Gamma Knife Surgery for Basal Ganglia AVMs.

Bengt Karlsson M.D.; Ph.D.
National University Hospital
Singapore

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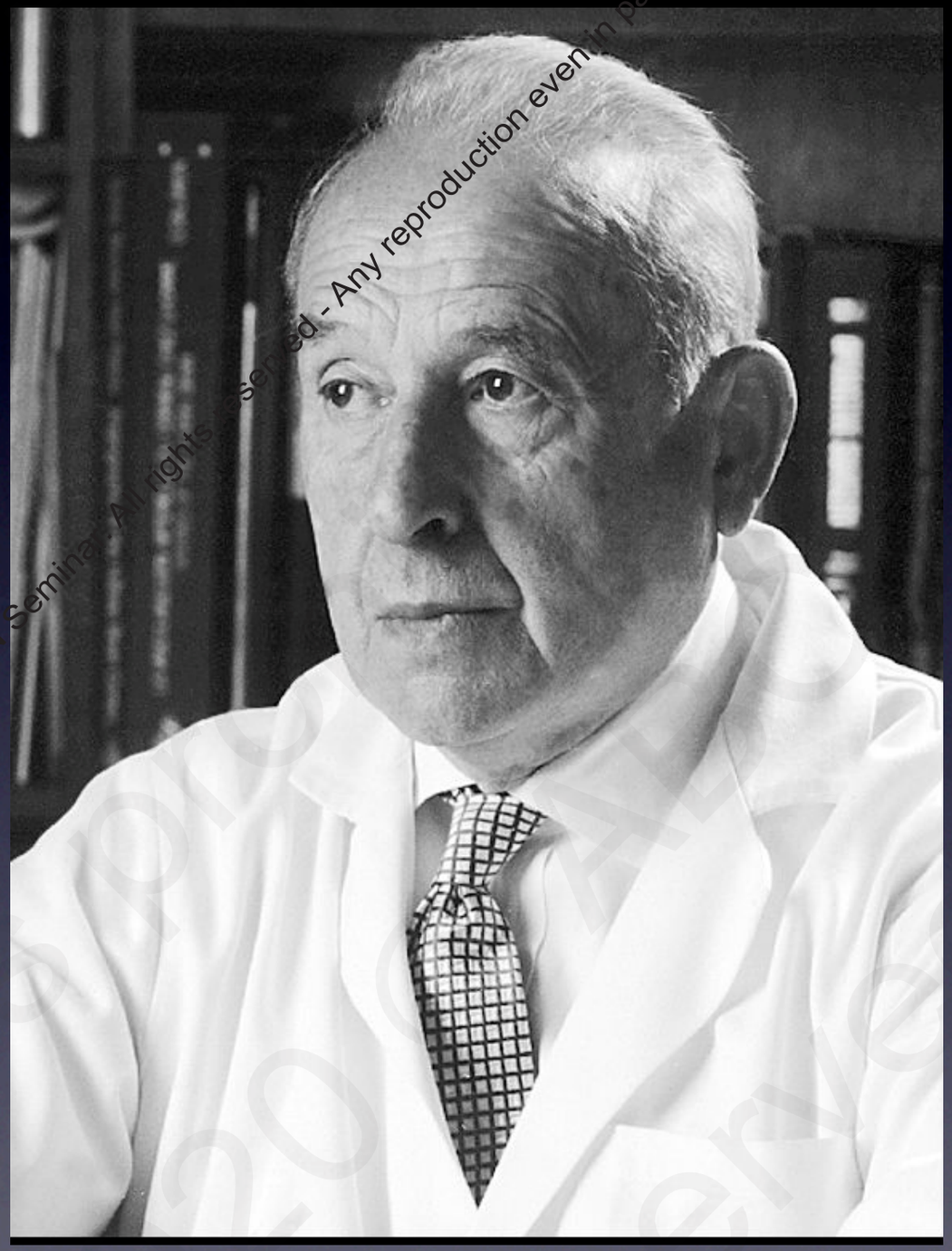
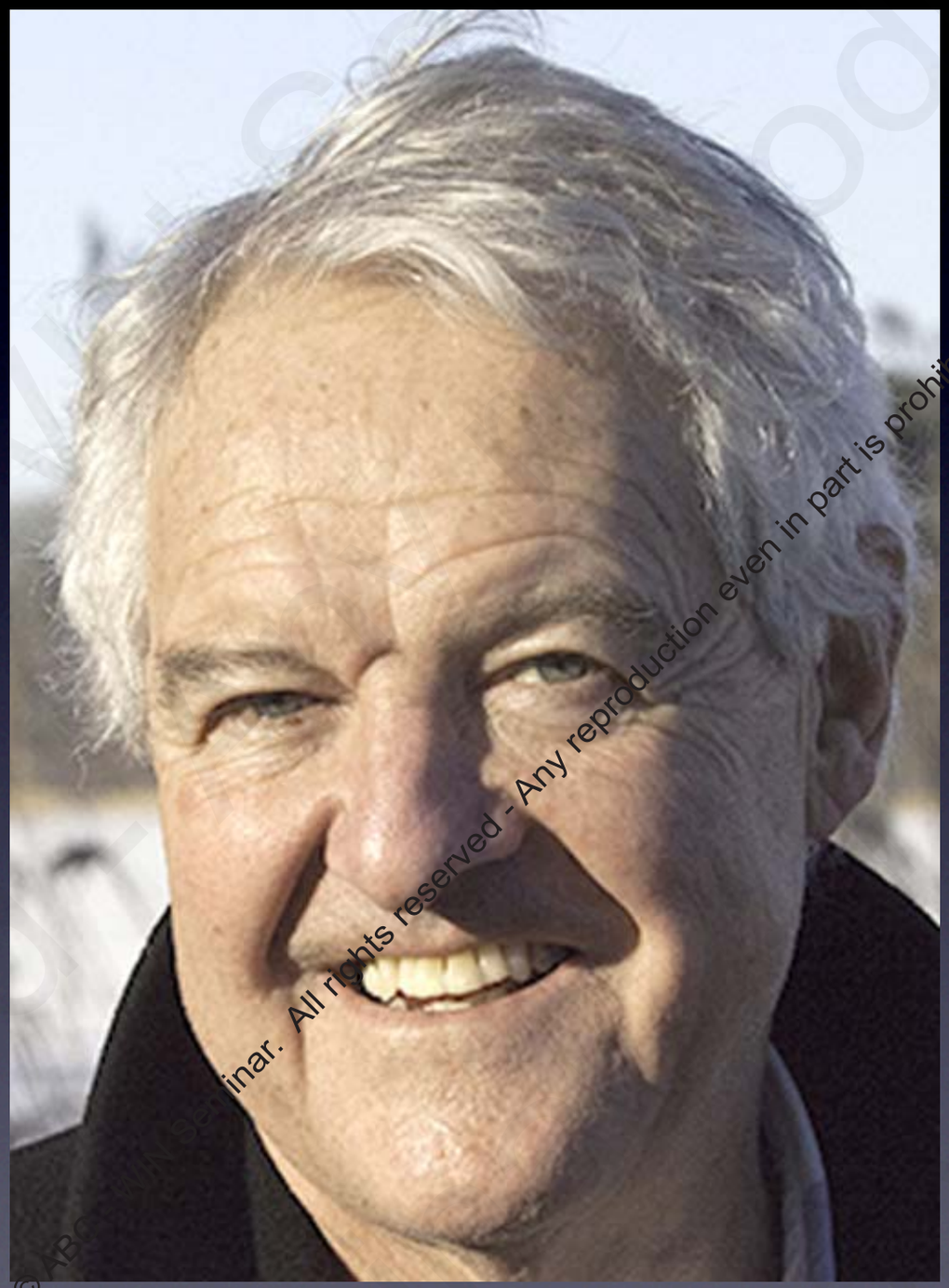
My sincere thanks and appreciation to:

Ladislau Steiner.



Christer Lindquist.



Without them Gamma Knife surgery would not be what it is today!

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Is there a need to study how the subgroup of basal ganglia AVMs respond to Gamma Knife Surgery (GKS)?

If yes, the respond to GKS must be related to AVM location.

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So, is the respond to GKS related to AVM location?

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Neurosurgery, Vol. 40, No. 3, March 1997

Prediction of Obliteration after Gamma Knife Surgery for Cerebral Arteriovenous Malformations

Bengt Karlsson, M.D., Ph.D.,
Christer Lindquist, M.D., Ph.D.,
Ladislau Steiner, M.D., Ph.D.

Department of Neurosurgery (BK, CL), Karolinska Hospital, Stockholm, Sweden, and
Department of Neurological Surgery (LS), The University of Virginia
School of Medicine, Charlottesville, Virginia

OBJECTIVE: To define the factors of importance for the obliteration of cerebral arteriovenous malformations (AVMs), thus making a prediction of the probability for obliteration possible.

METHODS: In 945 AVMs of a series of 1319 patients treated with the gamma knife during 1990 to 1990, the relationship between patient, AVMs, and treatment parameters on the one hand and the obliteration of the nidus on the other was analyzed.

RESULTS: The obliteration rate increased both with increased minimum (lowest peripheral) and average dose and decreased with increased AVM volume. The minimum dose to the AVMs was the decisive dose factor for the treatment result. The higher the minimum dose, the higher the chance for total obliteration. The curve illustrating this relation increased logarithmically to a value of 87%. A higher average dose shortened the latency to AVM obliteration. For the obliterated cases, the larger the malformation, the lower the minimum dose used. This prompted us to relate the obliteration rate to the product minimum dose (AVM volume)$^{1/3}$ (K index). The obliteration rate increased linearly with the K index up to a value of approximately 27, and for higher K values, the obliteration rate had a constant value of approximately 80%. For the group of 273 cases treated with a minimum dose of at least 25 Gy, the obliteration rate at the study end point (defined as 2-yr latency) was 80% (95% confidence interval = 75–85%). If obliterations that occurred beyond the end point are included, the obliteration rate increased to 85% (81–89%).

CONCLUSION: The probability of obliteration of AVMs after gamma knife surgery is related both to the lowest dose to the AVMs and the AVM volume, and it can be predicted using the K index. (Neurosurgery 40:425–431, 1997)

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AVM obliteration related to:

* AVM volume.
* Treatment dose to the AVM periphery.

but unrelated to:

* AVM location.

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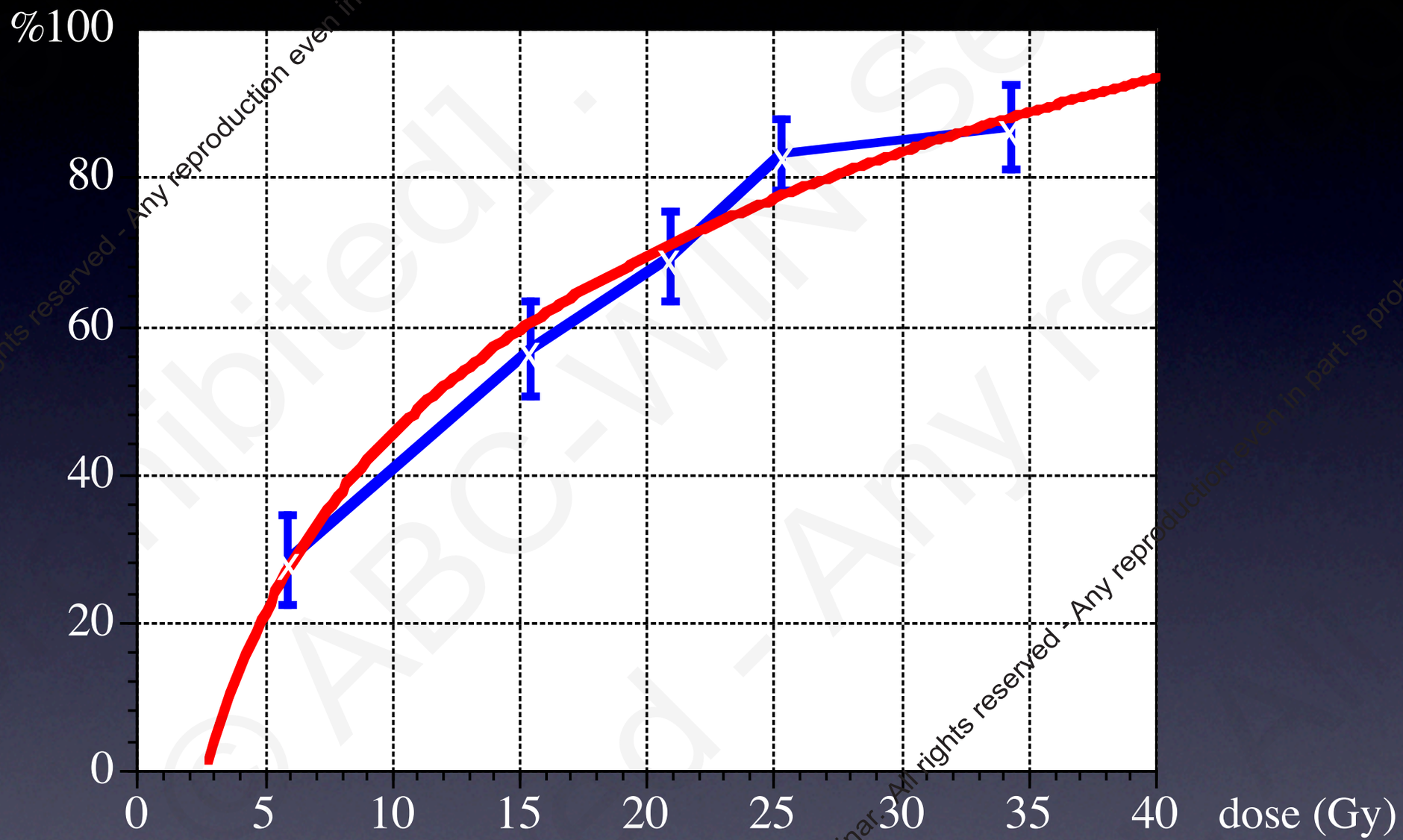
Obliteration rate versus periphery dose



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Radiotherapy and Oncology 43 (1997) 275–280

Factors influencing the risk for complications following Gamma Knife radiosurgery of cerebral arteriovenous malformations

Bengt Karlsson[a,*], Ingmar Lax[b], Michael Söderman[c]

Background and purpose: We reported previously a model predicting the risk for radiation-induced complications following Gamma Knife radiosurgery for AVM. No factor other than the dose distribution was related to the risk. The aim of this study was to define if other parameters are of importance for the risk of complications.

Material and methods: The model above was used to calculate the risk for complications in all 1128 AVM patients Gamma Knife-treated at the Karolinska Hospital 1970–1993. The number of predicted complications was compared to the number of observed ones for a number of different parameters.

Results: The model underestimated the risk of complications for patients previously given radiation with multiple or single fractions. Neither age nor gender influenced the risk of complications. Centrally located AVM had a higher, and peripheral a lower incidence of complications as compared to the calculated risk, and a previous hemorrhage reduced the risk of complications. From the observed number of complications, parameters in the model were determined by a fitting procedure separately for three groups of AVM: central and peripheral with and without a previous hemorrhage. It is also shown that the assumption of a serial functional architecture is valid in the model. This was investigated by the use of a relative seriality model with a combined serial-parallel functional architecture.

Conclusions: The risk of complications following radiosurgical treatment of AVM is dependent on the clinical history, AVM location and whether the patient has received radiation earlier. © 1997 Elsevier Science Ireland Ltd.

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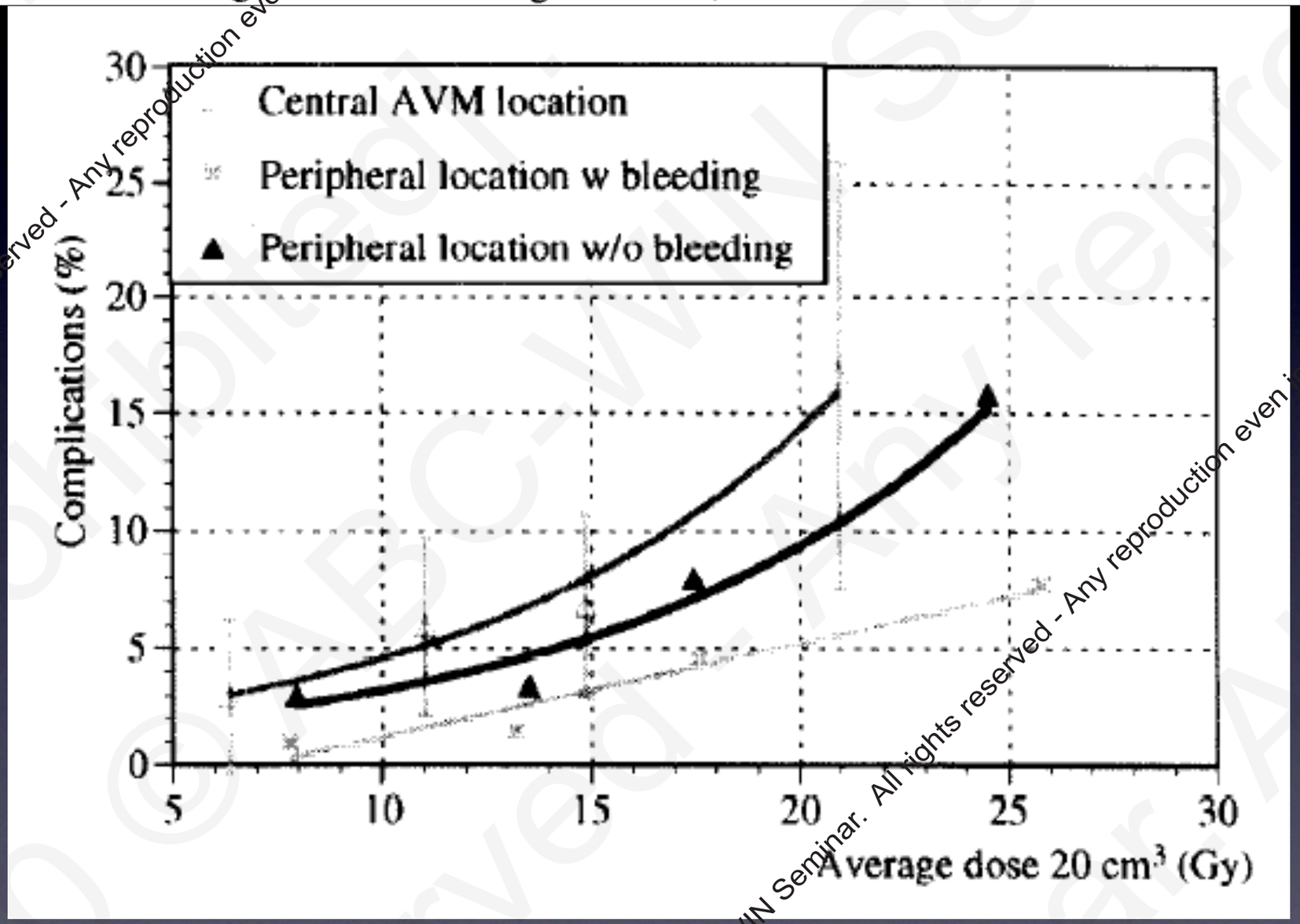
Radiotherapy and Oncology 43 (1997) 275–280

Factors influencing the risk for complications following Gamma Knife radiosurgery of cerebral arteriovenous malformations

Bengt Karlsson[a,*], Ingmar Lax[b], Michael Söderman[c]



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Conclusions:

* Obliteration is unrelated to AVM location.
* Risk for complications is related to AVM location.

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Can these conclusions be verified in a larger patient population?

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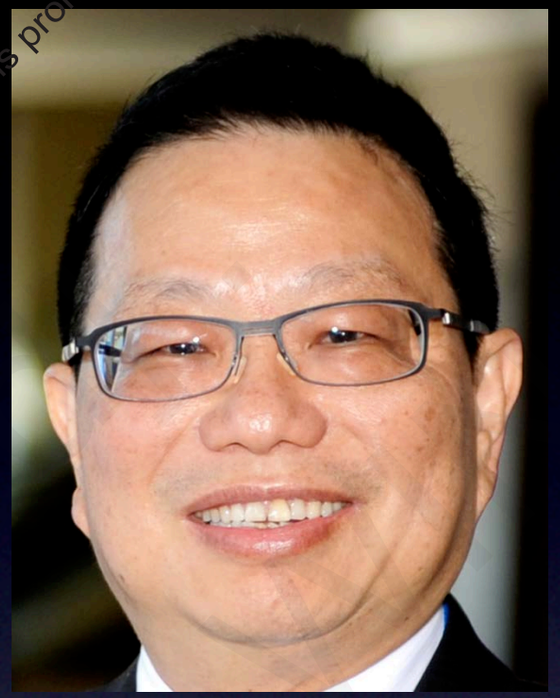
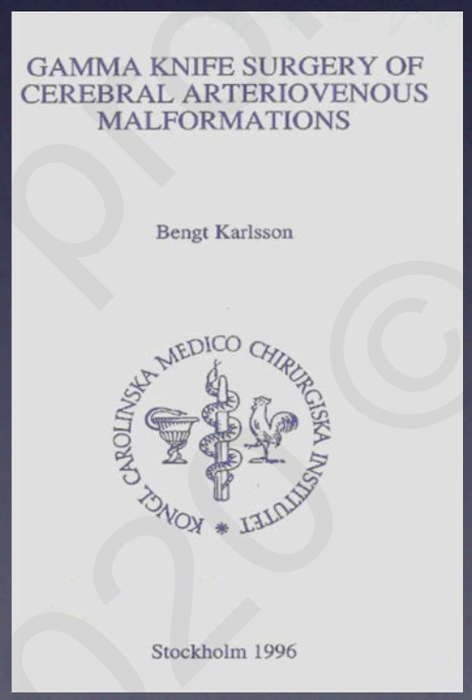
Combined database of 5060 patients with follow-up.

Sendai, Japan.

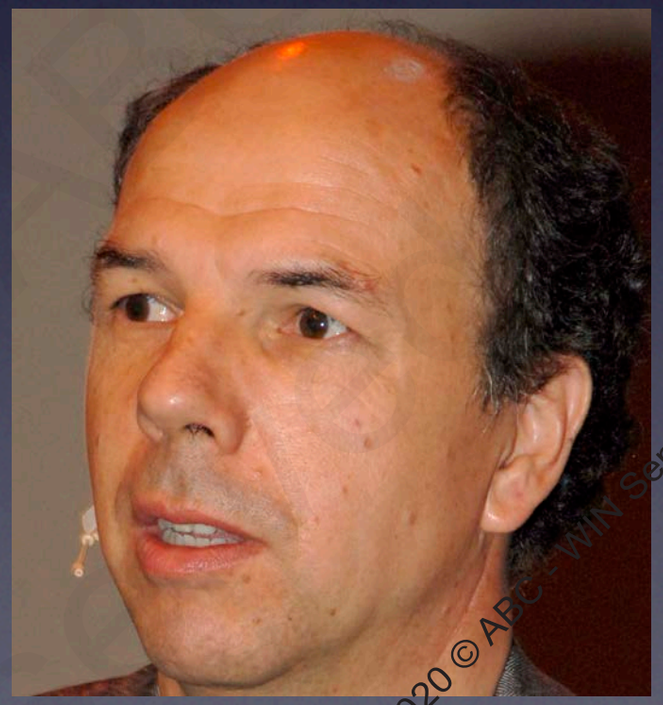


Taipei, Taiwan.

Madrid, Spain.



Karolinska and UVA.



Tilburg, the Netherlands.

Ibaraki, Japan.

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GKS for AVMs:
Central vs. peripheral vs. cerebellar. Patient parameters.

AVM location	N	age	male	pre bleed
Central	1434	31	52%	83%
Peripheral	3205	36	54%	46%
Cerebellar	421	41	52%	72%
Central vs. Peripher		P<0.01	P=0.16	P<0.01
Central vs. Cerebell		P<0.01	P=0.87	P<0.01
Cerebell vs. Peripher		P<0.01	P=0.28	P<0.01

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GKS for AVMs:

Central/peripheral/cerebellar. Treatment and outcome parameters.

AVM location	N	volume	min dose	oblit	compl	post 2 yr bleed
Central	1434	4.3 cc	19 Gy	59%	7.5%	5.0%
Peripheral	3205	7.1 cc	19 Gy	59%	5.3%	3.8%
Cerebellar	421	4.0 cc	20 Gy	55%	3.6%	4.0%
Central vs. Peripher		P<0.01	P=0.70	P=0.87	P<0.01	P=0.07
Central vs. Cerebell		P=0.05	P<0.01	P=0.14	P<0.01	P=0.44
Cerebell vs. Peripher		P<0.01	P<0.01	P=0.09	P=0.16	P=0.78

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Why are central AVMs more prone for post GKS rupture?

Because of history of pre treatment hemorrhage?

AVM location	pre GKS bleed	post 2 yr bleed
Central	83%	5.0%
Peripheral	46%	3.8%

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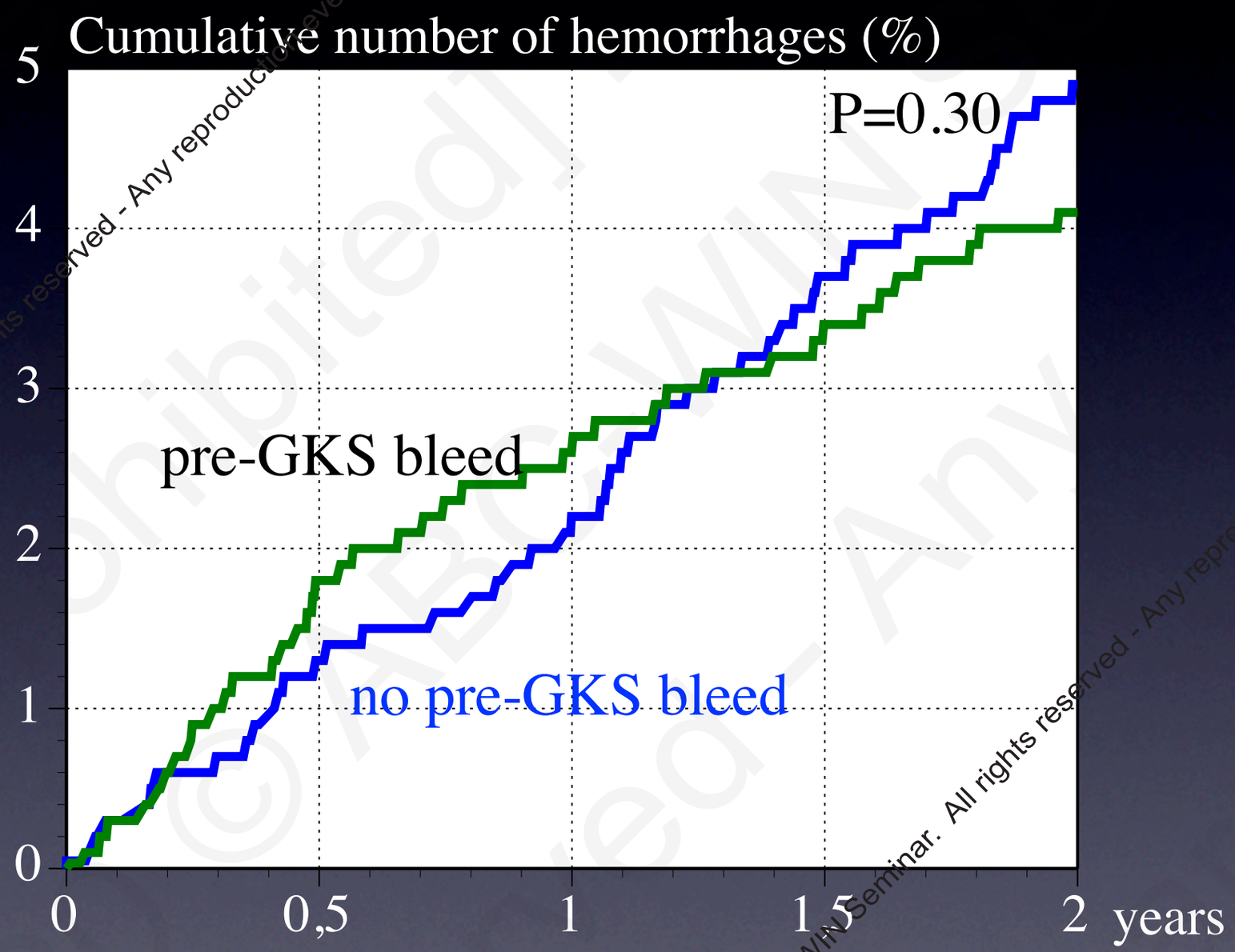
Why are central AVMs more prone for post GKS rupture?

Because of history of pre treatment hemorrhage? NO!



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Why are central AVMs more prone for post GKS rupture?

Because of AVM location?

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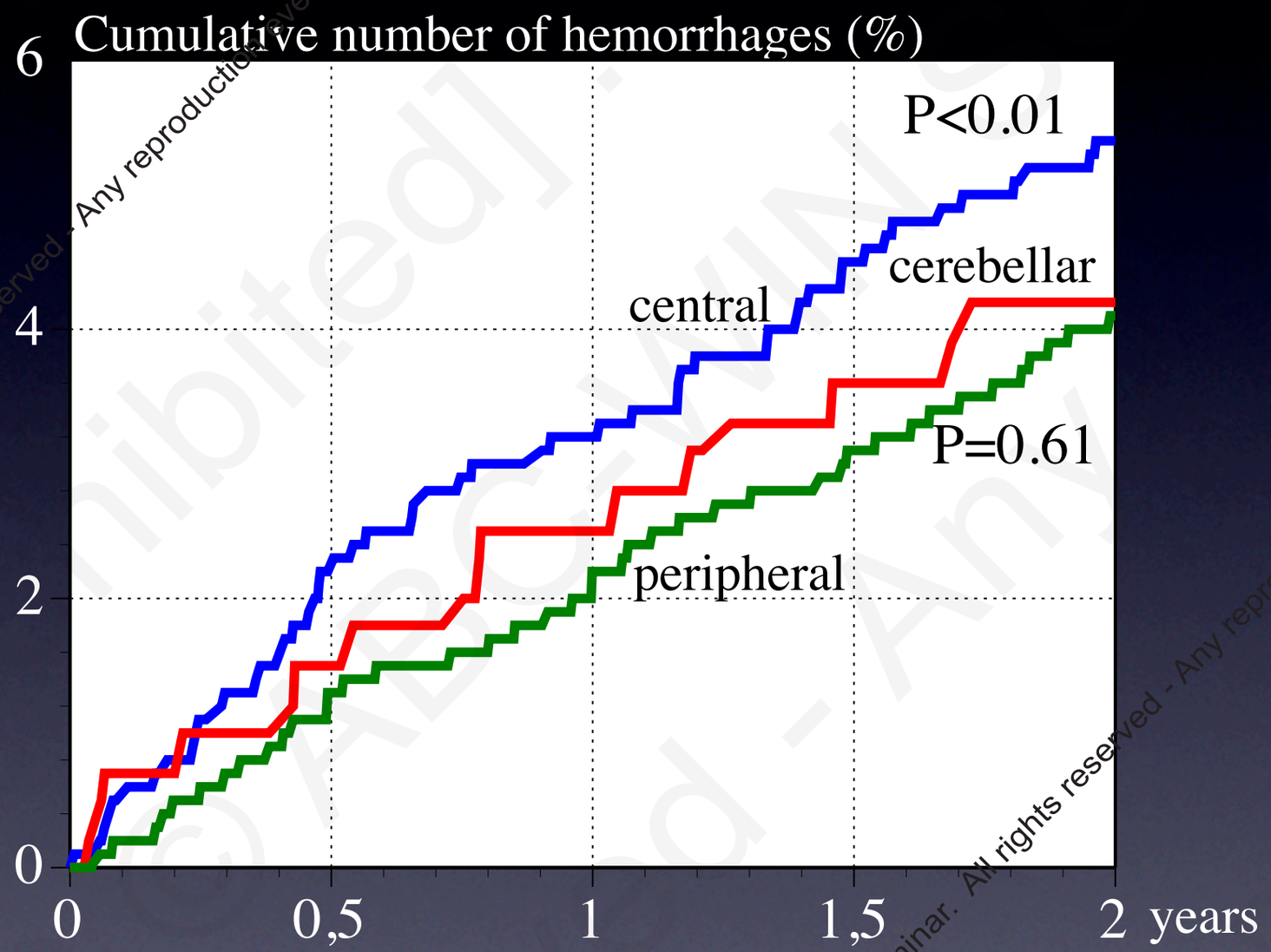
Why are central AVMs more prone for post GKS rupture?

Because of AVM location? YES!



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The findings support that:

* AVM obliteration is unrelated to AVM location.
* The risk for complications is higher for central AVMs.
* Central AVMs have a higher risk for (post GKS) hemorrhage.

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Thus, the outcome following GKS for AVMs is AVM location dependent.
Is this also true for subgroups of central AVMs?
Let us divide central AVMs in three groups:
* Brain stem/midbrain AVMs.
* Basal ganglia/thalamus AVMs.
* Other centrally located AVMs.

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The findings support that:

* AVM obliteration is unrelated to AVM location.
* The risk for complications is higher for central AVMs.
* Central AVMs have a higher risk for post GKS hemorrhage.

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GKS for central AVMs. Obliteration.

AVM location	N	volume	min dose	oblit
Basal ggl/thalamus	540	5.6 cc	19 Gy	57%
Brain stem/midbrain	302	2.6 cc	18 Gy	46%
Other central	367	4.5 cc	21 Gy	69%
Basal ggl vs. brain stem		P<0.01	P=0.13	P<0.01
Basal ganglia vs. other		P=0.25	P<0.01	P<0.01
Brain stem vs. other		P<0.01	P<0.01	P<0.01

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Are the differences caused by different doses, different AVM volumes, or different AVM locations?

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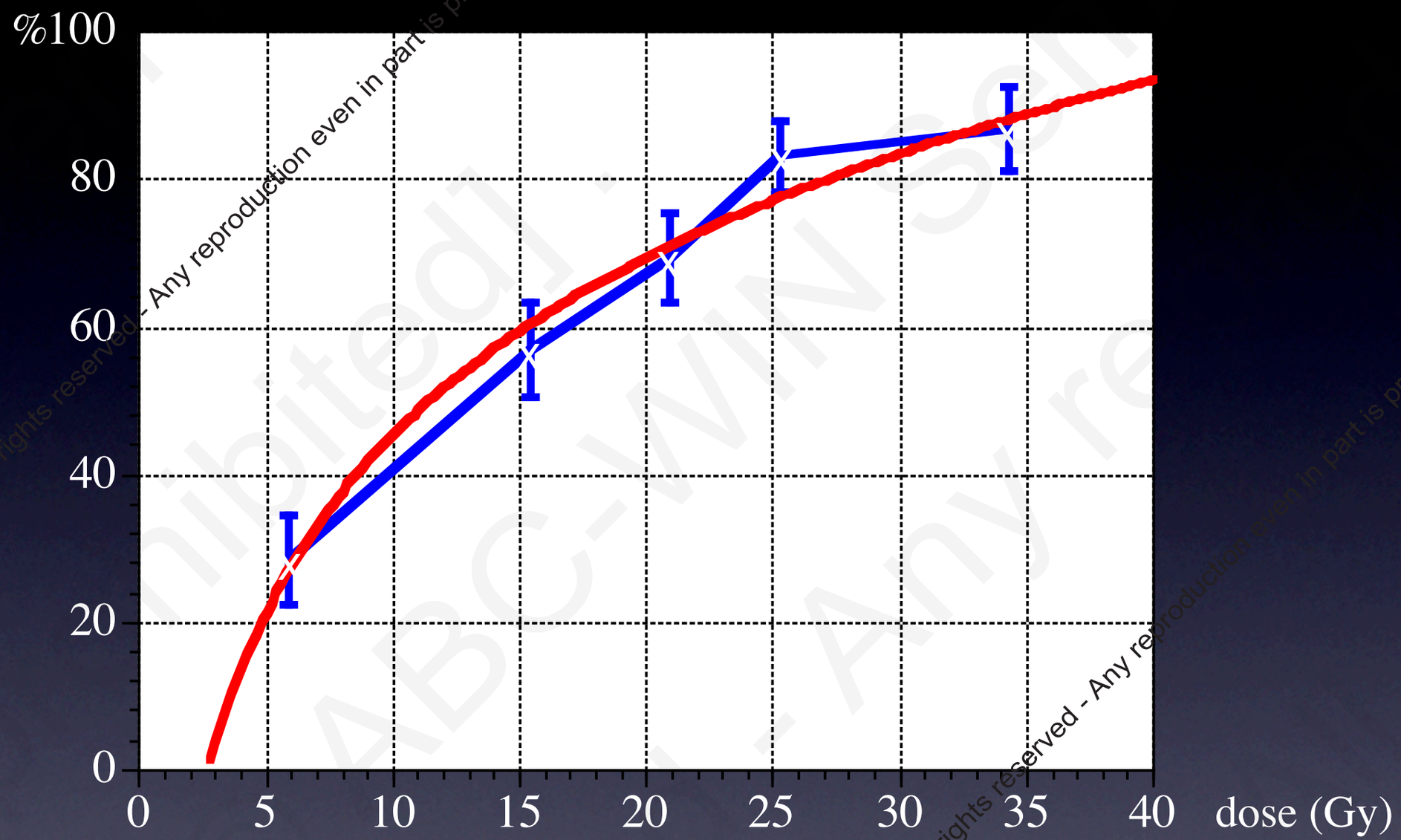
Obliteration rate versus periphery dose



logarithmic curve fit:

f(dose) = 35.68*ln(dose) - 39.66 $R^2 = 0.99$

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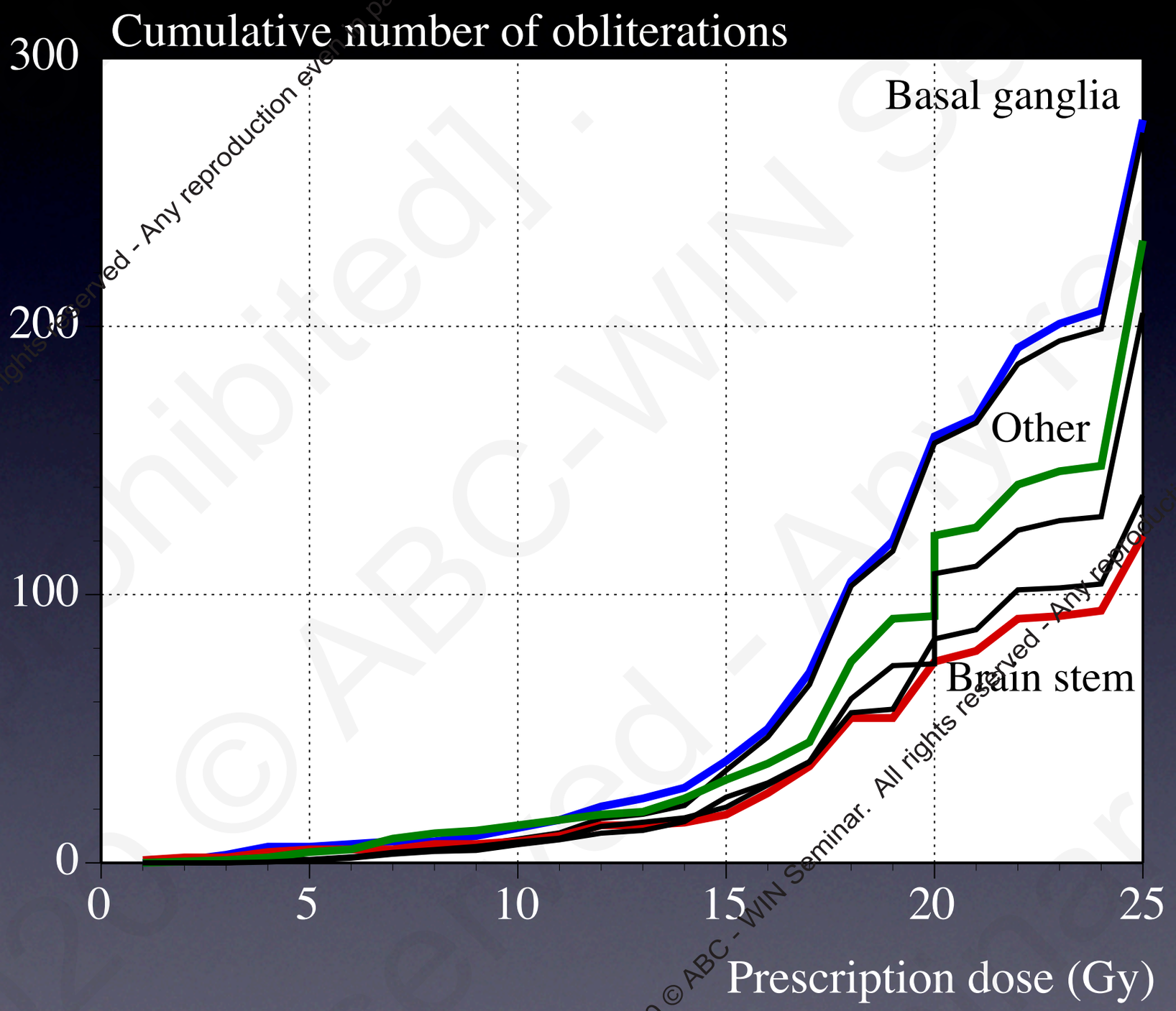
Observed vs. predicted number of obliterations.



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Conclusion obliteration:

* The prediction model is accurate also for subgroups of central AVMs.
* Obliteration is unrelated to AVM location.
* Basal ganglia AVMs respond to radiation as all other AVMs.

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The findings support that:

* AVM obliteration is unrelated to AVM location.
* The risk for complications is higher for central AVMs.
* Central AVMs have a higher risk for post GKS hemorrhage.

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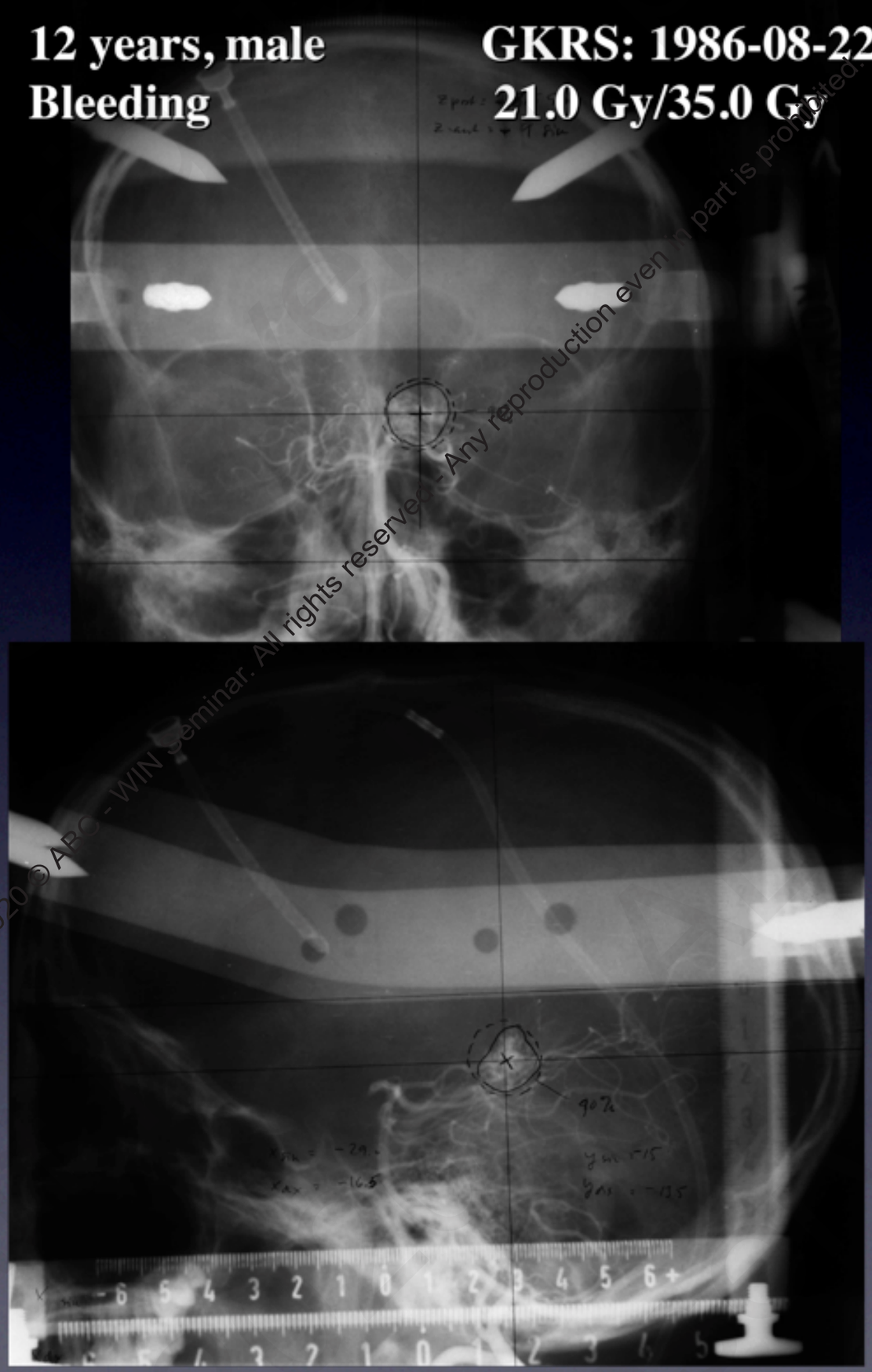
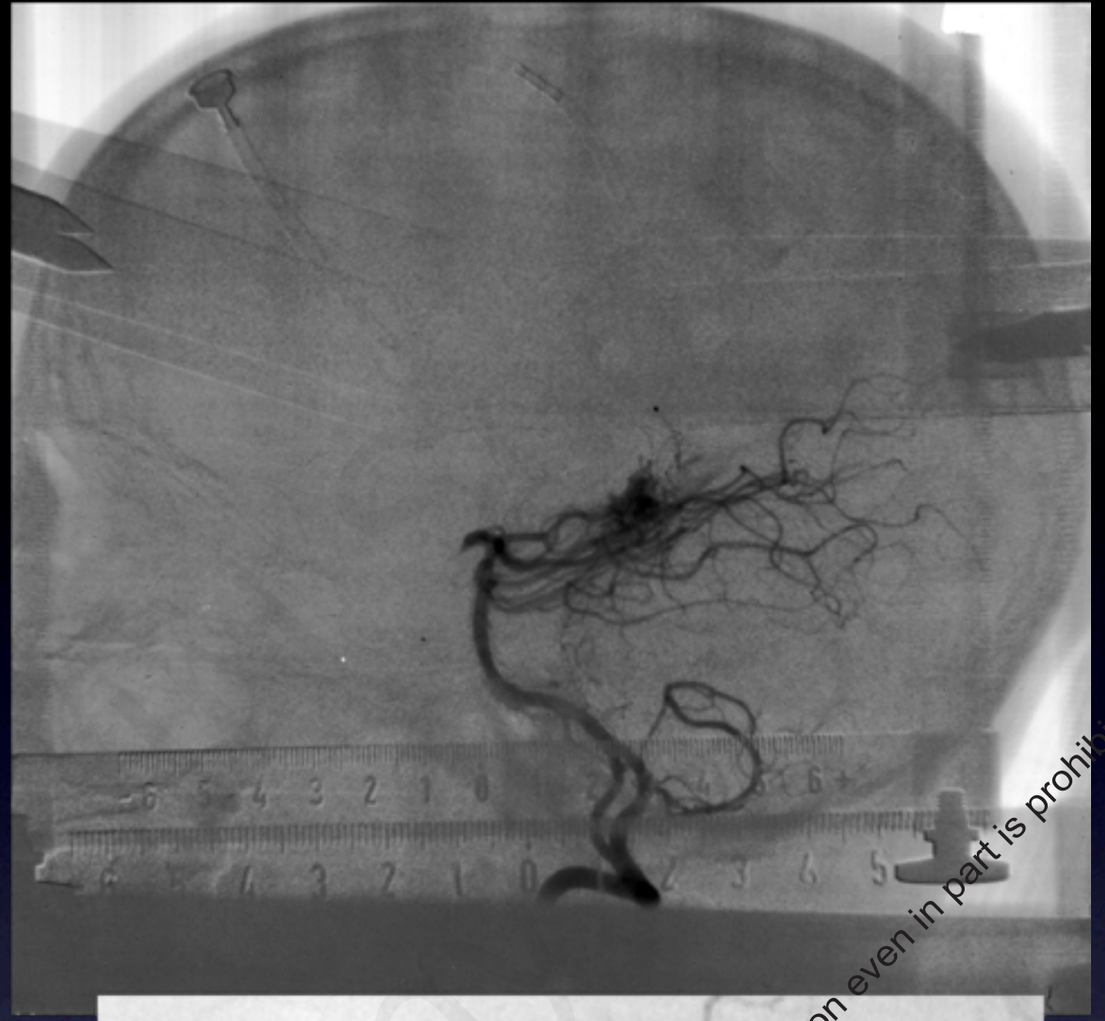
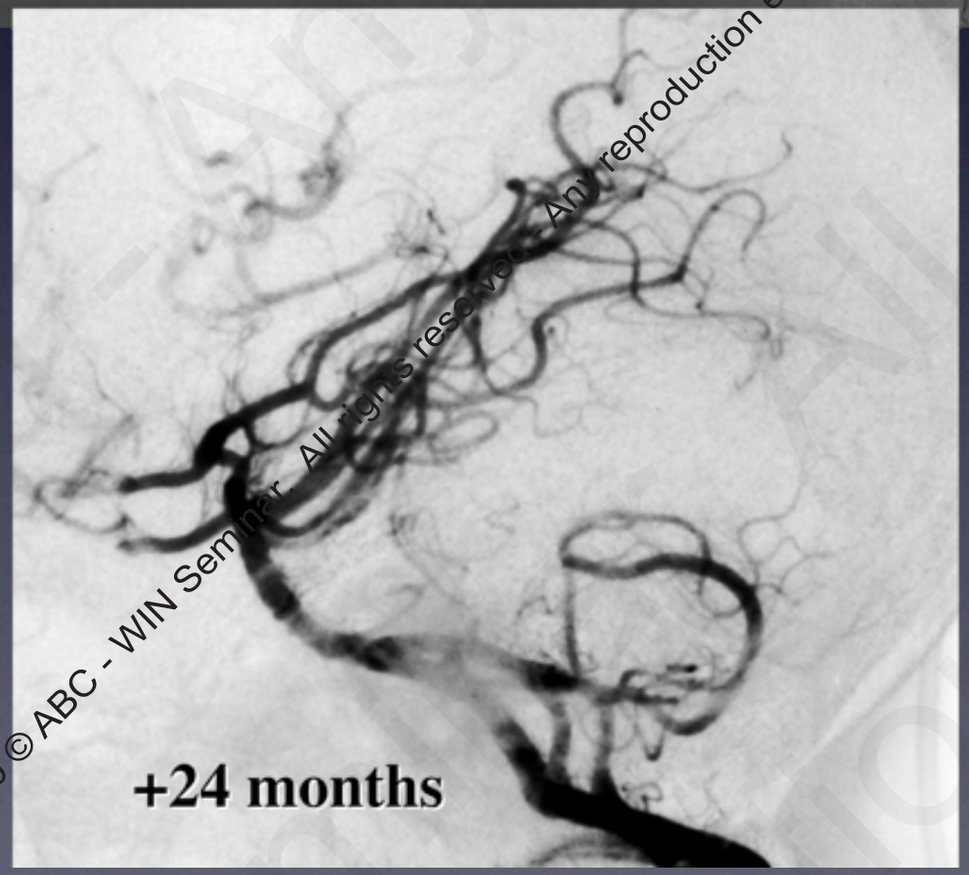
12 years, male
Bleeding

GKRS: 1986-08-22
21.0 Gy/35.0 Gy







courtesy Dr. Yamamoto

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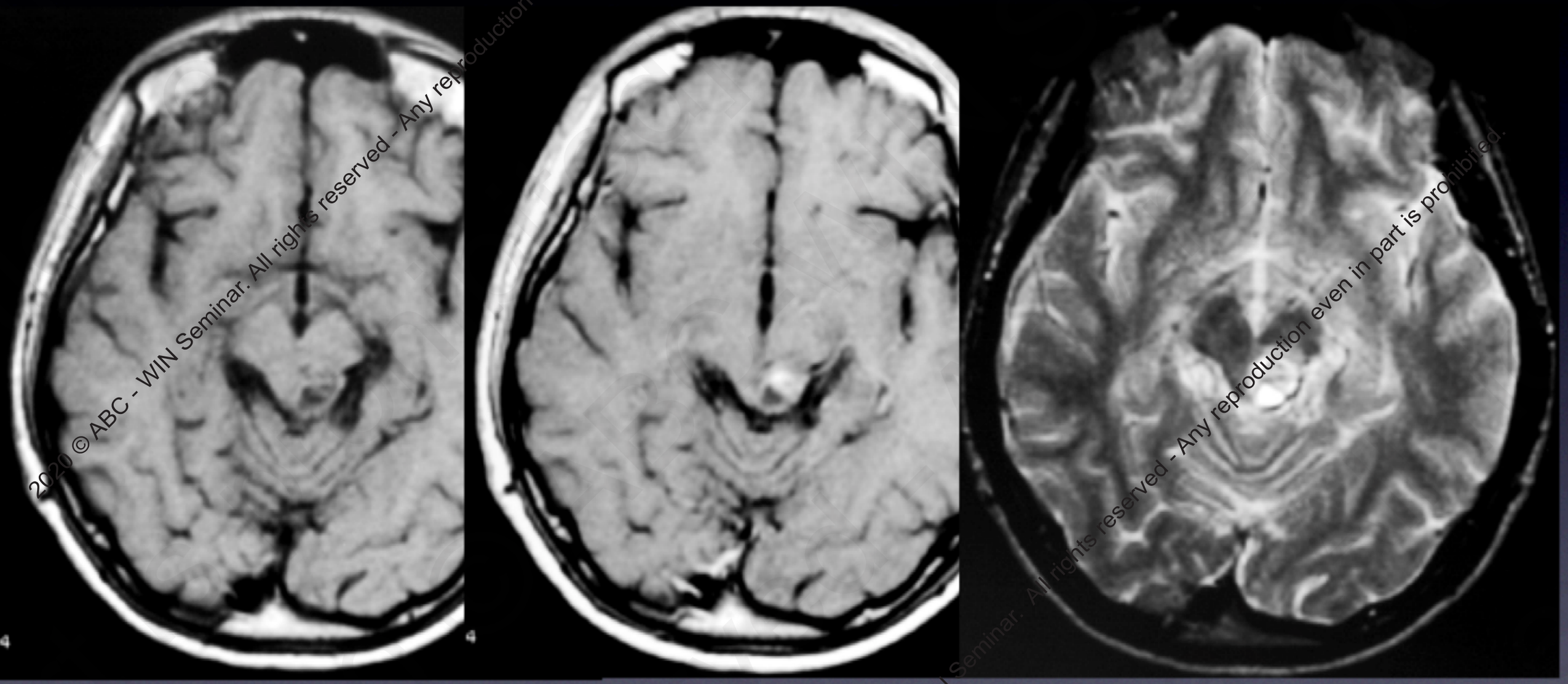
+123 months



T1 **T1-Gd** **T2**

courtesy Dr. Yamamoto

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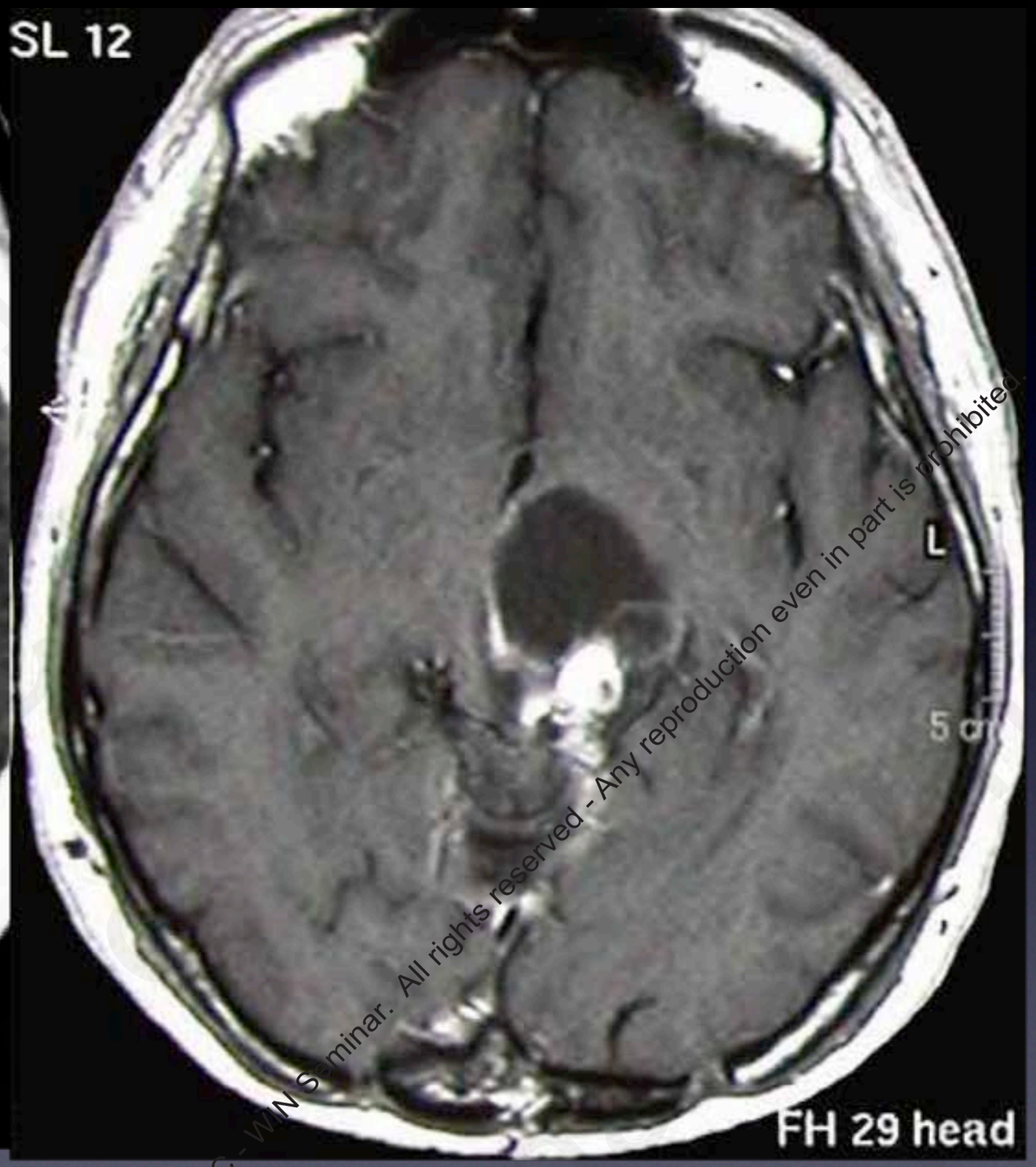
+177 months



+222 months

courtesy Dr. Yamamoto

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GKS for central AVMs. Complications.

AVM location	N	volume	min dose	complications
Basal ggl/thalamus	540	5.6 cc	19 Gy	10%
Brain stem/midbrain	302	2.6 cc	18 Gy	6%
Other central	367	4.5 cc	21 Gy	6%
Basal ggl vs. brain stem		P<0.01	P=0.13	P=0.03
Basal ganglia vs. other		P=0.25	P<0.01	P=0.03
Brain stem vs. other		P<0.01	P<0.01	P=0.87

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Are the differences caused by different doses, AVM volumes, or AVM locations?

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Factors influencing the risk for complications following Gamma Knife radiosurgery of cerebral arteriovenous malformations

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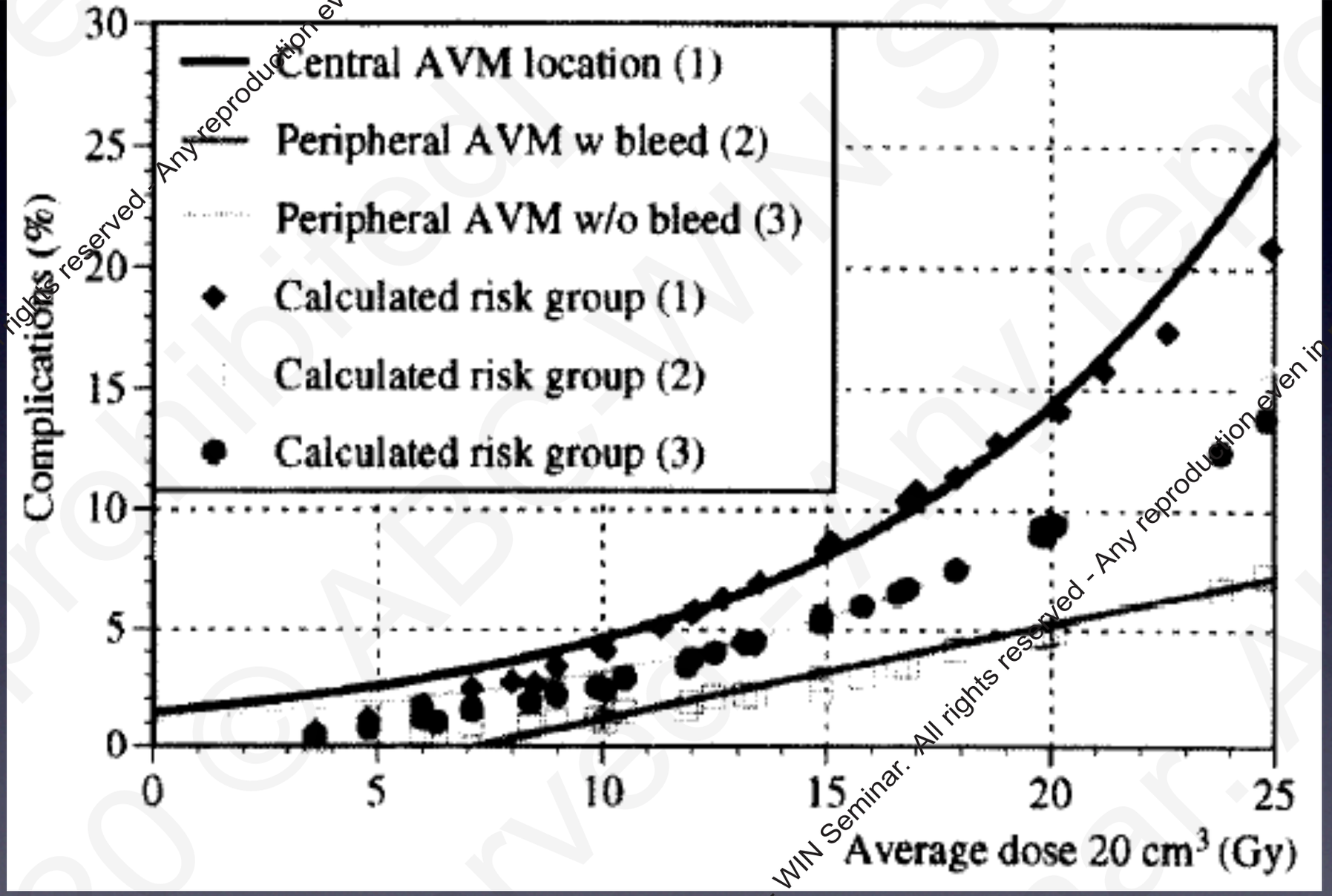

exponential curve fit:

f(dose20) = 1.446*exp(0.1114*dose20)

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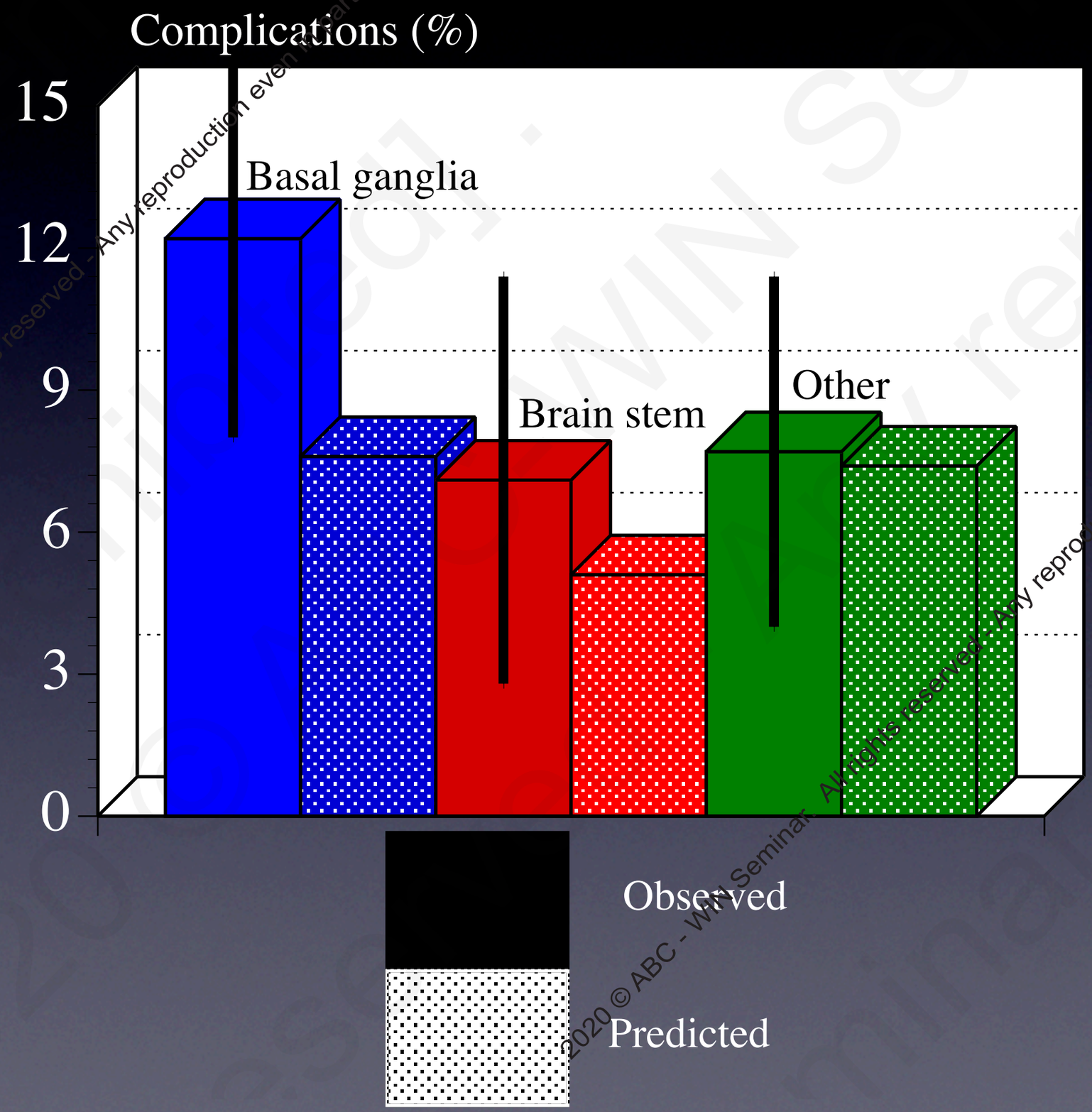
Observed vs. predicted number of obliterations.



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Conclusion complications:

* The prediction model seems to accurate predict the risk for complications for brain stem and other central AVMs.
* The prediction model seems to underestimate the risk for complications for basal ganglia/thalamic AVMs.

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GKS for central AVMs. Post treatment hemorrhages.

AVM location	N	pre GKS bleed	2 yr post GKS bleed
Basal ggl/thalamus	470	84%	5.4%
Brain stem/midbrain	243	77%	5.3%
Other central	325	89%	2.7%
Basal ggl vs. brain stem		P<0.01	P=0.99
Basal ganglia vs. other		P<0.01	P=0.07
Brain stem vs. other		P<0.01	P=0.11

No statistically significant relation between pre- and post GKS hemorrhages (P=0.18)

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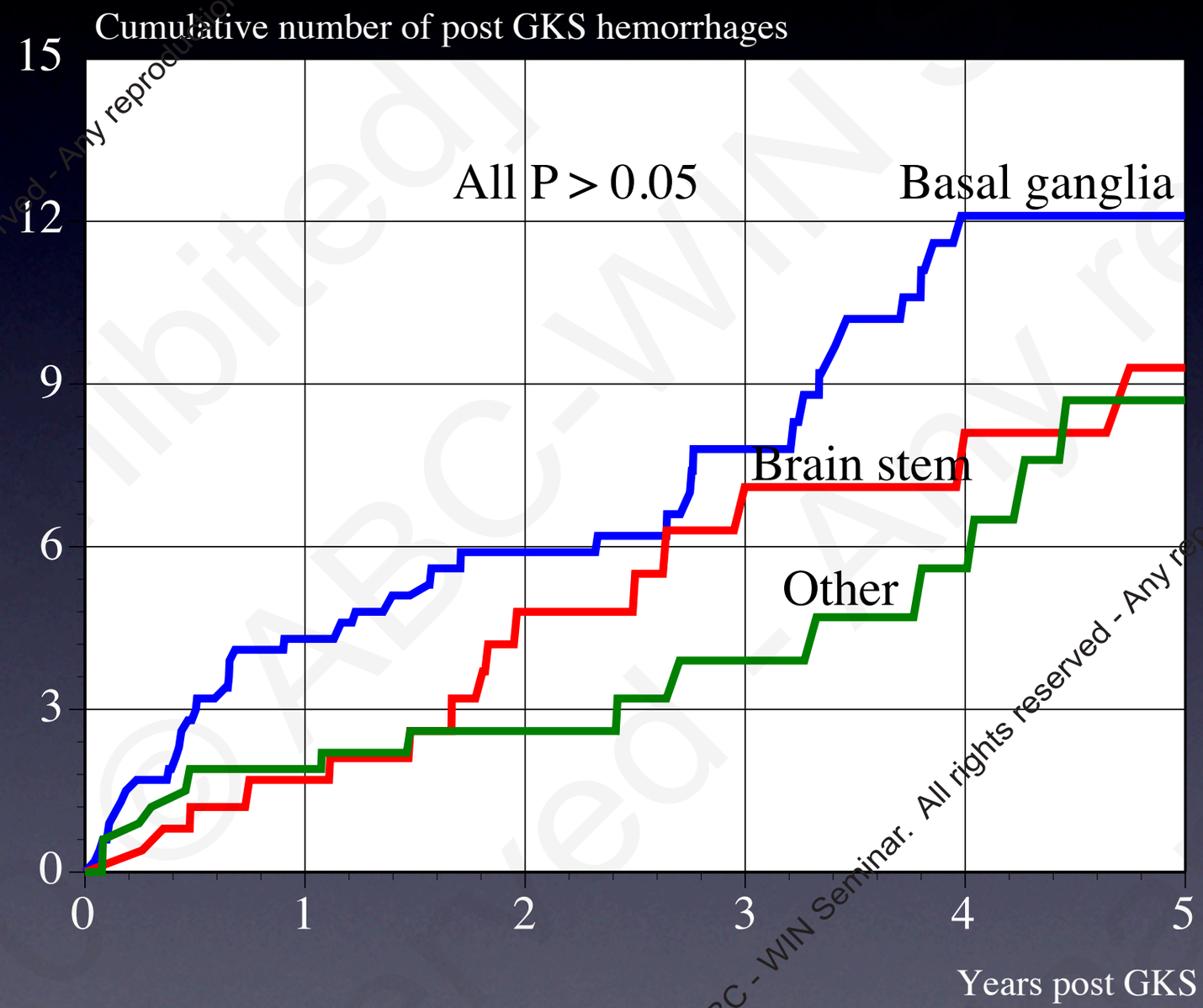
Cumulative incidence of post GKS hemorrhage:



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Conclusion post treatment hemorrhages:

* Trend that the risk of post treatment hemorrhage is higher in basal ganglia/thalamic AVMs.
* No difference between brain stem and other central AVMs.

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Conclusion basal ganglia/thalamic AVMs:

* Same probability for obliteration as AVMs in other locations.
* Much higher risk for complications than peripheral AVMs.
* Higher risk for complications than other central AVMs.
* Trend for higher post treatment hemorrhage rate?

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