	Method of determining obliteration ± no. of patients underwent imaging modality	Post-GKRS Haemorrhage (%)	Post-GKRS transient RIC (radiological or symptomatic)	Post-GKRS permanent RIC (radiological or permanent FND)	Post-GKRS new onset/ increase frequency seizures	Cyst formation (%)	Post-GKRS Mortality (%)	Patients who underwent repeat-GKRS (%)	Outcomes for repeat-GK cohort
Arslan *et al.* 2017 [2]	199	89 (45%)	32 (3-74)	Lobar: 150 (75.4) Deep 35 (17.6) -Basal ganglia 10 (5) -Thalamus 10 (5) -Brainstem 15 (8) Corpus callosum 5 (3) Cerebellar 5 (5%)	—	I 16 (8.04) II 45 (22.61) III 119 (59.8) IV 14 (7.04) V 5 (2.51)	—	—	7 (3.51)	1.07 (0.18 – 4.80)	Embolisation 22 (11%) Surgical Resection 20 (10) Shunt 4 (2) EVD 3 (2) Ventriculostomy 1 (0.5) Embolisation + RS 1 (0.5) Surgery + RS 1 (0.5) Surgery + Embolisation 1 (0.5)	86 (43)	42 (21)	1 (0.5)	2.50 (0.05-39)	22 (10-26 Gy)	60.2 (7–100.1)	199	—	141 /199 (71)	—	MRI AND Angiography: 153 (77%) MRI only: 46 (23%)	7 (3.5%)	Total 54 (27%) including symptomatic in 13 (6.5%)	0 (0)	7 (3.5)	—	4 (1.5). 3/4 ICH 1/4 Unrelated	29 (14.6)	10/29 obliteration
Bir *et al.* 2015 [4]	85	42 (49.5)	41 (17-76)	Cortical 68 (80) Deep 9 (10.6) -Thalamus 4/85 -Brain stem 3/85 -Basal ganglia 2/85 Cerebellum 9 (10.6) Corpus callosum 2/85 (2.35)	—	I 8 (9.41%) II 29 (34.1) III 25 (29.4%) IV 21 (24.71%) V 2 (2.4%)	—	3 (0.4–9.5)	—	—	Embolisation 8 (9.4%)	26 (30.5)	—	—	3 (0.4-9.5)	Mean: 18 (14–25)	32.65 (6–133)	85		67/85 (79)	31 (5–89)	MRI AND Angiography: 30 (35%) MRI: 85 (100)	5 (5.8%). annual rate 1.6%.	0 (0)	0 (0)	0 (0)	1 (1.2)	Total: 3 (3.56). 2/3 ICH 1/3 Hydrocephalus	17 (20)	—
Bose *et al.* 2015 [5]	96	34 (35.42)	Mean: 27.52 (±SD 14.48)	—	—	I 9 (9.38) II 31 (32.29) III 44(45.83) IV 11(11.46) V 1 (1.04)	—	—	—	—	Embolisation 23 (23.96) Surgical resection 4 (4.1) Gamma knife 10 (10.42)	57 (59.4)	0 (0)	—	Mean: 7.45 (1.01-71.2)	Mean 24.6 (15-25)	24.5 (6-48)	96	39 (72.2)	—	—	Angiography: 50	10 (10.42%)	Total transient or permanent symptomatic : 25 (26.04%)	Total transient or permanent symptomatic : 25 (26.04%)	—	—	Total: 2 (2.08%). ICH 2/2	—	—
Chang *et al.* 2000 [6]	278	117 (42)	Mean: 29.4 (2.8–68.1)	Lobar 156 (56.1%) Deep 62 (22.3%) Corpus Callosum 17(6.1%) Cerebellum 23 (8.3%) Cerebrospinal fluid pathways 20 (7.2%)	—	I 37 (14.1%) II 88 (33.6%) III 84 (32.1%) IV 50 (19.1%) V 3(1.2%)	Deep 155 (59.2) Superficial 107(40.8)	2.56	63 (26.3)	—	Embolisation 72 (25.9%) Surgical resection 20 (7.2) GK 23 (8.3%)	179 (64.6)	61 (21.9)	7 (2.5)	12.1 (0.15–109.5)	mean: 16.2 (8.4–30)	24.7 (0.4–90.2)	128 with radiological FU	/128 with 2 year+ follow-up: 101 (78.9%) 101/128 AVMs Obliteration rate at 2 years/3/4 post-GKRS was 42%/ 56.7/78.2	/128 with 2 year+ follow-up: 101 (78.9%) 101/128 AVMs Obliteration rate at 2 years/3/4 post-GK was 42%/ 56.7/78.2	—	Angiography	19 (6.8%)	symptomatic 4(4.68%)	symptomatic 1(0.04%)	8 (2.9)	1 (0.4)	—	23 (9.1)	—
Chen *et al.* 2018 [7]	1845	929 (50.4%)	40.4 (±SD 14.1)	Deep 384 (20.9%)	1292 (70%)	I 209 (11.3%) II 699 (37.9%) III 751 (40.7%) IV 168 (9.1%) V 18 (1%)	Deep 1033 (56) Superficial 811 (44)	Mean: 2.4 (±SD 1.2)	229/1845 (12.4%)	Mean: 1.4 (±SD 0.6)	Embolisation: 387 (21.3%) Surgical resection: 80 (4.4%) EBRT: 138 (7.5%)	999 (54.2)	—	—	MEAN 4.6 (±SD 5.3)	Mean: 20.4 (±SD 3.8)	Mean: 80.7 (±SD 62.5)	1845	896/1845 (48.6)	1147/1845 (62.2) Actuarial obliteration rates at 2/4/6/8/10 years were 13.7%/38.8/ 47.2/53.5/ 57.1	—	Angiography and MRI	147 (8%)	Total: 545 (29.6%) including symptomatic 130 (7.04%)	symptomatic 42 (2.28%)	—	—	Total: 96 (7.9) all-causes	—	—
Choe *et al.* 2008 [8]	100	48 (48)	Mean: 34 (5-66)	Cortical 67 (67%) Deep 18 (18) Cerebellum 11 (11) Corpus callosum 4 (4)	—	I 18 (18%) II 27 (27) III 36 (36) IV 11 (11) V 8 (8)	—	—	—	—	Embolisation 5 (5%) Surgical resection 2 (2) LINAC 3 (3)	34 (34)	25 (25)	8 (8)	mean: 4.3(0.1 -29.3)	20.8 (13-32)	Mean: 37.5 (5-63)	100	28 /48 (58) Min. 3 year angiography follow-up: 29/35 (83)	—	Mean: 25.3 (6-43)	Angiography: 48 patients	7 (7%). Annual rate 3.2%	Total /76 patients with MRI FU: Total: 24 (32%) including symptomatic 5 (6.6%)	0 (0)	—	—	Total: 1 (1). 1/1 ICH	16 (16)	—
Ding *et al.* 2014 [14]	110	53 (48.2%)	27.6 (4.7–75.1) Age <18: 28 (25.5%)	Superficial 62 (56.4%) Deep 48 (43.6%)	110 (100%)	IV 109 (99.1%) V 1 (0.9%)	Deep 110 (100)	3.4	—	1.38 (0.47 – 4.10)	Embolisation 32 (29.1%) Surgical Resection 16 (14.5%).	56 (50.9)	23 (23)	4 (3.6)	5.7 (1.2 – 33.0)	19 (10 – 25)	Clinical: 97.4 (6.5– 312.9) Radiological: 87.8 (17.3 – 261.6)		37/110 (33.6)	48/110 (43.64) Actuarial obliteration rates at 3/5years were and 5 years were 10/23%	42.7 (6.2–223.5)	Angiography and MRI	20 (18.2%) Annual hemorrhage rate 3.0%. (800 risk years)	Total: 49 (48.0%) including symptomatic 10 (9.1%)	symptomatic 3 (2.73%)	1 (1.3)	—	—	34 (30.9)	—
Ding *et al.* 2014 [15]	398	194 (48.7)	30.9 (3.7–81.1) Age <18 yrs: 75 (18.8%)	Superficial 214 (53.8) Deep: 184 (46.2%)	363 (91.2)	III 398 (100)	Deep 337 (84.7%) Multiple 169 (42.5%)	2.3 (0.4–5.5)	—	1.18 (0.21–3.70)	Embolisation 109 (27.4%) Surgical resection 44 (11.1%)	234 (58.8)	80 (20.1)	11 (2.8)	2.8 (0.1–27.8)	20 (5–32)	Clinical: 67.5 (6.2–239.2) Radiological: 54.3 (5.3–230.4)		222/398 (55.8)	276/398 (69.3) Actuarial obliteration rates: 3 and 5 years 38% and 60%,	45.5 months	Angiography and MRI	28 (7.03%). Annual hemorrhage rate 1.7%. (1897 risk-years)	Total /334 with 2 years+ follow-up: 115/334 (34.3%) including symptomatic 21/334 (6.3)	symptomatic 13/334 (3.9%)	7 (1.8)	—	Total: Two (0.5). 2/2 ICH	64 (16.1)	—
Ding *et al.* 2014 [16]	502	249 (49.6%)	35.2 (4.1-81.8) Age <18 yrs: 79 (15.7%)	Superficial 470 (93.6%) Deep 32 (6.4%)	204 (40.6%)	I 147 (29.3%) II 355 (70.7%)	Deep 111 (22.1) Superficial 391 (77.9)	2 (0.2–4.5)	—	1.03 (0.21–2.95)	Embolisation: 101 (20.1%) Surgical Resection: 55 (11.0%).	235 (46.8)	126 (25.1)	15 (3.0)	2.4 (0.1–22.5)	23 (7–36)	Clinical: 61.6 (6.8–239.4) Radiological: 47.9 (5.7–239.4)		304/502 (60.6)	382/502 (76.1) Actuarial obliteration rates: 3/5/7/10 are 41/66/75/80%	39.5 (5.7–192.8)	Angiography and MRI	28 (5.6%) Annual hemorrhage rate 1.4% (2158 risk-years)	Total /414 patients with 2 year+ Follow-up: 160 (38.6%) including symptomatic in 28 (6.8%)	Total /414 patients with 2 year+ FU: 6 symptomatic (1.45%)	15 (3.0)	6 (1.2)	—	50 (10.0)	—
Ditty *et al.* 2017 [18]	78	39 (50)	Mean: 38.5 (6.9–74.3 years)	Cortical 69 (89.6%) Cerebellar 1(1.3%) Deep 6 (7.8) -Basal Ganglia 4/78 -Thalamus 1/78 -Brainstem 1/78 Ventricular 2 (2.6)	—	I 5 (6.5%) II 18 (23.4%), III 36(46.8%), IV 17 (22.1%) V 1(1.3%)	—	—	—	—	Embolisation 0 (0) Surgical resection 5 (6.4%)	9 (14.3)	78 (100)	—	—	17.5 (17–22 Gy)	Mean: 36.4 (1–242.6)	78	—	/59 who underwent MRI or CTA or DSA: 34/59 (57.6)	—	MRI or CTA or DSA: 59 (75.6%)	6 (7.69%)	symptomatic (transient or permanent): 6 (7.69%)	Radiation necrosis 3 (3.85%)	5 (3)	—	—	10 (12.8)	—
Franzin *et al.* 2013 [24]	127	56 (44.1)	38.5 (6–76)	Lobar 106 (83.5) Deep 21 (16.5)	80 (63%)	I 21 (16.5%) II 46 (36.2%) III 51 (40.1%) IV/V 9 (7.1%)	Deep 70 (55.1) Superficial 57 (44.9)	1.8	—	1.08 (0.47–2.26)	Embolisation 24 (18.9) Surgical resection 7 (5.5) Radiosurgery 5 (3.9) Embolization + RS 6 (4.7) Embolization + Surgery 3 (2.4) Embolization + surgery + RS 1 (0.8)	55 (43.3)	40 (31.5)	28 (22)	2.74 (0.1–13)	22 (16 to 30)	Min. 36	104 radiological FU	/90 who underwent angiography: 54 (60)	/104 with MRI follow-up: 72 (69.2)	44 (43.9–53.1)	DSA: 90 MRI:104	11 (8.66 %) Annual bleeding rate 2.1 %.	—	8 (6.3%) permanent FND and 6 (4.9 %) radiation necrosis	15 (12.3)	2 (1.6)	Total 5 (4.1). 5/5 ICH	—	—
Han *et al.* 2008 [31]	218	73 (33.49)	Mean: 31 (±SD 15)	Peripheral 151 (69.3) Deep 50 (22.9) Cerebellum 17 (7.8)	—	I 54 (24.8) II 79 (36.2) III 68 (31.2) IV 15 (6.9) V 2 (0.9)	—	—	20 (9.2)	—	Embolisation 32 (14.7%) Surgical resection, evacuation of ICH from AVM and Aneurysm occlusion 33 (15.14)	106 (48.6)	58 (26.6)	15 (6.9)	3.4 (0.17–35.2)	18.0 (10.0–25.0)	Mean: 44 (±SD 20)	218	Min. 2 year follow-up /119: 79 (66.4) Angio rate; 79/218 total or 79/119 who underwent angiography at min. 2 years.	Min. 2 year follow-up: 131 / 183 (71.6)	24	Angiography: 119 MRI: 183	12 (5.5%) annual bleeding rate 1.9%. Four of these patients had permanent neurological deficits and 1 died. The neurological deficits in 7 of the patients improved completely within 2 years.	Total#: /157 with regular MRI FU: 30 (19.1) including symptomatic 9 (5.73)	8 (5.1%)	—	0 (0)	Total 4 (1.83). 1/4 ICH 3/4 Unrelated	24 (11)	—
Hasegawa *et al.* 2018 [32]	592	248 (42%)	38 (20–80)	Deep location 217 (37)	338 (57)	I–II 328 (55%)	Deep: 308 (52) Superficial 284 (48.0)	2.2 (0.5–6)	—	—	Embolisation 63 (11%) Surgical Resection 52 (9%)	311 (53)	—	—	2.7 (0.1–44.5)	20 (15–28)	92 (1–320)	592	391 (66). Actuarial obliteration rates at 2/3/4/6 years were 23/53/73/85%	391 (66). Actuarial obliteration rates at 2/3/4/6 years were 23/53/73/85%	30	Angiography: DSA	38(6.4%). Actuarial haemorrhage rate at 1/2/5/10 years were 2.9/4.9/ 5.5/6.4%.	Total: 1/2/3 years rate of 15/30/32%	Permanent symptomatic at 2/5/10/15 years of 3/4/4/7%	—	35(5.9) including encapsulated haematoma	—	37	—
Hirschmann *et al.* 2019 [35]	265	124 (47%)	40 (7–80)	—	144 (54%)	Spetzler-Ponce A 130 (49%) B 109 (41%) C 26 (10%)	Deep 165 (62%) Superficial 100 (38%)	—	—	1.3 (0.2–4.2)	Embolisation 19 (7.16%) Surgical Resection 8 (3.02%) Repeat GK 68 (26%)	81 (31)	—	—	2.3 (0.1–42.0)	19 (11–22)	66 (7.2–384)	265	—	Actuarial obliteration rate at 3/5/10 years were 51/63/74%	45.6	Angiography and MRI	24 /265 (9%) Annual haemorrhage rate 1.3%.	—	Total permanent: 13/265 (4.9%) **includes the occurrence of radiologically diagnosed edema or late onset cyst formation with or without new neurological symptoms	—	see transient RIC column	Total: 7 (1.5)	49 (18.9)	—
Hu *et al.* 2020 [36]	98	38 (38.8)	37 (4-80)	Lobar 81 (82.7) Deep location 29 (29.6) -Thalamus, basal ganglia 3/98 -Brainstem 7/98 Cerebellum 8 (8.2)	61 (62.2)	I 17 (17.35) II 33 (33.7) III 33 (33.7) IV 14 (14.29) V 1 (1.02)	Deep 57 (58.2) Superficial 41 ((41.8)	2.58	25 (25.5)	—	0 (0)	47 (48.0)	29 (29.6)	—	7.1 (0.1-42.6)	18 (16-21)	47.5 (3-93)	98	43 /98 (43.9)	63 (64.3)	31 (14-82)	Angiography: 43 (43.9%) MRI only: 20 (20.4%)	2 (2%)	Total: 62(63.3%) including symptomatic 7 (7.1%)	—	—	—	—	—	—
Izawa *et al.* 2005 [39]	237	93 (39.2%)	mean: 30.1 (6–74)	Lobar 159 (67%) Deep 65 (27.4) Cerebellum 13 (5.5%)	—	I 33 (13.9%) II 69 (29.1%) III 104 (43.9%) IV 31 (13.1%)	—	—	—	—	—	130 (54.9)	50 (21.1)	—	mean: 4.7 (0.1–28.5)	mean: 20.2 (12–26)	81.6 (24–150)	237	130 (54.9)	130 (54.9)	—	Angiography	8 (3.4%)	—	Total: 1 (0.4%) including symptomatic 0 (0)	4 (1.7)	8 (3.4)	Total: 3 (1.27%). 3/3 ICH	—	—
Kano *et al.* 2014 [41]	474	222 (46.8)	33 (±SD 1.32)	Cortical 250/474 (52.7) Deep 169 (35.7) -Thalamus 64/474 (13.5) -Brain stem 56/474 (11.8) -Basal ganglia 49 (10.3) cerebellum 34 (7.2) Corpus callosum 14 (3.0) ventricles 3 (0.6)	430 (90.7)	III 474 (100)	Deep 326 (68.8) Superficial 148 (31.2)	1.9 (0.6–2.9)	32 (6.8)	—	Embolisation alone: 67 (14.1%) Surgical resection alone: 44 (9.3%) Embolisation + resection: 14 (3)	268 (56.5)	—	—	3.8 (0.1–26.3)	20 (13–25)	89 (2–278)		Actuarial obliteration: 3/4/5/10 were 39%, 57%, 59%, 62%.	Actuarial obliteration: 3/4/5/10 years were 48%, 69%, 72%, 77%	—	Angiography: 198 MRI only:258	38 (8%). Annual hemorrhage rate 2.7% (1385 patient-years)	symptomatic 17 (3.58)	13 (2.74%) Sx	—	9 (1.9)	Total: 21 (4.4). 20/21 ICH 1/21 ARE	59 (12.4)	34/59 (58) obliteration
Kano *et al.* 2014 [43]	133	63 (47.4)	26 (3–69)	Deep 133 (100) -Basal Ganglia 56 (40) -Thalamus: 77 (55)	—	II 11 (8.3) III 48 (36.1) IV 20 (15.0) VI 54 (40.6)	—	2.0 (0.6–4.8)	7 (5%)	1.39 (±SD 0.56)	Embolisation 18 (13.5) Surgical Resection 20 (15.0).	113 (85)	3 (2)	3 (2)	2.7 (0.1–20.7)	20 (15–25)	Clinical: 81(2–265) Radiological: 61		Actuarial obliteration 3/4/5/10 years were 47%/60/ 63/63.	Actuarial obliteration 3/4/5/10 years 57%/ 70/72/72	DSA: 36.7 (95% CI 29.19–44.2)	Angiography: 63 MRI only:78	15 (11%). Annual hemorrhage rate 4.7% (364.4 patient-years)	symptomatic 13 (9.8%)	6 (4.5%) Sx	—	1 (0.8)	Total: 11 (8.3). 7/11 ICH 4/11 Un-related	18 (13.5)	9/18 obliteration
Kano *et al.* 2014 [44]	67	25 (37.3)	41 (6–79)	Deep 67 (100) Midbrain 40 (59.7) Pons 32 (47.8) Medulla 3 (4.5)	67 (100)	III 7 (10.4) IV 0 (0) V 0 (0) VI 60 (89.6)	—	—	7 (10.4)	1.45 (±SD 0.55)	Embolisation: 11 (16.4)	51 (76)	0 (0)	4 (6)	1.4 (0.1–13.4)	20 (14–25.6)	73.3 months (6–269)		Actuarial obliteration 3/4/5/10 years were 36%/ 63/63/63.	Actuarial obliteration 3/4/5/10 years were 41%/ 70/70/76	DSA:41.3 (95% CI 35.73–46.87)	Angiography: 28 MRI only:35	4 (6%). Annual hemorrhage rate 1.9% (206.7 patient-years)	Symptomatic 4 (6.0)	7 (10.4) Sx	—	2 (3.0)	Total: 10 (14.9). 4/10 ICH 1/10 hydrocephalus 5/10 unrelated	4/67 (6.0)	1/4 obliteration
Kano *et al.* 2012 [45]	217	106 (49)	38 (3–77	Cortical 174 (80.2) Deep 9 (4.1) -thalamus 7 (3.2) -basal ganglia 2 (0.9) pineal region 1 (0.5) intraventricular 4 (1.8) cerebellum 19 (8.8) corpus callosum 10 (4.6)	—	I 34 (16%) II 183 (84%)	—	1.9 (0.5-3.77)	21 (9.7)	1.12 (±SD 0.52)	0 (0)	78 (36)	61 (28)	30 (14)	2.3 (0.1–14.1)	22 (15–27)	64 (6–267)		Actuarial obliteration rates: 3/4/5/10 years were 41%, 66%, 77%, and 83%.	Actuarial obliteration: 3/4/5/10 years were 58%/ 87/90/93	DSA: 37 (95% CI 36–39). Obliteration time defined as halfway time-point between last MRI image and documented MRI/DSA obliteration	Angiography: 100 MRI only:148	13 (6%) Annual hemorrhage rate 2.3% (559.1 patient-years)	Total: 5 (2.3%) including symptomatic 5 (2.3%)	0 Permanent deficit 0 Radiation necrosis	3 (1.4) /5 who experienced transient symptomatic RICs	2 (0.9)	Total: 6 (2.8). 6/6 ICH	8 (3.7)	4/8 obliteration
Kim BS *et al.* 2019 [46]	264	98 (37.1)	Mean: 40.7 (±SD 12.0)	Supratentorial lobar 238 (90.2) Deep 7 (2.6) -Thalamus 4 (1.5) -Basal ganglia 3 (1.1) Corpus callosum 3 (1.1) Cerebellum 8 (3.0) Insula 5 (1.9) Intraventricular 3 (1.1)	121 (45.8)	I 52 (19.7) II 87 (32.9) III 87 (32.9) IV 38 (14.4)	Deep 65 (24.6) Superficial 199 (75.1)	3.6 (±SD 1.6)	53 (20.1)	Mean: 1.35 (0.46–3.54)	0 (0)	0 (0)	66 (25.0)	92 (34.8)	Mean: 4.8 (±SD 5.3)	Mean: 21 (12–30)	Mean: Clinical and Radiological were 55.5 and 44.7 (3.4–179.9)	264	115 /264 (43.5)	164 (62.1). Actuarial obliteration rates at 3/5/7/10 years: 37.1%/ 70.5/84.1/90.1	40.1 (95% CI: 37.0–45.5)	MRI alone: 49/164 (18.6%) DSA: 115/164 (43.5%)	19 (8.26%) Annual Rate 2.85% (644.6 person-years)	Total: 149 (56.4%) including symptomatic in 35 (13.3%)	symptomatic 3 (1.1%)	24 (9.1)	—	Total: 2 (0.76). 1/2 AVM-related causes, 1/2 unrelated	34 (12.9)	—
Kiran *et al.* 2009 [47]	53	12 (22.6)	Mean: 22.7 years (3–55)	Deep 53 (100) -Basal ganglia/ thalamus, 47; Brainstem, 6).	53 (100)	I 0 (0) II 0 (0) III 40 (75) IV 11 (21) V 2 (4)	—	—	—	—	Embolisation 5 (9%)	43 (81)	8 (15)	—	Mean: 4.3 (0.1–36.6)	Mean: 23.3 (16–25)	Mean: 28 (12–96)	53	Min. 4 year angiography follow-up /19: 14 (74%) Actuarial obliteration rates, 3 and 4 years: 68 and 74%	—	—	Angiography: 19	5 (9.4%)	Symptomatic 4 (7.54)	symptomatic 4 (7.54)	—	—	—	—	—
Liscák *et al.* 2007 [49]	330	152 (46.5%)	35 (3-78)	Lobar 250 (75.76%) Deep 42 (12.73%) Cerebellum and Corpus callosum 38 (11.52%)	—	I 39 (11.8%) II 156 (47.3%) III 100 (30.3%) IV 35 (10.6%) V 0 (0)	—	2.2 (0.6-6.1)	—	—	Embolisation 58 (17.6%) Surgical resection 64 (19.4%) fractionated radiotherapy 6 (1.8%) Resection+Embolisation 7 (2.12%)	207 (63)	105 (31.82)	—	3.9 (0.15-28.6)	20 (8-32)	38 (1-118)	300	222/300 (74)	222/300 (74)	25 (12-96)	Angiography 222	16/300 (5.33%)	—	8/300 (2.67%)	12/300 (4)	—	—	68/300 (22.67)	47/68 (69)

Study, year of publication	Total number of patients	Female patients (%)	Median age (range/ SD)	Location[2] (%)	Eloquent Location (%)	SM grade (%)	Venous Drainage (%)	Median Maximum Nidus Diameter, cm (range)	Associated flow-related or intranidal aneurysm (%)	Median RBAS OR VRAS Score	Pre-GKRS intervention (%)	Presentation with Haemorrhage (%)	Presentation with seizure (%)	Asymptomatic presentation (%)	Median Nidus Volume cm³ (range)	Median Prescription dose Gy (Range)	Median Duration of follow-up months(range)	Number of patients with follow-up	Complete Obliteration rate — Angiography-confirmed (%)	Complete Obliteration rate — Angiography or MRI confirmed (%)	Median Time to obliteration (months)	Method of determining obliteration ± no. of patients underwent imaging modality	Post-GKRS Haemorrhage (%)	Post-GKRS transient RIC (radiological or symptomatic)	Post-GKRS permanent RIC (radiological or permanent FND)	Post-GKRS new onset/ increase frequency seizures	Cyst formation (%)	Post-GKRS Mortality (%)	Patients who underwent repeat-GKRS (%)	Outcomes for repeat-GK cohort
Matsunaga et Shuto. 2014 [51]	82	28 (34.1)	mean 43.3 (±SD17.5)	Deep 27 (32.9) cerebellar vermis 20 (24.4) cerebellar hemispheres 35 (42.7)	60 (73.2)	I 14 (17.1%) II 37 (45.1%) III 30 (36.6) IV 1 (1.2%)	—	1.7 (0.4-5.5)	12 (14.6)	1.42 (0.58-3.22)	embolisation 11 (13.4%) surgical resection 5 (6.1%)	69 (84.1)	0 (0)	11 (13.4)	0.95 (0.03-22.9)	18 (12-25)	73.2 (60-219.6)	82	41 (50)	65 (79.3) Actuarial rate at 3/5 years is 58.5% and 78%	26.4 (6-63.6)	Angiography: 41 MRI: 24	2 (2.43%) Annual bleeding risk post GK was 1.2% at 1 year and 0.49% at 5 years.	Total: 20 (24.4%) patients including symptomatic in 6 (7.32%)	symptomatic 6 (7.31%) 1 radiation necrosis (1.2)	—	0 (0)	—	5 (6.1)	2/5 obliteration at 3 and 3.2 years post repeat-GK
Missios *et al.* 2014 [52]	165	82 (53.9)	Mean: 43.6 (±SD 17.4)	Cortical 125 (75.75) Deep 23 (13.9) -brainstem 9 (5.5) -thalamus/ basal ganglia 14 (8.5) cerebellum 13 (7.9) Other 4 (2.4)	—	I 11 (6.7) II 67 (40.6) III 69 (41.8) IV 18 (10.9)	—	Mean: 2.74 (0.8–5.6)	22 (13.3)	1–2 104 (63.1)	Embolisation 0 (0) Surgical resection 5 (3.0)	41 (24.8)	36 (21.8)	22 (13.3)	Mean: 6.3 (0.05–46.8)	Mean: 17.9 (10–28)	Mean: 36.2 (1–158)	165	70 (42.42) Actuarial rates for 3, 4, 5 years are: 44%/ 54/66	—	40 months (95% CI 28.4–51.6)	Angiography	7 (4.2%)	symptomatic 14 (9.03%)	—	8 (4.8)	—	Total: 3 (1.81). 1/3 ICH 1/3 cerebral edema 1/3 intractable seizure	38 (23.0)	—
Nicolato et al. 2002 [54]	242	102 (42.1)	Mean: 33.2 (5-74)	Cortical 209 (86.4) Deep 33 (13.6) -Basal Ganglia 33 (13.6)	—	I 14 (5.7) II 134 (55.4) III 89 (36.8) IV 5 (2.1)	—	—	—	—	Embolisation 116 (47.9) Surgical resection 9 (4.5) Previous RT 2 (1)	137 (56.6)	75 (36)	16 (8)	3.12 (0.1-10)	22.9 (14-28)	Not stated-"minimum 6 months"	191	111/131 (84.8) 131 had minimum 2 years follow-up.	111/131 (84.8) 131 had minimum 2 years follow-up.	Mean: 27.7 (6.2-76.5)	Angiography 131	5/191 (2.0.7%)	8/191 (4.2)	4/191 (2.1)	—	—	total 2/191 (1.04). 1/2 ICH 1/2 unrelated.	—	—
Orio *et al.* 2006 [56]	100	48 (52.7)	33 (9–66)	Cerebrum 91 (91%) Deep 9 (9.9) -Basal Ganglia 4 (4%) -Thalamus 3 (3%) -Brainstem 2 (2%)	—	*d*	—	—	—	—	Previous LINAC: 13 (14.3%) Repeat GK 4 (15.8%)	40 (44)	—	—	4.3 (0.2–27.2)	20 (13–24)	32	91	Actuarial obliteration rates: 3/5 year of 21/ 72%	Actuarial obliteration rates: 3/5 year of 21/ 72%	—	Angiography and MRI	12(12%)	—	8 (8%) including 5 radiation necrosis (5.5) and 3 symptomatic (3.3)	—	—	Total: 3 (3.3). 3/3 ICH	18 (20)	Overall primary and secondary GK: 3/5 year obliteration rates of 21 and 72%
Pan *et al.* 2000 [57]	240	104 (43.3)	Mean: 28 (2–77 years)	Lobar 133 (55) Deep 58 (24) -Basal ganglia 24 (10) -Brainstem 34 (14) corpus callosum 20 (8.3) cerebellum 21 (8.8) lat ventricle 8 (3.3)	—	I 8 (3.3) II 48 (20) III 87 (36.3) IV 74 (30.8) V 20 (8.3) VI 3 (1.25)	—	6.15	—	—	Embolisation: 5 (2.1) Surgical resection 33 (13.8) Radiotherapy 3 (1.25)	178 (74)	70 (29)	—	6.15 (±SD 8.01)	Mean: 19.1	26 (12–73)	240	/131 who underwent angiography: 115 (88). Actuarial obliteration rate 40 months is 75%	/131 who underwent angiography: 115 (88). Actuarial obliteration rate 40 months is 75%	—	Angiography: 131	10 (4.1%)	Total: 115 (47.9) including symptomatic 7 (2.9)	Symptomatic 8 (3.3)	—	—	Total: 1 (0.42)	15 (6.3)	Obliteration 9/15
Parkhutik *et al.* 2013 [58]	102	49 (48%)	34 years (IQR 22–50)	—	—	I 35 (34 %) II 34 (33%) III 26 (25 %) IV 8 (8%)	Deep 42 (41.2) Superficial 60 (59)	1.5	14 (14)	—	Embolisation 66 (64.7 %) Surgical resection 2 (2.0%) Endovascular and Surgical resection 1 (0.98%)	41 (40)	36 (35)	—	3.95 (IQR 0.95–5.9)	Mean: 18.5 (12–24)	63 months (IQR 35–103)	102	/82 who had 3 year angiographic follow-up: 50 (79)	/82 who had 3 year angiographic follow-up: 50 (79)	—	Angiography: 63 patients	3 (2.9%)	Total: 17[b] (16.6 %)	Necrosis 7 (6.9 %)	2 (1.9)	*Cyst incidence included in necrosis*	Total: 4 (3.9). 2/4 ICH and 2/4 of unrelated causes.	19 (18.6)	11/19
Pollock *et al.* 2016 [64] *1990-1999 cohort*	160	84 (52.5)	36 (3-82)	Deep 32 (20.0)	128 (80.0)	Spetzler-Ponce A 52 (32.5) B 73 (45.6) C 35 (21.9)	—	2.8 (0.9-6.2)	—	1.46 (0.41-5.92)	Embolisation: 12 (7.5) Surgical Resection: 15 (9.4)	55 (34.4)	—	—	5.7 (0.4-45.8)	18.0 (15.0-22.0)	Clinical: 93 (3-290)	160		130/160 (81.3). 4-year and 8-year obliteration rate of group 1 patients was 67.9% and 86.1%,	—	Angiography and MRI	37 (9.7%). Annual hemorrhage rate 1.3% (2966 person-years)	—	Symptomatic 23 (14.4%)	4 (1.05) /23 who experienced permanent RIC	—	Total: 14 (3.7). 13/14 ICH 1/14 radiation necrosis.	26 (16.3)	—
Pollock *et al.* 2016 [64] *1999-2009 cohort*	221	128 (57.9)	42 (5-71)	Deep 30 (13.6)	165 (74.7)	Spetzler-Ponce A 107 (48.4) B 85 (38.5) C 29 (13.1)	—	2.4 (0.6-6.1)	—	1.31 (0.21-4.40)	Embolisation: 8 (3.6) Surgical resection: 15 (6.9)	63 (28.5)	—	—	3.6 (0.1-35.4)	20.0 (15.0-25.0)	Clinical: 93 (3-290)	221		168/221 (76.0). 4-year and 8-year obliteration rate 52.7% and 84.3%	—	Angiography and MRI	37 (9.7%). Annual hemorrhage rate 1.3% (2966 person-years)	—	Symptomatic 8 (3.6%)	4 (1.05) /23 who experienced permanent RIC	—	Total: 14 (3.7). 13/14 ICH 1/14 radiation necrosis.	38 (17.2)	—
Raboud *et al.* 2018 [65b]	64	32 (50.0)	Mean: 46 (13–79)	—	—	I 9 (14.3) II 14 (22.2) III 29 (46.0) IV 7 (11) V 4 (6.3)	—	—	—	1.01–1.5 29 (46.0)	Embolisation 16 (25.0) Surgical resection 1 (1.6) Previous Gk 2 (3.1) LINAC 7 (10.9)	32 (50.0)	12 (18.8)	6 (9.4)	1.2 (0.032–11.3)	24 (18–24)	38 (12–75)	64	30 /64 total (46.9) 30 /55 who underwent DSA (54.5)	39 (61) Actuarial rates at 3/4/5years were 37.4/63.6/78.4%,	Mean: 35 (8–56)	Angiography: 55 MRI only: 9	3 (4.7%)	Total: 1 (1.56%) including symptomatic in 1 (1.56%)	0	0	1 (1.6)	Total: 1 (1.75). 1/1 ICH	—	—
Tuleasca *et al.* 2020 [71]	149	82 (55)	40 (18–68)	Supratentorial lobar 128 (85.9) Deep 7 (4.7) -Thalamus 6 (4) -Brainstem 1 (0.7) Infratentorial 8 (5.4) Ventricular 6 (4)	95 (63.8)	I 42 (28.2%) II 71 (47.7) III 36 (24.2) IV 0 (0)	Deep 32 (21.5) Superficial 117 (78.5)	—	10 (6.7)	2002 Median: 1.52 (0.4–2.9)	Embolisation 0 (0)	0 (0)	66 (44.3)	32 (21.5)	2 (0.09–10)	24 (18–25)	48 (12–154)	149	—	104 (69.8) Actuarial obliteration at 3/4/5/6/8 years were 37.9%/ 55.6/ 63.3/72/76	36 (12–96)	MRI only: 30 (20%) Angiography: 119 (80%)	3 (2%)	Total: 20 (13.4%)	symptomatic 5 (3.4%)	1 (0.7%)	—	—	—	—
Zeiler *et al.* 2011 [74]	41	17 (41.5%)	40.9 (14-74)	Cortical: 34 (82.9) Deep 8 (19.5) -Brainstem 2/41 (4.9) -Basal ganglia 6/41 (14.6) Cerebellar 4 (9.8)	—	I 7 (17.1%) II 9 (22.0%) III 21 (51.2%) IV 4 (9.8%) V 0 (0)	—	2.36	—	1.68	Embolisation 1 (2.44%) Embolisation and partial resection 1 (2.44%) Repeat GK 7 (17.1)	18 (43.9)	24 (58.5)	9 (22.0)	5.05 cm3	20.3 (16 – 26.4)	43.1	41		MRI OR CTA OR DSA: 36 (87.8)	27.6	MRI OR CTA AND DSA: 20 MRI OR CTA: 16	2 (4.88%)	Total: 11 (26.8%) including symptomatic in 7 (17.1%)	1 (2.44%)	—	—	3 (7.32)	5	1/5 obliteration
Zhao *et al.* 2008 [75]	341	106 (31.1)	Mean: 24.2 (1.1 - 79)	Lobar 243 (71.3%) Deep 47 (13.8) -Basal ganglia 19 (5.6%), -Thalamus 14 (4.1%), -Brain stem 14 (4.1%), Corpus callosum and ventricular 26 (7.6%) Cerebellum 25 (7.3%)	—	*d*	—	—	—	—	Embolisation 54 (15.8%) Surgical Resection 26 (7.6%)	171 (50.2)	78 (22.9)	24 (7.0)	Mean: 5.4	Mean: 20.5 (10 to 30)	76.8 (±SD 16.8)	341	—	267 (78.4) (follow-up 18 months +)	—	DSA (31/341) MR/MRA (298/341) CT (12/341)	10 (2.9%)	Symptomatic 12 (3.52%)	symptomatic 3 (0.88%)	—	2 (0.6)	Total: 4 (1/17). 3 ICH 1 ARE	3 (0.9)	—

Abbreviations: AVM = arteriovenous malformation; EBRT = fractionated external beam radiation therapy; Magnetic Resonance Imaging (MRI); RBAS = modified Radiosurgery Based Arteriovenous malformation Score; SM = Spetzler-Martin; Stereotactic Radiosurgery (SRS); Virginia Radiosurgery AVM Score (VRAS)— or NA = Data not available.

[1] explicitly not stated that there were no mortalities secondary to GKS treatment;[2]Eloquent locations, as defined by the Spetzler-Martin (SM) grading system, included sensorimotor, language, and visual cortex, hypothalamus and thalamus, internal capsule, brain stem, cerebellar peduncles, and deep cerebellar nuclei. Deep locations, as defined by the modified radiosurgery-based AVM score (RBAS), included the thalamus, basal ganglia, and brain stem, unless stated otherwise. [c] Chang *et al.* 2000 [6]: Brainstem-located AVMs have been totalled alongside author's definition of deep location which includes the thalamus, lentiform nucleus, caudate nucleus, and internal capsule but excludes brainstem [b]Defined "major radiological injury" that included moderate or severe edema and radiation necrosis (excluded minor/perilesional oedema). Was not possible to reliably extract whether RICs were transient or permanent so excluded from final statistical analysis. [a]Spetzler martin grade could not be calculated (venous drainage not stated). [d]Hasegawa *et al.* 2018 [32]: Deep location includes basal ganglia, thalamus, brainstem, cerebellum, interventricular regions, and corpus callosum. [f]Han *et al.* 2008 [31]. Deep location includes corpus callosum (in addition to Basal Ganglia/Brainstem/Thalamus). [f]Han *et al.* 2008 [31]. classified 'severe' post-radiosurgery injury as significant and this has been reflected in the data included in this analysis. [s]Superficial includes cerebral hemispheres, lateral ventricles, parasagittal/paraventricular regions, corpus callosum, cerebellar tentorium.

APPENDIX 7. Summary of methodological characteristics of the included studies

Study set-up	
Multi-center	1 (3%)
Single-center	33 (97%)
Continent (Single-centre only)	
North-America	13 (39%)
Europe	8 (24%)
Asia	12 (36%)
Reporting of the selection criteria of the study	
Specified	23 (68%)
No specified	33 (32%)
Participant identification	
Retrospective	33 (97%)
Prospective	1 (3%)
Unspecified	0 (0%)
Reporting of consecutive patients	
Yes	8 (24%)
No	7 (21%)
Not specified	19 (56%)
Participant follow-up	
Retrospective	33 (88%)
Prospective	4 (12%)
Unspecified	0 (0%)

APPENDIX 8. Moderator analysis/Meta-regression

Characteristic	Haemorrhage	PRIC	TRIC	Angio-obliteration	Angio/MRI-obliteration
Age, %				0.018	
Male, %					
Study Midyear				0.021	
Margin Dose, Gy					
AVM Volume, cm^3					
Deep venous drainage, %	0.005				0.035
Eloquent location, %	0.026				
Deep location, %		0.005	0.002		

Cells shaded green indicate statistical significance (P<0.05) with actual values of significance stated within corresponding cells.

APPENDIX 9. Funnel Plots