

# **The 8th Meeting of the Asian Leksell Gamma Knife Society**

**Resilience**

**Program & Abstracts**



## Welcome Message

Dear colleagues and friends,

On behalf of the board members of Asian Leksell Gamma Knife Society and the Japanese Leksell Gamma Knife Society, we are delighted to announce that the 8th Asian Leksell Gamma Knife Society Meeting (ALGKS) in conjunction with the 20th Japanese society meeting will be held jointly in Kochi, Japan, from February 10-12, 2023 at Kochi Prefectural Culture Hall.

The first Gamma Knife was introduced in Japan in 1999. Gamma Knife has spread rapidly in Asia, including Japan, and treatment technology has been constantly advancing by improvement of Gamma Knife machine. With the progress of minimally invasive treatment in neurosurgery, stereotactic radiotherapy such as Gamma Knife is expected to occupy more important position in the future.

In particular, the development of the Icon has made it easier to perform fractionated irradiation, and the range of treatments that can be treated with Gamma Knife has expanded.

Fractionation for metastatic brain tumors with Gamma Knife is one of the hottest topics, but the optimal dose and optimal number of fractionation remain unclear. There are many unclear points about fractionated irradiation for benign tumors. Large AVMs are still difficult to treat.

We hope that the information on Gamma Knife will be updated by discussing the experience of experts from Asian countries on many difficult clinical issues.

Kochi prefecture is located in the south of Shikoku, one of four main islands of Japan. Ryoma Sakamoto, one of the most popular samurai in Japan, was born in Kochi. Kochi Ryoma Airport, the only airport in Kochi, is named after him. There are a lot of various tourist attractions in Kochi, and the food is delicious. We hope you will take this opportunity to enjoy the winter in Kochi as well.

Globally, the pandemic of the covid-19 is still far from being well controlled, but we look forward to meeting our Asian friends in 2023.

We sincerely look forward to your participation.

With warmest regards,



A stylized, handwritten signature in black ink, appearing to read 'T. Shuto'.

President,  
The 8th Meeting of Asian Leksell Gamma Knife Society  
Takashi Shuto, M. D.  
Vice president, Yokohama Rosai Hospital,  
Director, Department of Neurosurgery, Yokohama Rosai Hospital

## Board Members

### ◆ Board Members of Asian LGK Society

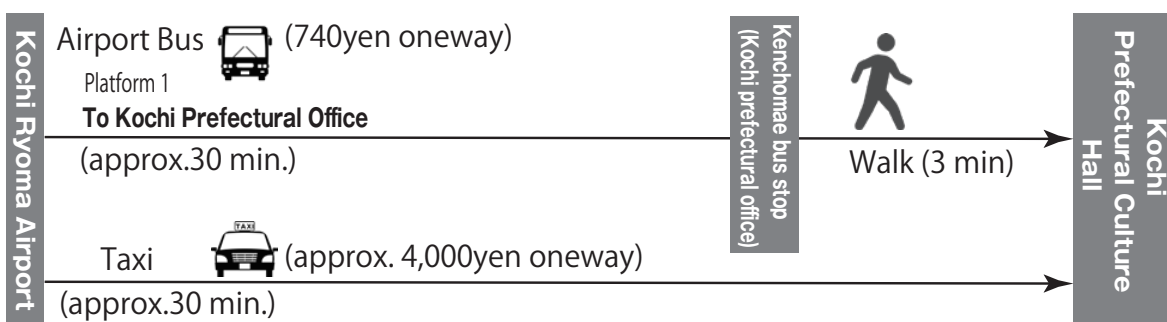
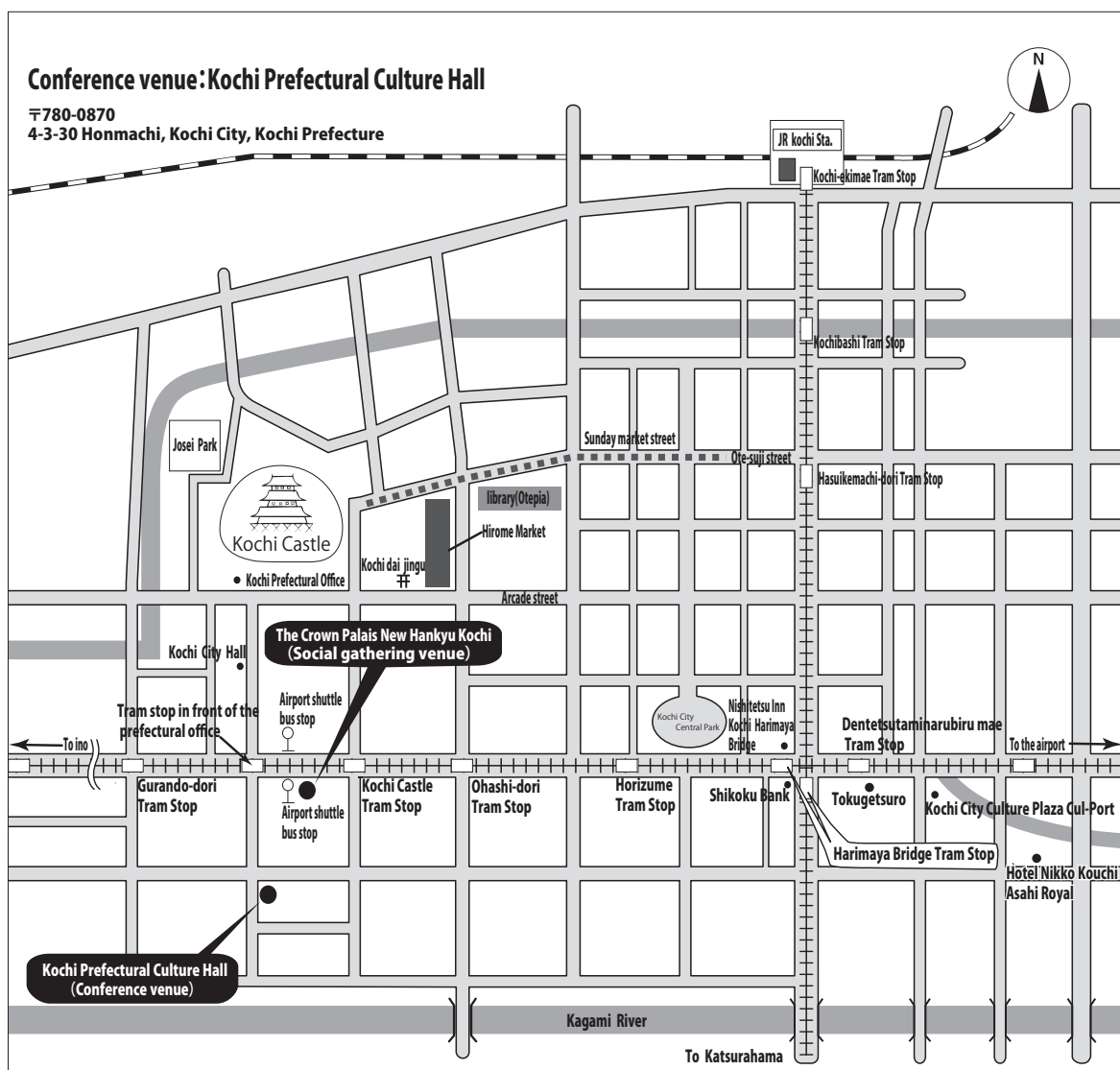
1	Wen-Yuh Chung	Veterans General Hospital-Taipei, National Yang-Ming University, Taiwan
2	Wan-Yuo Guo	Veterans General Hospital-Taipei, National Yang-Ming University, Taiwan
3	Yoshiyasu Iwai	Tominaga Hospital, Japan
4	Hidefumi Jokura	Jiro Suzuki Memorial Gamma House, Furukawa Seiryō Hospital, Japan
5	Bengt Karlsson	National University Hospital, Singapore
6	Jung-Il Lee	Samsung Medical Center, Sungkyunkwan University School of Medicine, Korea
7	Sun-Ha Paek	Seoul National University, Korea
8	David Hung-Chi Pan	Shuang Ho Hospital, Taiwan Medical University, Taiwan
9	Li Pan	Shanghai Gamma Knife Center, China
10	Toru Serizawa	Tsukiji Neurological Clinic, Japan
11	Takashi Shuto	Yokohama Rosai Hospital, Japan
12	Theodor S. Vesagas	The Philippine Gamma Knife Center, Cardinal Santos Medical Center, Philippines
13	Masaaki Yamamoto	Southern Tohoku Hospital, Japan
14	Chung Ping Yu	Gamma Knife Centre, Canossa Hospital, Hong Kong, Clinical Neuroscience Centre, Neurosurgery Centre, Hong Kong Sanatorium and Hospital, Hong Kong

## Past Presidents

### ◆ Succesive Presidents of Asian Leksell Gamma Knife Society

	Year	President	Venue
1st	2009	Dong Gyu Kim	Seoul, Korea
2nd	2010	Yoshihisa Kida	Nagoya, Japan
3rd	2012	David Hung-Chi Pan	Taipei, Taiwan
4th	2015	Masaaki Yamamoto	Yokohama, Japan
5th	2017	Young Jin Lim	Jeju, Korea
6th	2019	Hidefumi Jokura	Sendai, Japan
7th	2020	Wan-Yuo Guo, Wen-Yuh Chung	Taipei, Taiwan
8th	2023	Takashi Shuto	Kochi, Japan

# Access Map



## ■ By air

Domestic		
Tokyo	Haneda Airport	1h30m
Chiba	Narita Airport	1h30m
Nagoya	Nagoya komaki Airport	1h
Osaka	Itami Airport	50m
Kobe	Kobe Airport	50m
Fukuoka	Fukuoka Airport	55m

※No direct flights

※Please note it may take time to make a transfer

Foreign Countries		
Seoul		1h40m
Beijing		1h40m
Shanghai		2h35m
Taipei		3h

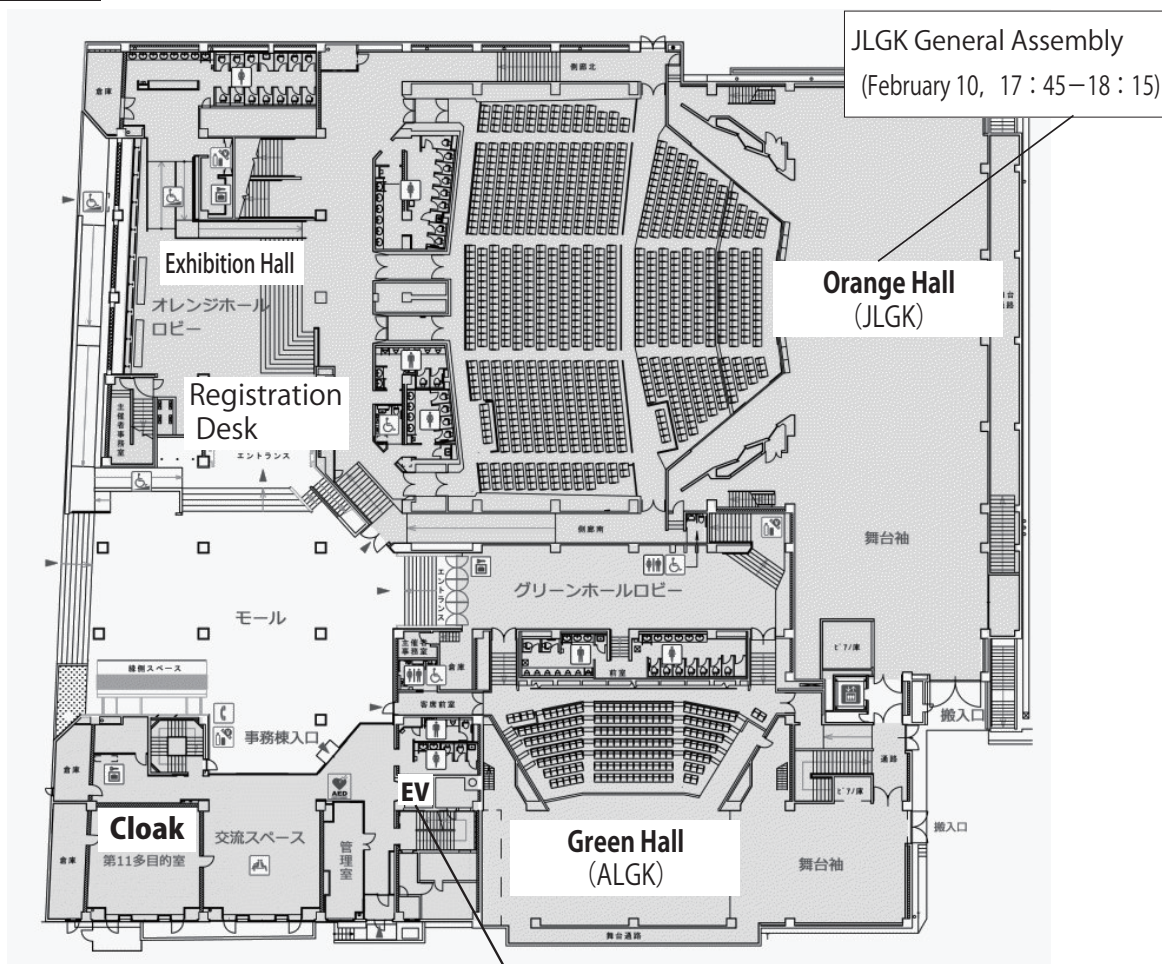
Fukuoka Airport	55m	Kochi Ryoma Airport
Narita Airport	1h30m	Kochi Ryoma Airport

# Congress Site Map

## Room Location

### Kochi Prefectural Culture Hall (1F • 4F)

**1F**



take the elevator to the 4th floor

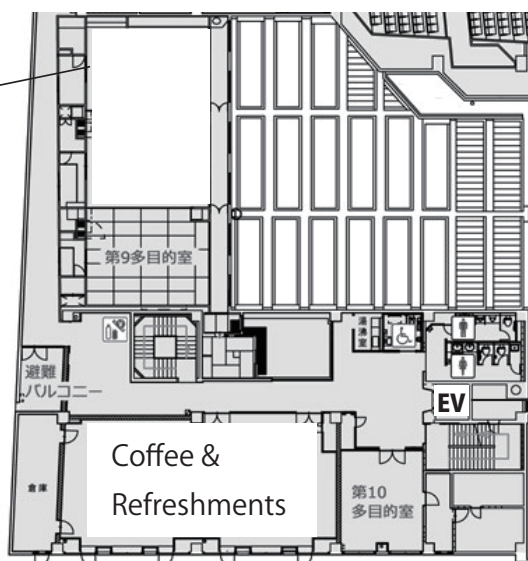
### Administration Building 4F

JLGK Board Meeting  
(February 10, 16:40-17:40)

※Different Venue

◇Get-together Party (3F banquet hall)  
(The Crown Palais New Hankyu Kochi,  
February 10, 19:00-21:00)

◇ALGK Board Meeting (3F Rose room)  
(The Crown Palais New Hankyu Kochi,  
February 11, 8:00-9:00)



## General Information

### ◆Date

February 10 (Fri) ~ 12 (Sun), 2023

### ◆Venue

Kochi Prefectural Culture Hall (Green Hall · Orange Hall )

4-3-30, Honmachi, Kochi-city, Kochi 780-0870 Japan

TEL: +81-88-824-5321

<https://kkb-hall.jp/index.html> (in Japanese only)

### ◆Official language

English

### ◆Registration Desk

Registration desk will be located at the Orange Hall lobby (1<sup>st</sup> floor).

Open hours:

February 10 (Fri) 12 : 00 ~ 18 : 00

February 11 (Sat) 9 : 15 ~ 18 : 40

February 12 (Sun) 9 : 15 ~ 10 : 40

### ◆Name Badges

A name badge will be provided to all participants at the registration desk.

The name badge is mandatory for access to all Scientific Sessions, Exhibition and Social Program during the meeting.

### ◆Program & Abstracts Book

For those who participate in ALGK, one abstracts book will be distributed to each participant at the reception. If you need more than one copy, it will be sold for 2,000JPY, but in limited number.

### ◆Registration Fee

Onsite registration: February 10 to 12, 2023

Doctor JPY 22,000

Medical staff JPY 8,000

### ◆Registration fee includes the following:

- Admission to all scientific sessions including luncheon seminar
- Program and abstracts book
- Get-together Party ※Pre-registration only

### ◆Payment Method

Registration fee can be paid by credit card only (VISA, Master, AMEX and JCB are accepted).

Cash payment is not possible for on-site registration on the day. Please prepare your credit card information and register and pay for participation on the web at the reception desk.

### ◆Congress Etiquette

Participants are advised not to photograph or video recording any sessions without the author's consent. Participants are also advised to obtain consent from authors before citing any of their work

presented at the congress.

#### ◆Wi-Fi Connection

Wi-Fi is not available in Green and Orange Hall, but is available in the following limited areas in the venue.

・ Orange Hall Lobby ・ Green Hall Lobby ・ 4F multipurpose room ※Drink Service

The ID and Password for connection will be posted in the venue.

#### ◆Luncheon Seminar

A luncheon seminar will be held on February 11. Japanese style lunch box (avoiding beef and pork) will be served. Lunch box for vegetarian (no meat, no fish, no egg) and halal options are also available, but limited in number.

#### ◆Drink Service

Free coffee and refreshments will be available in multi-purpose room 6 (4<sup>th</sup> floor), Administration Building.

#### ◆Cloak

Cloak is available at multi-purpose room 11, 1F, Administration Building.

#### ◆Get-together Party (included in the registration fee)

It will be a sit-down party in order to prevent infection. Pre-registration in advance is necessary to attend the party. Please note that we will check your name tag at the reception.

Date & Time: February 10 (Fri) 19 : 00 ~ 21 : 00

Place: The Crown Palais New Hankyu Kochi 3F: Flower Room

Attire: Casual and informal

#### ◆ALGK Board Meeting

Date & Time: February 11 (Sat) 8 : 00 ~ 9 : 00

Place: Rose room, 3F, The Crown Palais New Hankyu Kochi

#### ◆Secretariat of ALGKS2023

Medical corporation Jikyukai Mominoki Hospital

6-1 Tsukanohara, Kochi-shi, Kochi-ken, 780-0952, Japan

E-mail: asia@ajlgks2023.com



# For Moderators & Speakers

## Instructions for Moderators

1. Please come to the room 15 minutes before your session starts. The seat for next moderator will be in the front row on the right.
2. Please proceed with the session per the following time allocation.

## Instructions for Oral Presentation

1. The time allotted for each presentation is scheduled as follows:
  - Educational Lectures ..... Presentation 60 min incl. Q&A
  - Symposia ..... Presentation 10 min + Q&A 3 min.
  - General Sessions ..... Presentation 8 min + Q&A 2 min

\*You will be notified by a yellow lamp 1 minute before the end of your oral presentation, and will be notified by a red lamp of the end time.
2. All presentations will be done on PC.
3. Please bring your PC or PC data to the PC Preview Desk at least 30 minutes prior to your presentation to register and submit it to test the connection and view your file.  
The PC Preview Desk will be located and be open as follows:

Date	Time	Place
February 10 (Fri)	12 : 00 ~ 17 : 30	Lobby, 1F, Orange Hall
February 11 (Sat)	9 : 15 ~ 17 : 30	
February 12 (Sun)	9 : 15 ~ 10 : 40	

4. Please come to the room 15 minutes before your session starts. The seat for next speaker will be in the front row on the left.
5. Please use the mouse and keyboard on the podium for your presentation. You are required to handle your data yourself, using the mouse or keyboard connected to the PC.
6. The image resolution is Full HD (1920 x 1080 pixels). If it is larger than this size, the edges of the slide will be cut off, so please adjust the slide show settings to Full HD.
7. Sound functions will not be available.
8. Presenter View functions will not be available.
9. If your presentation includes movies and if you use Macintosh, you are advised to bring your own laptop.

## [To bring and submit your presentation data (for Windows only)]

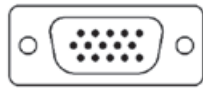
- Please bring your presentation data (PPT). The only PC media that will be available is USB flash drive.
- Any media other than above cannot be used.  
We will prepare a PC with Windows 10 installed at the presentation venue. Application software must be PowerPoint 2019 for Windows (playable with the latest Media Player initial codec, WMV format recommended).
- Your presentation data and pictures and graphs linked thereto are to be saved in the same folder.
- Standard PC fonts for Windows should be used, such as Century and Times New Roman.
- Please scan your presentation data for viruses and check if the data works properly in other PCs beforehand.
- The copied data for your presentation will be deleted by the secretariat after the congress.

[To bring your own laptop (PC or Macintosh)]

- Please bring a backup data (PPT) in CD-R or USB memory stick.
- Please make sure to bring an AC adaptor (standard 2 -pin type).

The connector shape of the cable to be connected at the venue is Mini D-sub 15pin or HDMI. Please prepare a computer that fits this shape, or bring a connector that converts to this shape.

Mini D-sub 15pin



HDMI



- Please cancel your password, screen saver and power saving settings in advance.
- Please pick up your laptop at the PC operators' desk in the presentation room after your presentation.

# Program

## Day 1: Friday, February 10

	Green Hall ALGK	Orange Hall JLGK	4F Multipurpose room
09:00			
10:00			
11:00			
12:00	12:00 <b>Reception</b>	12:00 <b>Reception</b>	
13:00	12:55 <b>Opening Ceremony</b>	12:55 <b>Opening Ceremony</b>	
	13:10 <b>General Session 1</b> Benign tumors Moderators : Motohiro Hayashi Hung-Chuan Pan	13:00 <b>Educational Lecture 1 (JLGK)</b> Moderator : Akihito Moriki Speaker : Katsunobu Aoyama	
14:00	14:30 <b>ALGK/JLGK Symposium 1</b> SRT for metastatic brain tumors - optimal number of fraction and dose Moderators : Yoshiyasu Iwai Se-Hyuk Kim	14:00 <b>Japanese General Session 1 (JLGK)</b> Nursing, team medicine Moderators : Koichi Hasui Kaori Toda	
15:00	16:00 <b>ALGK/JLGK joint announcement</b>		
16:00	16:15 <b>General Session 2</b> Vascular disorders 1 Moderator : Chain-Fa-Su	16:15 <b>General Session 3 (ALGK)</b> Functional disorders and others ※ALGK On-site Only Moderator : Jung-Il Lee	
17:00	17:05 <b>General Session 4</b> Imaging, Dose planning, and Physics Moderator : Hyun-Tai Chung	17:25	
18:00			
19:00	19:00	19:00	
20:00	<b>ALGK/JLGK Get-together Party</b> (The Crown Palace New Hankyu Kochi)	<b>ALGK/JLGK Get-together Party</b> (The Crown Palace New Hankyu Kochi)	
21:00	21:00	21:00	

Drink Service

ALGK Program

# Program

## Day 2: Saturday, February 11

	Green Hall ALGK	Orange Hall JLGK	4F Multipurpose room
08:00			
09:00			
9:15	<b>Reception</b>	9:15 <b>Reception</b>	
9:45	<b>Elekta Seminar</b> Moderator : Bengt Karlsson Speaker : James McInerney Sponsored by Elekta K.K.	9:45 <b>Cultural Lecture (JLGK)</b> Moderator : Masaaki Yamamoto Speaker : Makoto Arimitsu (Current Topics) Koreaki Mori	Sponsored by Novartis Pharma K.K.
10:45		10:45	<b>Drink Service</b>
10:55	<b>Educational Lecture 1</b> Moderator : Hidefumi Jokura Speaker : Bengt Karlsson	10:55 <b>Japanese General Session 2 (JLGK)</b> Metastatic brain tumors 1 Moderators : Shoji Yomo, Tatsuo Hirai	
11:55		11:55	
12:05	<b>ALGK/JLGK Luncheon Seminar</b> Moderator : Takashi Shuto Speaker : Motohiro Hayashi Sponsored by Brainlab K.K.		
13:05			
13:15	<b>ALGK/JLGK Symposium 2</b> Gamma Knife radiosurgery for large AVM Moderators : Hisae Mori Wan-Yuo Guo		
14:20		Moderators : Atsuya Akabane Maheep Singh Gaur	<b>Metastatic brain tumors 1</b> Moderator : Yoshiyasu Iwai
14:30	<b>General Session 5</b> Vascular disorders 2	14:30 <b>Japanese General Session 3 (JLGK)</b>	
15:10		15:10	<b>Light meals of Kochi</b>
15:20	<b>General Session 6</b> Metastatic brain tumors 1 Moderators : Masatoshi Hasegawa Young Seok Park	15:20 <b>Educational Lecture 2 (JLGK)</b> Moderator : Akihito Moriki Speaker : Takeki Sugimoto	
16:20		16:20	
16:30	<b>General Session 7</b> Metastatic brain tumors 2 Moderators : Shoji Yomo Theodor S. Vesagas	16:30 <b>Japanese General Session 4 (JLGK)</b> Benign tumors and other malignant tumors Moderators : Yoshinori Higuchi, Kyoko Aoyagi	
17:30		17:30	
17:40	<b>Educational Lecture 2</b> Moderator : Nobuhito Saito Speaker : Wan-Yuo Guo	17:40 <b>Japanese General Session 5 (JLGK)</b> AVM and others Moderators : Toshinori Hasegawa Atsuya Akabane	
18:40			
19:00			
20:00			
21:00			

# Program

## Day 3: Sunday February 12

	Green Hall ALGK	Orange Hall JLGK	4F Multipurpose room
09:00			
	9 : 15 <b>Reception</b>	9 : 15 <b>Reception</b>	
10:00	9 : 30 <b>General Session 8</b> Metastatic brain tumors 3 Moderators : Yoshinori Higuchi Huai-che Yang	9 : 30 <b>Educational Lecture 3 (JLGK)</b> Moderator : Masanori Morimoto Speaker : Toru Hirano Sponsored by AMIN Co.,Ltd.	Drink Service
11:00	10 : 35 <b>ALGK/JLGK Symposium 3</b> Long term results of Gamma Knife radiosurgery for benign lesions – efficacy and complication Moderators : Toshinori Hasegawa Wen-Yuh Chung	10 : 35 <b>Japanese General Session 6 (JLGK)</b> Icon, technology Moderators : Kazuhiro Yamanaka Kiyomi Minakuchi	
12:00	12 : 20	11 : 45 Moderators : Kazutaka Yatsushiro Szu-Hao Andrew Liu	Light meals of Kochi
	12 : 25 <b>General Session 9</b> Vascular disorders 3	12 : 25 <b>Special Symposium (JLGK)</b> Moderators : Hidefumi Jokura Akihito Moriki	
13:00	13 : 05 <b>Closing Ceremony</b>	13 : 05 <b>Closing Ceremony</b>	
14:00			
15:00			
16:00			
17:00			
18:00			
19:00			
20:00			

# 10th February, Friday

## Green Hall

### English Session

12 : 55 ~ 13 : 00    **Opening Ceremony**

13 : 10 ~ 14 : 30    **General Session 1 : Benign tumors**

Moderators : Motohiro Hayashi (Tokyo Women's Medical University, Japan)  
Hung-Chuan Pan (Taichung Veterans General Hospital, Taiwan)

**AG1-1 Long-term outcomes of Gamma Knife radiosurgery for central neurocytoma**

Hyun Joo Park

Department of Neurosurgery, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea

**AG1-2 Central neurocytoma with hemorrhage during Gamma Knife surgery: Case reports and review of the literature**

Ji-Eyon Kwon

Department of Neurosurgery, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

**AG1-3 Stereotactic radiosurgery for orbital cavernous hemangiomas: a single-center experience over a 22-year period**

You-Cong Chen

Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan  
School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan

**AG1-4 Reasonable timing to treat vestibular schwannomas with gamma knife surgery: serial observation of untreated small tumors and remnants after surgery**

Yoshinori Higuchi

Department of Neurological Surgery, Chiba University Graduate School of Medicine, Japan

**AG1-5 Gamma Knife radiosurgery treatment results for older (age of  $\geq 75$ ) patients with vestibular schwannoma**

Kyoko Aoyagi

Gamma Knife House, Chiba Cerebral and Cardiovascular Center, Japan

**AG1-6 Long-lasting transient volume expansion of sporadic vestibular schwannomas after stereotactic radiosurgery: Is it tumor progression?**

So Young Ji

Department of Neurosurgery, Seoul National University Bundang Hospital, Gyeonggi-do, S. Korea

**AG1-7 Using the deformity index of vital structures to predict outcome of patients with large vestibular schwannomas after Gamma Knife radiosurgery**

Hung-Chuan Pan

Department of Neurosurgery, Taichung Veterans General Hospital, Taichung, Taiwan

**AG1-8 Quantification of tumor response of cystic vestibular schwannoma to Gamma Knife radiosurgery by using artificial intelligence**

Chih-Ying Huang

Department of Radiology, Taipei Veterans General Hospital, Taiwan

**14 : 40 ~ 16 : 00 Symposium 1 : SRT for metastatic brain tumors – optimal number of fraction and dose**

Moderators : Yoshiyasu Iwai (Tominaga Hospital, Japan)

Se-Hyuk Kim (Ajou University School of Medicine, Korea)

**AS1-1 Results of 2-staged Gamma Knife radiosurgery for large brain metastases at Ha Noi, Viet Nam**

Nguyen Duc Lien

Department of Neurosurgery, National cancer hospital (K hospital), Ha Noi, Viet Nam.

**AS1-2 Neoadjuvant stereotactic radiosurgery for brain metastases: single-fraction and hypofractionation experience**

Cristian Udovicich

Department of Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia

**AS1-3 Hypofractionated irradiation with Gamma Knife Icon for large metastatic brain tumors**

Kazutaka Yatsushiro

Department of Neurosurgery, Fujimoto General Hospital, Japan

**AS1-4 Fractionated radiotherapy for metastatic brain tumors using mask system of Leksell Gamma Knife Icon**

Takuya Kawabe

Department of Neurosurgery, Rakusai Shimizu Hospital, Japan

**AS1-5 Interfractional change of tumor volume during fractionated stereotactic radiotherapy using gamma knife for brain metastases**

Mariko Kawashima

Gamma Knife Center, NTT Medical Center Tokyo, Japan

**AS1-6 Gamma knife radiosurgery and radiotherapy for brain metastases in non-small cell lung cancer harboring driver gene alterations**

Mariko Kawashima

Gamma Knife Center, NTT Medical Center Tokyo, Japan

**16 : 15 ~ 17 : 05 General Session 2 : Vascular disorders 1**

Moderator : Chain-Fa-Su (Buddhist Tzu-Chi Medical Center, Tzu-Chi University, Taiwan)

**AG2-1 (Keynote Lecture)**

**Brain arteriovenous malformations and dural arteriovenous fistulas: risk evaluations and radiosurgical outcome prediction**

Yong-Sin Hu

Department of Radiology, Taipei Hospital, Ministry of Health and Welfare, Taiwan

**AG2-2 Gamma Knife radiosurgery for the clival epidural-osseous dural arteriovenous fistulas**

Cheng-Chia Lee

Departments of Neurosurgery, Taipei Veterans General Hospital, Taipei, Taiwan  
School of Medicine, National Yang-Ming University, Taipei, Taiwan

**AG2-3   Radiosurgical outcome of intracranial avms planned on DSA and MRI for Gamma Knife stereotactic radiosurgery versus MRI alone**

Kanwaljeet Garg

Department of Neurosurgery, All India Institute of Medical Sciences, New Delhi, India

**17 : 10 ~ 18 : 00    General Session 4 : Imaging, Dose planning, and Physics**

Moderator : Hyun-Tai Chung (Seoul National University College of Medicine, Korea)

**AG4-1   Efficient timer errors measurements for all three collimators in Gamma Knife (GK) ICON**

Tanxia Qu

Center for Advanced Radiosurgery, NYU Langone Health, USA

Department of Radiation Oncology, NYU Langone Health, USA

**AG4-2   Use an electrometer's time-series data logger function in Gamma Knife ICON QA**

Tanxia Qu

Center for Advanced Radiosurgery, NYU Langone Health, USA

Department of Radiation Oncology, NYU Langone Health, USA

**AG4-3   Use an electrometer's time-series data logger function to measure a beam profile**

Tanxia Qu

Center for Advanced Radiosurgery, NYU Langone Health, USA

Department of Radiation Oncology, NYU Langone Health, USA

**AG4-4   Verification of the absorbed energy calculation procedure of the Leksell Gamma Plan**

Hyun-Tai Chung

Department of Medical Device Development, Seoul National University College of Medicine, Seoul, Korea

Department of Neurosurgery, Seoul National University Hospital, Seoul, Korea

**AG4-5   Error analysis of probe measurements in extend treatment procedures**

Eliseo Dela Cruz, Jr

Philippine Gamma Knife Center, Cardinal Santos Medical Center, San Juan City, Metro Manila, Philippines



10th February, Friday

Orange Hall

English Session

16 : 15 ~ 17 : 25    **General Session 3 : Functional disorders and others**

Moderator : Jung-Il Lee (Samsung Medical Center, Sungkyunkwan University School of Medicine, Korea)

**AG3-1    Usefulness of Elements workstation (Brainlab) in stereotactic radiosurgery/stereotactic radiotherapy treatment planning**

Yoshimasa Mori  
Center for Advanced IGRT, Shin-Yurigaoka General Hospital, Japan

**AG3-2    Long term results of Gamma knife radiosurgery for essential trigeminal neuralgia: final clinical evaluation of the role and needs according to more than 100 patients with at least 10 years follow up**

Motohiro Hayashi  
Section of Stereotactic Radiosurgery, Department of Neurosurgery, Tokyo Women's Medical University, Japan

**AG3-3    Outcome of Gamma Knife thalamotomy and biologically effective dose (BED)**

Jung-Il Lee  
Department of Neurosurgery, Samsung Medical Center, Sungkyukwan Univerity School of Medicine, Korea

**AG3-4    Dynamic radiation-induced imaging changes more than 20 years following Gamma Knife surgery**

Ai Peng Tan  
Department of Radiology, National University Hospital, Singapore

**AG3-5    Adverse radiation effects (ARE): The major challenging complication after stereotactic radiosurgery on intracranial lesions**

Szu-Hao Andrew Liu  
Gamma knife center and Department of Neurosurgery, Kaohsiung Veterans General Hospital, Taiwan

**AG3-6    Ventralis oralis anterior (Voa) deep brain stimulation plus Gamma Knife thalamotomy in an elderly patient with essential tremor**

Young Seok Park  
Department of Neurosurgery, Gamma Knife Icon Center, Chungbuk National University Hospital, Cheongju, Republic of Korea  
Department of Medical Neuroscience, College of Medicine, Chungbuk National University, Cheongju, Republic of Korea  
Department of Neurosurgery, College of Medicine, Chungbuk National University, Cheongju, Republic of Korea

**AG3-7    Gamma knife radiosurgery multisession providing long term tumor control of skull base meningioma**

Abdul Sattar M Hashim  
Department of Neurosurgery, Neurospinal and Cancer Care Institute, Pakistan

# 11th February, Saturday

## Green Hall

### English Session

9 : 45 ~ 10 : 45    **Elekta Seminar**

**【Sponsored by Elekta Co.,Ltd.】**

Moderator : Bengt Karlsson (National University Hospital, Singapore)

Speaker : James McInerney

(Professor of Neurosurgery, Neurosurgical Residency Program Director, Director of Stereotactic and Functional Neurosurgery Fellowship)

Neurosurgical Director, Penn State Hershey Gamma Knife Center, Department of Neurosurgery, Penn State Hershey Medical Center (USA))

10 : 55 ~ 11 : 55    **Educational Lecture 1**

Moderator : Hidefumi Jokura (Jiro Suzuki Memorial Gamma House, Furukawa Seiryō Hospital, Japan)

**Factors related to the risk for hemorrhage following GKS – which are treatment and which are natural course related?**

Speaker : Bengt Karlsson

(National University Hospital, Singapore)

12 : 05 ~ 13 : 05    **ALGK/JLGK Luncheon Seminar**

Sponsored by Brainlab K.K.

Moderator : Takashi Shuto (Yokohama Rosai Hospital, Japan)

**Treatment strategy and clinical results of Gamma Knife stereotactic radiosurgery for high grade pediatric arteriovenous malformation: Utility and the role of Brainlab “Vascular ELEMENTS” software associated with modern Gamma knife system (Icon)**

Speaker : Motohiro Hayashi

(Section of Stereotactic Radiosurgery, Department of Neurosurgery, Tokyo Women's Medical University, Japan)

13 : 15 ~ 14 : 20    **Symposium 2 : Gamma Knife radiosurgery for large AVM**

Moderators : Hisae Mori (National Cerebral and Cardiovascular Center Hospital, Japan)

Wan-Yuo Guo

(Veterans General Hospital-Taipei, National Yang-Ming University, Taiwan)

**AS2-1    The role of gamma knife surgery in the treatment of high-grade ruptured cerebral AVMs**

Hisae Mori

Department of Neurosurgery, National Cerebral and Cardiovascular Center Hospital, Japan

- AS2-2 Change of therapeutic strategies with GKS and other interventional therapies for unruptured brain arteriovenous malformation after the publication of the ARUBA trial  
Taichi Ikedo  
Department of Neurosurgery, National Cerebral and Cardiovascular Center, Japan
- AS2-3 The irradiated brain volume within 12 Gy is a predictor for radiation-induced changes after stereotactic radiosurgery in patients with unruptured cerebral arteriovenous malformations  
Huai-Che Yang  
Institute of Brain Science, National Yang-Ming Chiao Tung University, Taipei, Taiwan  
School of Medicine, National Yang-Ming Chiao Tung University, Taipei, Taiwan  
Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan
- AS2-4 Efficacy of embolization before stereotactic radiosurgery for brain arteriovenous malformations  
Saori Kubota  
Department of Neurological Surgery, Chiba University, Japan
- AS2-5 Against controversy: Long-term outcomes of gamma knife radiosurgery for non-hemorrhagic large AVM based on the over 1,000 cases in 30 years at our institution  
Yuki Shinya  
Department of Neurosurgery, The University of Tokyo Hospital, Japan

14 : 30 ~ 15 : 10    **General Session 5 : Vascular disorders 2**

Moderators : Atsuya Akabane (NTT Medical Center Tokyo, Japan)  
Maheep Singh Gaur (Vimhans Hospital New Delhi, India)

- AG5-1 Hemorrhage risk of unruptured brain arteriovenous malformation after Gamma Knife radiosurgery: Significance of vascular compactness  
Po-Wei Huang  
Department of Radiation Oncology, Shuang Ho Hospital, Taipei Medical University, Taiwan
- AG5-2 Gamma Knife radiosurgery for brain arteriovenous malformations: a 15-year single center experience in Southern Vietnam  
Binh Thanh Nguyen  
Department of Neurosurgery, Cho Ray Hospital, Ho Chi Minh City, Vietnam
- AG5-3 Comparison of the outcomes after Gamma Knife radiosurgery for arteriovenous malformations in pediatric and adult patients  
Jun Kawagishi  
Jiro Suzuki Memorial Gamma House, Furukawa Seiryō Hospital, Japan
- AG5-4 A case of spontaneous obliteration of medium-sized unruptured cerebral arteriovenous malformation accompanied by reduced activity of protein S  
Atsuya Akabane  
Gamma Knife Center, NTT Medical Center Tokyo, Japan

Moderators : Masatoshi Hasegawa (Hidaka Hospital, Japan)  
Young Seok Park (Chungbuk National University, Korea)

- AG6-1** Improved prognosis for NSCLC patients with wildtype/mutant EGFR and brain metastases following stereotactic radiosurgery and immune/targeted therapy  
Ai Seon Kuan  
Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan
- AG6-2** Can we alleviate the radiation treatment for brain metastasis in the lung cancer patient with EGFR mutation in the era of targeted therapy?  
Guan-Ying Chiou  
Neurosurgery, Department of Surgery, Fu Jen Catholic University Hospital, New Taipei City, Taiwan
- AG6-3** VEGFR-TKI treatment for radiation-induced brain injury after gamma knife radiosurgery for brain metastases from renal cell carcinomas  
Ryuichi Noda  
Gamma Knife Center, NTT Medical Center Tokyo, Japan  
Department of Neurosurgery, NTT Medical Center Tokyo, Japan
- AG6-4** Effectiveness of immune checkpoint inhibitors in combination with stereotactic radiosurgery for patients with brain metastases from lung cancer: a propensity score-matched analysis  
Shoji Yomo  
Division of Radiation Oncology, Aizawa Comprehensive Cancer Center, Aizawa Hospital, Japan
- AG6-5** Gamma Knife radiosurgery for surgical cavity of brain metastases: factor analysis and gene consideration  
Huang Yi-Han  
Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan
- AG6-6** Gamma knife radiosurgery for metastatic brain tumors from ovarian cancer (JLGK1801)  
Shigeo Matsunaga  
Department of Neurosurgery and Stereotactic Radiotherapy Center, Yokohama Rosai Hospital, Japan
- AG6-7** Volume prediction for large brain metastases after hypofractionated gamma knife radiosurgery through artificial neural network  
Hyeong Cheol Moon  
Department of Neurosurgery, Gamma Knife Icon Center, Chungbuk National University Hospital, Cheongju, Republic of Korea

16 : 30 ~ 17 : 30    **General Session 7 : Metastatic brain tumors 2**

Moderators : Shoji Yomo (Aizawa Hospital, Japan)

Theodor S. Vesagas (The Philippine Gamma Knife Center, Cardinal Santos Medical Center, Philippines)

**AG7-1    Natural history of lung squamous cell brain metastases in patients treated with radiosurgery: a thirty-year experience at a Tertiary Medical Center**

Yu-Chi Chen

Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan

**AG7-2    withdrawn**

**AG7-3    Large cystic brain metastases are treatable without drainage by hypofractionated or staged radiosurgery**

Takeshi Kondoh

Department of Neurosurgery, Shinsuma General Hospital, Japan

**AG7-4    Fractionated Gamma Knife radiosurgery after cyst aspiration for large cystic brain metastases: case series and literature review**

Ryuichi Noda

Gamma Knife Center, NTT Medical Center Tokyo, Japan

Department of Neurosurgery, NTT Medical Center Tokyo, Japan

**AG7-5    Usefulness of Gamma Knife stereotactic radiotherapy for repeat brain metastasis in the choroid plexus from renal cell carcinoma: a case report**

Kazunori Koyama

Gamma Knife Center, Okuma Hospital, Japan

**AG7-6    Gamma Knife radiosurgery: A safe and effective treatment for brain metastases in pregnancy**

Beehong Soon

Neurosurgery Unit, Department of Surgery, Faculty of Medicine, National University of Malaysia, Kuala Lumpur, Malaysia

17 : 40 ~ 18 : 40    **Educational Lecture 2**

Moderator : Nobuhito Saito (The University of Tokyo Hospital, Japan)

**Brain Metastasis: AI Assisted Detection and Beyond**

Speaker : Wan-Yuo Guo

(Department of Radiology, Taipei Veterans General Hospital, Taiwan

Taiwan AI Labs, Taipei, Taiwan

China Medical University Hospital, Taichung, Taiwan)

# 12th February, Sunday

## Green Hall

### English Session

#### 9 : 30 ~ 10 : 30 General Session 8 : Metastatic brain tumors 3

Moderators : Yoshinori Higuchi (Chiba University Graduate School of Medicine, Japan)  
Huai-che Yang (Taipei Veterans General Hospital, Taiwan)

- AG8-1** Gamma Knife Surgery for twenty or more brain metastases - a pilot and feasibility study  
Jiani Sherry Liu  
Department of Surgery, Division of Neurosurgery, National University Hospital, Singapore
- AG8-2** Multi-session radiosurgery for numerous small brain metastases  
Yasuhiro Matsushita  
Gamma Knife Center, Okuma Hospital, Japan
- AG8-3** Leukoencephalopathy in patients with brain metastases who received radiosurgery with or without whole brain radiotherapy  
Chan-Wei Liu  
Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan
- AG8-4** Whole-brain radiotherapy vs. Localized radiotherapy after resection of brain metastases in the era of targeted therapy: a retrospective Study  
Se-Hyuk Kim  
Gamma Knife Center, Brain Tumor Center, Department of Neurosurgery, Ajou University Medical Center, Suwon, Korea
- AG8-5** Treatment results of post-stereotactic radiosurgical recurrence in patients with brain metastases  
Masaaki Yamamoto  
Department of Neurosurgery, Southern Tohoku Hospital, Japan  
Katsuta Hospital Mito GammaHouse, Japan
- AG8-6** A new tool for assessing risks of systemic and neurologic death in brain metastasis patients undergoing Gamma Knife radiosurgery  
Toru Serizawa  
Tokyo Gamma Unit Center, Tsukiji Neurological Clinic, Japan

#### 10 : 35 ~ 12 : 20 Symposium 3 : Long term results of Gamma Knife radiosurgery for benign lesions – efficacy and complication

Moderators : Toshinori Hasegawa (Komaki City Hospital, Japan)  
Wen-Yuh Chung (Veterans General Hospital-Taipei, National Yang-Ming University, Taiwan)

- AS3-1** Hearing preservation after planned partial resection followed by gamma knife radiosurgery for large vestibular schwannomas  
Yoshiyasu Iwai  
Department of Neurosurgery, Tominaga Hospital, Japan

- AS3-2 Gamma knife radiosurgery for vestibular schwannomas: Looking back 30 years of our experience**  
 Hidefumi Jokura  
 Jiro Suzuki Memorial Gamma House, Furukawa Seiryō hospital, Japan  
 Department of Neurosurgery, Tohoku University School of Medicine, Japan
- AS3-3 Stereotactic radiosurgery for post-operative residual vestibular schwannomas: immediate irradiation versus at time of confirmed growth**  
 Shinya Watanabe  
 Department of Neurosurgery, Mito Kyodo General Hospital, Tsukuba University Hospital Mito  
 Area Medical Education Center, Japan  
 Department of Neurosurgery, Faculty of Medicine, University of Tsukuba, Japan
- AS3-4 Long term results of Gamma knife micro-radiosurgery for acoustic tumors in Neurofibromatosis type 2 patients: treatment policy, strategy, and clinical results for maintenance of serviceable hearing**  
 Motohiro Hayashi  
 Section of Stereotactic Radiosurgery, Department of Neurosurgery, Tokyo Women's Medical University, Japan
- AS3-5 Long term effects of Gamma Knife radiosurgery for skull base meningiomas**  
 Maheep Singh Gaur  
 Gamma Knife Centre, Vimhans Hospital, India
- AS3-6 Long-term outcomes of stereotactic radiosurgery for skull base tumors involving the cavernous sinus**  
 Motoyuki Umekawa  
 Department of Neurosurgery, The University of Tokyo Hospital, Japan
- AS3-7 Long-term risks of hemorrhage and adverse radiation effects of stereotactic radiosurgery for brain arteriovenous malformations**  
 Toshinori Hasegawa  
 Department of Neurosurgery, Komaki City Hospital, Japan
- AS3-8 Multimodal treatment for ruptured arteriovenous malformations at our institution with three modalities**  
 Akihiro Niwa  
 Department of Neurosurgery, National Cerebral and Cardiovascular Center Hospital, Japan

**12 : 25 ~ 13 : 05      General Session 9 : Vascular disorders 3**

Moderators : Kazutaka Yatsushiro (Fujimoto General Hospital, Japan)  
 Szu-Hao Andrew Liu (Kaohsiung Veterans General Hospital, Taiwan)

- AG9-1 Development of expanding hematoma and expanding cysts in AVMs after GKS**  
 Han-Song Tseng  
 Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan
- AG9-2 Long-term results of gamma knife radiosurgery for pediatric arteriovenous malformations**  
 Kazuhiro Yamanaka  
 Department of Neurosurgery, Osaka City General Hospital, Japan

**AG93 Effect of treatment of cerebral arteriovenous malformations (AVMs) on AVM-associated epilepsy**

Etsuko Yamamoto Hattori

Department of Neurosurgery, National Cerebral and Cardiovascular Center, Japan

**AG94 Two cases of response to gamma knife radiosurgery for arteriovenous malformation complicated by Moyamoya disease**

Junji Fukumori

Department of Neurosurgery, National Cerebral and Cardiovascular Center Hospital, Japan

13 : 10 ~ 13 : 15    **Closing Ceremony**



# Educational Lecture

Curriculum Vitae

Abstracts

Name : Bengt Karlsson

Education:

1972 - 1974 : University Studies in Technical and Theoretical Physics,  
Royal Institute of Technology, Stockholm, Sweden  
1975 - 1980 : Medical studies, Karolinska Institute, Stockholm, Sweden  
1980 : Examined from the Karolinska Institute Medical School, Stockholm,  
Sweden  
1996 : Successful defense of doctoral thesis (Ph.D.) "Gamma Knife surgery for  
Arteriovenous malformations" at the Karolinska Institute, Stockholm,  
Sweden, 1996



Positions:

1983 - 1988 : residency in Neurosurgery, South Hospital, Stockholm, Sweden  
1988 - 2001 : consultant at the department of Neurosurgery, Karolinska Hospital, Stockholm Sweden  
1991 - 1998 : Assistant Director, Karolinska Gamma Knife center  
1998 - 2001 : Director, Karolinska Gamma Knife Center, Karolinska, Hospital, Stockholm, Sweden  
2001 - 2004 : Board certified Neurosurgeon in Germany and head, Gamma Knife Center at the Goethe  
University Frankfurt, Frankfurt am Main, Germany  
2004 - 2009 : Head of Gamma Knife and Full Professor of Neurosurgery, dep of Neurosurgery, West  
Virginia University, Morgantown WV USA  
2009 - at present : Visiting consultant, National University Hospital, Singapore and director, Parkway  
Gamma Knife Centre  
Working with Gamma Knife Surgery since 1985

Medical Licenses:

Sweden M.D. since 1982. Active  
Germany M.D. since 2001. Active  
West Virginia USA M.D. since 2005. Passive  
Pennsylvania USA M.D. since 2007. Passive  
Singapore M.D. since 2008. Active

Visiting professor to the following places:

Dep of Neurosurgery, Armed Forces Hospital Riyadh KSA (Dec 1997)  
Dep of Neurosurgery, University at Buffalo, NY USA (May 1999)  
Dep of Neurosurgery, Cleveland Clinic, Cleveland, OH USA (Nov 2007)  
Dep of Neurosurgery, Riyadh Military Hospital, Riyadh, Saudi Arabia (October 2009)

Factors related to the risk for hemorrhage following GKS – which are treatment and which are natural course related?

Bengt Karlsson, M.D., Ph.D.

National University Hospital, Singapore

The risk for hemorrhage between GKS and obliteration was analyzed in a recent study based on data from 5037 patients. It could be shown that the risk is independently related to the lowest dose to the AVM nidus, the AVM volume, the age of the patient and the AVM location. We could also show that females in their child bearing ages had a lower risk for hemorrhage as compared to males in the same age group.

Which of the parameters above are treatment and which are AVM or patient related? This is important, as this information allows us to objectively compare the risk/benefit ratios between GKS and other management modalities. In order to answer this question, information about the natural course for AVMs is necessary. We could in an earlier study show that the AVM volume and the age of the patient are unrelated to the hemorrhage risk for untreated patients. We could also show that females in their child bearing ages have a higher risk for hemorrhage as compared to males in the same age group. Thus, the increase in post GKS risk for hemorrhage caused by larger AVM volumes and older ages must be treatment related. The lower risk for hemorrhage for females in the child bearing ages is indirectly related to the treatment, as pregnancy has been postponed until the AVMs are occluded. Our data shows that the risk for AVM hemorrhage during pregnancy is 3-4 times higher during pregnancy, or around 10% per year.

In conclusion, the higher risk for hemorrhage for centrally located AVMs reflect the natural course and is not treatment related. Low dose to any part of the AVM Indus, large AVM volume and old age are all independent factors increasing the risk for post GKS hemorrhage. These relations can be quantified, allowing us to accurately predict the risk for hemorrhage during the first two years following GKS.

Name : Wan-Yuo Guo, M.D., Ph.D. (郭萬祐)

### I. Current Position:

Emeritus Professor, Department of Radiology, Taipei Veterans General Hospital (VGH-TPE)

Professor, School of Medicine, National Yang Ming Chiao Tung University, Taiwan

Head, Medical Solutions, Taiwan AI Labs, Taipei, Taiwan

Consultant, AI Center for Medical Diagnosis, CMU Hospital, Taichung, Taiwan

President, The World Federation of Neuroradiological Societies (WFNRS)



### II. Education

#### a) Undergraduate

1974 - 1981 Medical Doctor, China Medical University (CMU), Taiwan

#### b) Graduate

1989 - 1993 PhD, Karolinska Institute (KI), Stockholm, Sweden

### III. Professional Experience

1981 - 1983 Military Surgeon

1983 - 1986 Residency in Dept. of Radiology, VGH-TPE

1986 - 1987 Chief Residency, Dept. of Radiology, VGH-TPE

1987 - 1988 Fellowship, Division of Neuroradiology, Dept. of Radiology, VGH-TPE

1988 - 1989 Attending Radiologist, Division of Neuroradiology, VGH-TPE

1989 - 1993 Fellowship, Dept. of Neuroradiology, Karolinska Hospital, KI, Stockholm, Sweden

1994 - 2006 Chief, Division of MRI, Dept. of Radiology, VGH-TPE

2006 - 2016 Chief, Division of Neuroradiology, Dept. of Radiology, VGH-TPE

1987 - 1989 Deputy Secretary General, The Chinese Taipei Society of Radiology (CTSR)

1995 - 1998 Secretary General, The Neuroradiological Society of Taiwan (NRST)

2008 - 2010 Secretary General, CTSR

2006 - 2010 Member-at-large, World Federation of Neuroradiological Societies (WFNRS)

2010 - 2013 President, NRST

2013 - 2016 President, CTSR

2014 - 2018 Member, Executive Committee, WFNRS

2014 - 2018 President, XXI SNR-Symposium Neuroradiologicum

(2018 World Congress of Neuroradiology, Taipei, Taiwan)

2018 - 2022 President-Elect/Vice President, WFNRS

2016 - 2022 Professor and Chairman, Department of Radiology, VGH-TPE, Taiwan

2005 - present Professor, School of Medicine, National Yang Ming Chiao Tung University, Taiwan

### IV. Honors

1. Derek Harwood-Nash Pediatric Neuroradiology Scholarship 1998, The Hospital for Sick Children university of Toronto, Toronto, Canada

2. Visiting Professor, Division of Pediatric Neurosurgery, Department of Neurosurgery, Jikei University, School of Medicine, Tokyo, Japan, Aug 14-21, 2004

3. Honorary Member, American Society of Neuroradiology (2014)

4. Honorary Member, American Roentgen Ray Society (2015)

5. Honorary Member, KCR-AOCR (2022)

### V. Publications and Lectures

2 Hundreds of publications and hundreds of domestic and international invited speeches.

2 Five SCI Journals cover story papers

## Brain Metastasis: AI Assisted Detection and Beyond

Wan-Yuo Guo<sup>1,2,3</sup>, Myron Li<sup>2</sup>, Ethan Tu<sup>2</sup>, Kei Yamada<sup>4</sup>

<sup>1</sup>) Department of Radiology, Taipei Veterans General Hospital, Taiwan

<sup>2</sup>) Taiwan AI Labs, Taipei, Taiwan

<sup>3</sup>) China Medical University Hospital, Taichung, Taiwan

<sup>4</sup>) Department of Radiology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Japan

**Introduction** The majority of deep learning artificial intelligence (AI) models for imaging diagnosis demonstrate diminished model performance on external dataset. We employ multiple steps in model development, refinement, validation on MRI from wide-ranging vendors and hospitals and results in a clinically applicable vendor agnostic AI model for brain metastasis detection on MRI.

**Methods** AI model training based on MRI of 1029 patients with brain metastases from a single institute and single MRI brand was conducted. A benchmark algorithm of 2D Mask R-CNN was used and resulted in an initial model, DeepMets<sup>®</sup> (Step I). Model generalization of DeepMets<sup>®</sup> was then carried out over a nationwide population-based dataset (from 23 hospitals) via deep active learning on 559 patients (randomized from 3125) from National Health Insurance Administration (NHIA) medi-cloud, Taiwan. Iterative refining process using the ResNext50 U-Net architecture with attention mechanisms were undertaken and resulted in a newer version model, DeepMets-Plus<sup>®</sup> (Step II). Final testing of the model was conducted on a dataset of brain metastasis consisted of 152 patients (489 metastases). They were referred from 19 hospitals for considering radiosurgery on their brain metastasis. Their diagnostic MRI were conducted from three vendors. Sizes of the metastases were median 7 (4-40) mm in maximum diameters. The ground truth of the final test was obtained from a consensus of three experienced neuroradiologists, with 30 (25-36) years professional experience in neuroradiology (Step III).

**Results** The performance of DeepMets<sup>®</sup> were: sensitivity 96%, precision 86%, and f1 91% (Step I). It dropped to sensitivity 76%, precision 45% and f1 48%, initially, on the NHIA dataset. After three active learning rounds with Ensemble & Post, DeepMets-Plus<sup>®</sup> yielded the final performance of sensitivity 0.86%, precision 0.90%, and f1 0.87% (Step II). For DeepMets-Plus<sup>®</sup>, the intersection over union between ground truth and model inference were 0.718, 0.210-0.904 (median, range). The centroid and Hausdorff distances were, respectively, 0.617, 0.124-2.154 mm and 2.512, 0.469-7.469 mm. The final model performance was: sensitivity 85%, precision 93%, f1 89%, and false positive rate of 0.21/patient (Step III).

**Discussion and Conclusion** The initial model, DeepMets<sup>®</sup>, has high performance in detecting brain metastases on in-house homogeneous MRI dataset. However, the performance of DeepMets<sup>®</sup> initially dropped when applied to the heterogeneous imaging datasets in NHIA. After the model refinement conducted on the NHIA imaging datasets, DeepMets-Plus<sup>®</sup> gains model generalization and results in model performance as good as in the step I. The access to a national-scale dataset demonstrates significant improvements in performance and model generalization across vendors and imaging parameters for brain metastasis detection. The model is now applicable for assisting brain metastasis detection and contouring for clinical use.

One of the solutions for generalization of an AI model is to train a model on dataset from multiple sources with heterogeneity in data properties. In real world scenario, however, it is not feasible to collect and centralize datasets due to privacy and autonomy concerns. Federated learning, a way of model training and refinement based on non-centralized smaller datasets, opens a new window for reaching our goal of sharing the weights of models rather than datasets *per se* and resulting in the final model weights with the input of bigger datasets.

Regulatory approval AI models and their business promotion are the last but not least steps of AI application in clinical scenarios. They are also the critical steps that decide the sustainability of AI ecosystem. To the year of 2022, the global majority of medical AI models that have received regulatory approval for clinical use are imaging-related products. Among them, only not many are reimbursed globally, e.g., in the US and Japan. If we believe that medical AI is one of the savors of the medical communities to overcome the global problem of medical manpower shortage, the last steps of obtaining regulatory approval and business promotion and reimbursement for using AI in clinical service will be the keys to the success.



# Luncheon Seminar

Curriculum Vitae

Abstract

Name : Motohiro Hayashi, MD, DMSc



Motohiro Hayashi, MD, DMSc is a Professor of Neurosurgery at Tokyo Women's Medical University, a Visiting Associate Professor of Neurosurgery at National defense medical college, a Visiting Associate Professor of Heavy Particle Ion Center at Gunma University, and a visiting researcher at National Institutes for Quantum Science and Technology. He is the Director of the section of Stereotactic Radiosurgery at Tokyo Women's Medical University. Dr Hayashi earned both his MD and DMSc in Neurosurgery from Tokyo Women's Medical University. He then completed clinical training of both Neurosurgery and Stereotactic Radiosurgery Program at Tokyo Women's Medical University and is board-certified in Neurosurgery in 1997. Dr.Hayashi obtained "Diplome d'AFSA de Neurochirurgie" at Marseille University Timone Hospital in 2000, and experienced 1014 cases with Gamma knife from professor Jean Regis. His previous research involved tissue regeneration after stereotactic radiosurgery with animal models, focusing on elucidating the action mechanism of functional disorders in radiosurgery. Dr Hayashi's current research interests are focused on clinical improvement in both intractable skull base tumors and intractable functional disorders in stereotactic radiosurgery, and development Carbon knife (establishing micro-beam of heavy particle ion) at National Institutes for Quantum Science and Technology, funded through National Government grants. He is active in many societies and is currently a executive member of the Japanese Neurosurgery Society, and was board member of both World Federation of Neurosurgery Society in 2010-2017, and International Stereotactic Radiosurgery Society in 2013-2017, and host 12th International Stereotactic Radiosurgery Society Congress as a chairman in Yokohama, Japan in 2015.

#### Scientific Achievements:

Editorial review board of "*NEUROSUGERY*" in 2022-2024. 257articles (including 3 editorial books/ Total IF: 327.386) in the international journals and medico/radiosurgical textbooks, 216 invited and symposium presentations including 118 of international conferences. 12000 therapeutic experience with Gamma Knife and ZAP-X, and organized 31 official training courses as an official trainer designated from Elekta KK.



Treatment strategy and clinical results of Gamma Knife stereotactic radiosurgery for high grade pediatric arteriovenous malformation: Utility and the role of Brainlab “Vascular ELEMENTS” software associated with modern Gamma knife system (Icon).

Motohiro Hayashi, Ayako Horiba, and Mieko Oka

Section of Stereotactic Radiosurgery, Department of Neurosurgery, Tokyo Women's Medical University, Japan

The management of high grade pediatric arteriovenous malformation (AVM) with Gamma knife surgery had been very complicated, and complete disappearance without any complication, such as radiation necrosis and delayed cyst formation, was very rare. Therefore, we have been tried to sophisticate the treatment system itself for pediatric cases to cause in favorable clinical results, morphology and complication point of view. In recent cases, we have tried to apply MAC anesthesia, which was no intubation in general anesthesia not to give fear emotion to all infant patients. And then, we installed Gamma knife ICON system (ELEKTA Instruments AB), which has no need for frame application, with association of the dedicated software of “Vascular ELEMNTS” delivered by Brainlab. There is advantage to use this system that the previous angiography could be used with preoperative 3DCTA and MRI/A in the unique platform, and we can contour the target as 4D (3D + flow) before dose planning in Gamma Plan (ELEKTA Instruments AB). In practice, we don't need both angiography with frame application and oral intubation under general anesthesia at the day of Gamma knife surgery. Some pediatric patients didn't need hospitalization. In this lecture presentation, we would like to demonstrate our institutional experience, treatment policy, strategy, and clinical results for pediatric AVM cases, especially high grade AVM.



# Symposium

## Abstracts



## Results of 2-staged Gamma Knife radiosurgery for large brain metastases at Ha Noi, Viet Nam

Nguyen Duc Lien, Nguyen Minh Thuan, Phan Thanh Duong, Pham Hong Phuc

Department of Neurosurgery, National cancer hospital (K hospital), Ha Noi, Viet Nam

**Introduction** The optimal interfraction intervals for fractionated radiosurgery has yet to be established. Our study aimed to evaluate the preliminary treatment result of 2-staged stereotactic radiosurgery by Gamma Knife for large brain metastases.

**Methods** Between July 2019 to June 2021, a total of 50 patients underwent 2-staged Gamma Knife radiosurgery for large brain metastases using the ICON unit at K hospital, Hanoi, Viet Nam. All patients had at least 1 large brain metastasis with the largest diameter > 3cm or the volume >10cc, and their KPS score was  $\geq 60$ . Two-staged radiosurgery was performed with the median dose of 12 Gy at 50% isodose line, and the time interval between 2 treatments was 2 weeks.

**Results** The most common primary tumor site was the lung (35/50, 70%), and followed by the breast (16%). Number of metastatic tumors in the brain: 1 foci (44%), 2-5 foci 28/50 patients (56%). The mean tumor volume was  $18.13 \pm 6.98 \text{ cm}^3$  at the first treatment, and  $13.24 \pm 6.56 \text{ cm}^3$  at the second treatment (volume reduction 27.24%,  $p = 0.0001$ ). The local tumor control rate of 50 large brain metastases was 94% at 3 months, 34% complete response, 52% partial response, 8% stable disease. The estimated local control rate was 88% and 76% at 6 months and 12 months, respectively. New brain metastases have not developed during 3 months follow up period. Among 50 lesions, 6 (12%) show radiation-induced adverse effects (8% Grade 1 and 2 toxicity, 4% Grade 3). The estimated overall survival rates at 6 and 12 months were  $92\% \pm 4\%$  and  $74\% \pm 6\%$ , respectively.

**Conclusions** According to our results, we suggest that 2-staged Gamma Knife radiosurgery with a 2 weeks interval can be one of the effective treatment method for large brain metastases.

## AS1-2

## Neoadjuvant stereotactic radiosurgery for brain metastases: single-fraction and hypofractionation experience

Cristian Udovicich<sup>1,2</sup>, Damien Tange<sup>3</sup>, Kendrick Koo<sup>1</sup>, Neda Haghighi<sup>1,4</sup>

<sup>1</sup> Department of Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia

<sup>2</sup> Sir Peter MacCallum Department of Oncology, The University of Melbourne, Australia

<sup>3</sup> Department of Neurosurgery, Peter MacCallum Cancer Centre, Melbourne, Australia

<sup>4</sup> Icon Cancer Centre, Epworth Hospital, Richmond, Australia

**Introduction** The standard of care after resection of brain metastases is post-operative stereotactic radiosurgery (PoSRS). However, PoSRS has limitations with high rates of leptomeningeal disease (LMD) ~15-30%. Additionally, there are challenges with potential radionecrosis (RN) and inaccurate target volume delineation. Neoadjuvant SRS (NaSRS) has been proposed as an alternative approach to decrease these potential toxicities. The majority of previous evidence for NaSRS has been single-fraction SRS. The aim of the study was to report outcomes in patients undergoing single-fraction and hypofractionated NaSRS for brain metastases.

**Methods** Patients undergoing SRS followed by resection of intracranial lesions with a confirmed primary malignancy were included in our retrospective multi-centre case series. Exclusion criteria included previous local treatment to the NaSRS metastasis, current/previous LMD and ECOG  $\geq 3$ . Primary endpoints included LC and LMD. LMD was classified as classical or nodular. Secondary endpoints included RN, distant intracranial control (DC) and overall survival (OS). RN was graded as per CTCAE Version 5.0. LC and RN were calculated on a per-lesion analysis. LMD, DC and OS were calculated on a per-patient analysis. Time-to-event outcomes were estimated using the Kaplan-Meier method.

**Results** Overall, 41 patients with 44 metastases were eligible. Median follow-up was 10.5 months (IQR 7.4-31.6). The mean age was 62.9 years (range 36-80) and 27 (66%) were ECOG 0-1. The most common primary malignancies included non-small cell lung cancer (39%), melanoma (18%) and breast (14%). Hypofractionated SRS was utilised in 70%. There were two local failures (4.5%) with a 12-month LC rate of 93.9%. Four patients (9.8%) developed LMD, three classical and one nodular. The 12-month LMD rate was 7.8%. The 12-month RN rate was 5.6%, with only one metastasis (2.2%) developing Grade 2 RN. The 12-month DC and OS rate was 55.1% and 60.6%, respectively.

**Conclusions** We present one of the largest cohorts of patients in which the majority of patients were treated with hypofractionated SRS. We found a high rate of local control comparable to post-operative SRS with low rates of LMD and RN. NaSRS is a promising approach for appropriate patients where surgical resection is a component of local therapy.

## Hypofractionated irradiation with Gamma Knife Icon for large metastatic brain tumors

Kazutaka Yatsushiro<sup>1)</sup>, Hiroyuki Uchida<sup>2)</sup>, Masaki Sato<sup>1)</sup>, Ichiro Yamasaki<sup>1)</sup>, Toshiaki Otsubo<sup>1)</sup>, Takao Horinouchi<sup>3)</sup>, Masaomi Ijuin<sup>3)</sup>

<sup>1)</sup> Department of Neurosurgery, Fujimoto General Hospital, Japan

<sup>2)</sup> Department of Neurosurgery, Kagoshima University Hospital, Japan

<sup>3)</sup> Department of Radiology, Fujimoto General Hospital, Japan

**Introduction** In November 2016, we started hypofractionated irradiation with the Leksell Gamma Knife Icon (ICON) for large metastatic brain tumors. In this paper, we investigated the therapeutic effect and the rate and timing of occurrence of radiation injury.

**Methods** From December 2016 to June 2021, the subjects consisted of 194 patients (111 men and 83 women) who underwent fractionated irradiation at ICON in our hospital due to large tumor volume and were able to follow up for more than 6 months. Primary cancer was located in the lung in 118 patients, the colorectal in 23, the breast in 18, and other locations in 35. Three irradiation methods were selected for each tumor volume. Survival rate was evaluated using the Kaplan-Meier method, and recurrence rate and rate of radiation injury were evaluated using competing risk analysis.

**Results** We used 30 Gy / 3 fx, 35 Gy / 5 fx, and 40-42 Gy / 8-10 fx for fractionated irradiation. The number of cases for each division was 26, 110, and 58, and the average tumor volumes were 7.4 cm<sup>3</sup>, 11.8 cm<sup>3</sup>, and 25.2 cm<sup>3</sup>, respectively. The median survival times were 72, 36, and 53 weeks, respectively, with no significant difference. On the other hand, the recurrence rates at 1 year and 2 years were 7.9 / 16.1 %, 5.2 / 6.5 % and 9.5 / 12.1 %, respectively. The incidence of radiation injury requiring medical treatment was 12.2 / 17.0 %, 7.2 / 8.8 %, and 5.5 / 7.7 %. Radiation injury occurred on average 7.7 months after treatment, while recurrence occurred on average 10.1 months after treatment.

**Conclusions** Hypofractionated irradiation with ICON was shown to be an effective and safe treatment even for large metastatic brain tumors.

## Fractionated radiotherapy for metastatic brain tumors using mask system of Leksell Gamma Knife Icon

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**Introduction** Leksell Gamma Knife Icon enables us to apply new methods of immobilization using mask fixation and the option of fractionated treatment.

**Methods** We retrospectively analyzed 537 patients (668 times) with brain metastases who underwent fractionated radiotherapies using mask system of Icon between September 25th, 2017 and September 24th, 2022 at Rakusai Shimizu Hospital and for whom radiological and clinical follow-up data were available. If the tumor volume was larger than 5.0 ml, recurrence, or the location was in an eloquent area, we applied a fractionated schedule. The most common origin was lung (310 patients), followed by breast (84), gastro-intestinal tracts (64), kidney (21), and others (78).

**Results** The reasons for the select of fractionated schedule (including duplication) were large volume (378 times), recurrence (226), and near the eloquent area (218). For large tumors, we selected fractionated schedules as follows; 7.0 Gy x 5Fr (5-10 ml), 4.2(-4.7)Gy x 10Fr (10-20ml), 3.7(-4.2)Gy x 10Fr (20-30ml), 3.2(-4.7)Gy x 10Fr (30ml-). Median survival times after Icon treatment was 28.4 months, with only 4/5/6% of neurological deaths at 12/24/36 months after treatment. Poor local control was 11/25/35% at 6/12/24 months post-treatment. Preservation of neurological function was 89/84/83% at 12/24/36 months post-treatment. Serious complications occurred in only 1/3/5% of patients at 12/24/36 months post-treatment.

**Conclusions** Although these results are limited to short periods, survival rates, local control rates and qualitative survival rated in patients unsuitable for stereotactic radiosurgery, such as those with large, recurrent, and eloquent site lesions, were within the acceptable ranges.

## Interfractional change of tumor volume during fractionated stereotactic radiotherapy using gamma knife for brain metastases

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**Introduction** Fractionated stereotactic radiotherapy (FSRT) using gamma knife is useful for brain metastases. However, several uncertainties derived from fractionation pose issues for maintaining high-level accuracy. This study analyzed interfractional tumor change by performing radiological reassessment at the midterm of FSRT with  $\geq 10$  fractions, and the significance of replanning was evaluated.

**Methods** Data of FSRT using gamma knife with  $\geq 10$  fractions were retrospectively collected. Interfractional volume changes in MRI at the midterm of the irradiation period were analyzed. Radiological changes after FSRT and final outcomes were also investigated.

**Results** Overall, 114 lesions in 74 treatments from 66 patients were included, with previously irradiated lesions accounting for 46%. The median interval between planning and the interfractional MRI was 7 days. The interfractional change rates of tumor volume ranged from  $-48$  to  $+72\%$ . Significant interfractional enlargement was observed in 16 lesions (14%); evident regression was confirmed in 17 lesions (15%). Predictive factors for interfractional enlargement were small tumor and cystic lesion; high biologically effective dose was associated with regression. After FSRT, most lesions regressed within 6 months despite interfractional change type. The incidences of tumor control and radiation necrosis indicated no differences between interfractionally-regressed lesions and others.

**Conclusions** This is the first study to evaluate interfractional tumor change in FSRT using gamma knife with  $\geq 10$  fractions, indicating significant volume changes in 29% of the lesions. These preliminary results suggest that interfractional reassessment of a treatment plan in FSRT with irradiation periods exceeding a week is necessary for more adaptive treatment.

## Gamma knife radiosurgery and radiotherapy for brain metastases in non-small cell lung cancer harboring driver gene alterations

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**Introduction** While fractionated gamma knife radiotherapy (F-GK) is effective for large brain metastases (BMs), other potential candidates for F-GK have not been elucidated. Patients with non-small cell lung cancer (NSCLC), especially those harboring driver gene alterations, can now survive longer than before because of advancements in targeted therapy. Consequently, they require long-term safety. This study aimed to analyze the outcomes of single-fraction gamma knife radiosurgery (S-GK) and F-GK for NSCLC-BMs.

**Methods** Data of consecutive patients who underwent S-GK or F-GK as the first local treatment for NSCLC-BMs between May 2018 and December 2021 at our institution were retrospectively collected. We excluded patients whose gene alteration status was unknown, those who underwent staged radiosurgery, and those with only BMs of  $< 5$  mm diameter. F-GK was generally selected for patients with large tumors, those located in eloquent regions, and those whose border was ambiguously enhanced.

**Results** Among 97 patients with 282 lesions, 44 patients with 125 lesions harbored the following driver gene alterations: EGFR mutation in 34 patients and ALK or ROS1 rearrangements in 10. S-GK was performed in 63 patients, while F-GK (3–15 in fractions) was performed in 34 patients. The lesions treated with F-GK were slightly but significantly larger than those treated with S-GK ( $p = 0.048$ ). After treatment, the overall survival of patients with driver gene alteration was 97% at 1 year and 88% at 2 years, which was significantly higher than those in patients without it ( $p = 0.008$ ). Higher local control rates were observed in smaller BMs ( $p = 0.002$ ) and lesions with driver gene alterations ( $p = 0.036$ ). Radiation-induced adverse effects (RAEs) appeared more frequently in patients with larger BMs ( $p = 0.012$ ) and those treated with S-GK ( $p = 0.036$ ) in the multivariate analysis; driver gene alteration was not a predictive factor for RAEs.

**Conclusions** Both S-GK and F-GK achieved high local control for NSCLC-BMs. F-GK could be more suitable in terms of RAE risk, especially for patients with driver gene alteration, and is expected for long survival in the era of the third-generation tyrosine kinase inhibitors.

## The role of gamma knife surgery in the treatment of high-grade ruptured cerebral AVMs

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**Introduction** High-grade ruptured arteriovenous malformations (rAVMs) are difficult to treat, even when surgery and embolization are combined. The purpose of this study is to investigate the current state and future challenges of gamma knife radiosurgery (GKRS) in high-grade rAVMs.

**Methods** From April 2002 to September 2021, treatment method and prognosis were retrospectively examined for all 518 AVMs treated by inpatient exploration, 27 of which were the Spetzler-Martin Grade (S-M) IV, V ruptured and treated.

**Results** The study included 17 male patients (62.9%) with a mean age of  $29.3 \pm 18.7$  years and a mean follow-up period of  $89.9 \pm 73.7$  months were studied. S-M grade IV was present in 25 patients (92.6%). All patients had IVR combination. 9 (75%) of 12 (54.5%) patients treated with the combination of GKRS and IVR were cured. There were 12 occlusions (54.5%), of which 9 were occlusions (75%) All nine instances of rebleeding following therapy were GKRS ( $p=0.03$ ). Irradiation strategies included dose staging (D; target volume; TV  $7.1 \pm 3.7$ cc), volume staging (V; TV  $14.2 \pm 6.0$ cc), and irradiation with the bleeding source as the target (T;  $p=0.03$ ). Posttreatment bleeding in cases D3 and V5 did not differ significantly, and the occlusion rate was 54.5% in case D6, 25% in case V2, and 33.3% in case T1. The incidence of occlusion was comparable between the three groups. mRS0-2 was 60% in the three removed patients and 68% in the fifteen GKRS cases at the last follow-up. At the most recent follow-up, mRS0-2 levels were not significantly different.

**Discussion** The lesions located on the surface of the brain without involvement of the perforating arteries were cured by a combination of direct surgery and IVR, whereas the majority of the other lesions were treated with GKRS.

In instances treated with combined IVR and GKRS, the occlusion rate is significant, and IVR treatment after GKRS is an alternative. Although bleeding can be lethal, the prevention of rebleeding should take precedence over the risk of delayed radiation injury.

**Conclusions** Currently, GKRS is the most effective treatment for high-grade rAVMs, and it is important to tailor treatment to individual nidus characteristics.

## Change of therapeutic strategies with GKS and other interventional therapies for unruptured brain arteriovenous malformation after the publication of the ARUBA trial

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**Introduction** Although the ARUBA trial demonstrated superiority of medical treatment for unruptured brain arteriovenous malformation (bAVM), researchers have criticized its research design and interpretations. We examined whether the publication of the ARUBA trial changed therapeutic strategies and outcomes of treatment for unruptured bAVM with multimodalities including gamma knife surgery (GKS) and microsurgery.

**Methods** We reviewed 226 consecutive patients with unruptured bAVM admitted to our institute from 2002 to 2022. Patients were divided into pre-ARUBA group (125 patients, before February 2014) and post-ARUBA group (101 patients, after March 2014). Symptomatic stroke or death were evaluated for the primary outcome. Strategic choice including medical treatment or interventional therapies including GKS, microsurgery, embolization was compared between the two groups.

**Results** 73% of patients had therapeutic interventions in pre-ARUBA group, and 84% in post-ARUBA group ( $p = 0.053$ ). Strategic choice of microsurgery remains unchanged after the publication of ARUBA study (pre vs. post: 16% vs. 10%,  $p = 0.24$ ), whereas SRS slightly increased (57% vs. 74%,  $p < 0.01$ ). Although microsurgery for high grade bAVMs with SM grade of 3–5 decreased from 30% to 10% in post-ARUBA ( $p < 0.01$ ), GKS did not decrease even for high SM grade bAVMs (38% vs. 40%,  $p = 0.87$ ). Rate of stroke or death was higher in patients with medical treatment (medical vs. intervention: 22% vs. 9.7%,  $p = 0.022$ ). The annual incidence of stroke or death decreased by interventional therapies (total: 4.3%/y vs. 1.8%/y,  $p = 0.032$ , pre: 4.3%/y vs. 1.5%/y,  $p = 0.033$ , post: 4.0% vs. 2.8%,  $p = 0.64$ ). In interventional therapies, GKS significantly reduced the development of bAVM rupture compared with medical treatment in the long term (4.3% vs. 1.2%,  $p < 0.01$ , HR = 3.1)

**Conclusions** Therapeutic intervention rate including GKS did not decrease even after the publication of the ARUBA trial. The superiority of interventional therapies over medical treatment was demonstrated in our single institutional study.



## The irradiated brain volume within 12 Gy is a predictor for radiation-induced changes after stereotactic radiosurgery in patients with unruptured cerebral arteriovenous malformations

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**Introduction** To determine whether the coverage of brain parenchyma within the 12Gy radiosurgical volume (V12) correlates with the development of radiation-induced changes (RICs) in patients with unruptured cerebral arteriovenous malformations (AVM) after undergoing stereotactic radiosurgery (SRS).

**Methods** This study conducted regular follow-up examinations of 165 patients with unruptured AVMs who had previously undergone SRS. The RICs identified in T2-weighted MRI scans at any time point in the first 3 years after SRS was labeled early RICs. The RICs remain identified in T2-weighted MRI scans at 5-years follow-up brain images was labeled late RICs. Fully automated segmentation was used to analyze the MRI scans from these patients, whereupon the volume and proportion of brain parenchyma within the V12 was calculated. Logistic regression analysis was used to characterize the factors affecting the incidence of early and late RICs of any grade following SRS.

**Results** The median duration of follow-up was 70 months (range, 36-222). Early RICs were identified in 124 of the 165 patients with the highest grade as followed: Grade 1 (103 patients), Grade 2 (19 patients), and Grade 3 (2 patients). Only 103 patients had more than 5 years follow-up and late RICs were identified in 70 of 103 patients. 17 of 70 patients with late RICs were symptomatic. The median volume and proportion of brain parenchyma within the V12 was 22.4 cm<sup>3</sup> (range, 0.6-63.9) and 58.7% (range, 18.4-76.8). Univariate analysis revealed that AVM volume and the brain volume within the V12 were correlated with the incidence of both early and late RICs after SRS. Multivariable analysis revealed that only the brain volume within the V12 was significantly associated with the incidence of early and late RICs after SRS.

**Conclusions** In patients with unruptured AVM, the volume of brain parenchyma within the V12 was an important factor associated with the incidence of early and late RICs following SRS. Prior to SRS, meticulous radiosurgical planning to reduce brain parenchyma coverage within the V12 could reduce the risk of complications.

## AS2-4

### Efficacy of embolization before stereotactic radiosurgery for brain arteriovenous malformations

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**Objective** This study aims to evaluate the effect of endovascular embolization prior to stereotactic radiosurgery on the outcome of patients with arteriovenous malformations (AVM).

**Method** A total of 420 patients with AVM treated with single session Gamma Knife radiosurgery (GK) were included in this study. Of these patients, 261 were treated with GK only, and 159 were treated with embolization followed by GK (GK+E). Comparing clinical characteristics between patients treated with GK only and GK+E, these groups were matched in a 1:1 ratio using propensity score matching to eliminate differences in basic characteristics. The primary outcome was to compare the nidus obliteration rates between the GK only and GK+E groups. The secondary outcomes were the comparison of cumulative hemorrhage rates and the incidence of delayed radiation injury after GK between these groups.

**Results** In the unmatched cohorts, the AVMs in the GK+E group had a larger nidus volume, higher Spetzler-Martin Grade, and lower peripheral prescription dose than those in the GK-only group. In the matched cohort of 136 patients in each group, the nidus obliteration rate 5 years after GK was 67.9% in GK only group and 75.4% in GK+E group (p=0.54). There was no significant difference in the cumulative delayed radiation injury rate between the two groups (GK only 5.2%, GK+E 7.3%, 10 years after GK, p=0.20), whereas GK+E group had a lower cumulative incidence of hemorrhage compared to GK only group (GK only 10.1%, GK+E 3.8%, 10 years after GK, p=0.04).

**Conclusions** Endovascular embolization prior to GK did not affect nidus obliteration rates or the incidence of delayed radiation injury, while the cumulative incidence of hemorrhage tended to be lower in GK+E group.

## Against controversy: Long-term outcomes of gamma knife radiosurgery for non-hemorrhagic large AVM based on the over 1,000 cases in 30 years at our institution

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**Introduction** Treatment strategies for AVMs have changed dramatically since ARUBA study. In particular, the intervention for large unruptured AVMs is controversial. We are committed to single-session GK whenever possible, and our policy is to perform single GK for a nidus volume of up to 20 mL. In this study, we analyzed 1070 GK treatments for AVMs over 32 years at our institution, aiming to report the current status and future prospects of GK for large unruptured AVMs.

**Methods** We retrospectively analyzed 1070 cases of GK for AVMs at our hospital from 1990 to 2022. The endpoints were AVM obliteration, post-GK hemorrhage, adverse events, and disease-specific survival (DSS). They were classified into three groups by nidus volume: small (<5 mL), medium (5-10 mL), and large (>10 mL). The outcomes of large AVMs were compared and validated with those of small and medium-sized lesions.

**Results** Cumulative AVM obliteration rates in the entire cohort were 80% at 5 years and 90% at 10 years; post-GK hemorrhage rates were 3.4% at 5 years, 4.5% at 10 years, and 7.0% at 20 years; and DSS were 99% at 10 years, 98% at 15 years, 92% at 20 years. For unruptured AVMs, the prescription dose was significantly lower in the order of small, medium, and large groups (mean 20.3 Gy vs. 19.9 Gy vs. 18.7 Gy,  $P = 0.001$ ). Previous embolization tended to be less common in the small group (7.6% vs. 15.6% vs. 12.3%,  $P = 0.081$ ). There was a trend toward longer latency period for AVM obliteration in the unruptured large AVM group (52% at 3 years, 81% at 5 years, and 93% at 10 years in the small group vs. 42% at 3 years, 87% at 5 years, and 93% at 10 years in the medium group vs. 30% at 3 years, 71% at 5 years, and 96% at 10 years in the large group,  $P = 0.052$ ). The unruptured medium AVM group showed a trend toward higher post-GK hemorrhage rates 12 years after GK (2.2% at 5 years and 3.9% at 10-15 years in the small group vs. 7.4% at 5-10 years and 13.0% at 15 years in the medium group vs. 6.3% at 5-15 years in the large group,  $P = 0.089$ ). The cumulative neurological preservation rates were significantly worse in the unruptured large AVM group (99% at 5 years, and 96% at 10-15 years in the small group vs. 94% at 5 years, 92% at 10 years, and 86% at 15 years in the medium group vs. 89% at 5-10 years and 84% at 15 years in the large group,  $P = 0.005$ ).

**Conclusions** Although the intervention for unruptured large AVMs is controversial, our long-term outcomes of the single-session GK for those with over 10mL nidus volume were acceptable. Abundant treatment data, clarification of long-term results, and the addition of new technologies could continue to optimize treatment.

## AS3-1

### Hearing preservation after planned partial resection followed by gamma knife radiosurgery for large vestibular schwannomas

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**Introduction** We have been performing planned partial surgical resections followed by gamma knife radiosurgery (GKS) for large vestibular schwannomas (VSs), and we could achieve the hearing preservation and/or hearing improvement after this strategy.

**Methods** From January 2000 to September 2021, we treated 50 patients with large unilateral VSs with planned partial tumor removal followed by GKS. At the time of surgical resection, the internal auditory canal is not opened and part of the ventral tumor is left in order to preserve the functions of the facial and cochlear nerves. GKS is performed at a marginal dose of 12 Gy, 3 months after surgery when the residual tumor has a shape suitable for GKS. In order to preserve hearing function, dose planning is performed so that the average cochlear exposure dose is 4 Gy or less. The median maximum diameter of the tumors was 32 mm. The median tumor volume at GKS was 2.7 cm<sup>3</sup> and the median prescribed dose was 12 Gy. The median follow-up period was 74 months.

**Results** At the final follow-up, facial nerve preservation (HB grade I - II) was achieved in 47 patients (94%; HB grade I: 92%, II: 2%). Among the patients with preoperative serviceable hearing (PTA ≤ 50 dB; 16 patients), 13 patients (81%) can maintain serviceable hearing postoperatively. At the last follow-up, 7 of preoperative serviceable hearing preservation (44%) maintained serviceable hearing. Among 34 patients without serviceable hearing, three patients (9%) improved to serviceable hearing postoperatively. Five-, 10-year and 15-year tumor growth control without additional treatment occurred in 86% of patients. Four patients (8.5%) required salvage surgery.

**Conclusions** Planned partial removal of large VSs followed by GKS achieved a high rate of facial nerve and hearing preservation. Furthermore, some patients with severe hearing loss before treatment have the chance of hearing improvement, even those with large VSs.

## Gamma knife radiosurgery for vestibular schwannomas: Looking back 30 years of our experience

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**Introduction** Gamma knife radiosurgery (GKRS) has established a role as a primary treatment modality for small to medium sized vestibular schwannomas (VSs). Nevertheless, considering that the tumor is benign and more and more young patients are treated, information of long-term follow up is still insufficient. We will summarize our 30-year-experience of GKRS for VSs.

**Methods** Materials are 626 cases of unilateral VSs treated between November 1991 and December 2020.

**Results** The median age was 60 years (17-84 years) and 41% of the patients were male. The median tumor volume was 2.7cm<sup>3</sup> (0.12 – 20.2 cm<sup>3</sup>) and the median marginal dose was 12.0 Gy (range, 10–17Gy). The median follow-up period was 83 months (range, 0.4–363.0 months). Tumor control (not requiring salvage surgery) rate at 5, 10, and 15 years were 94.0%, 91.6%, and 88.4%, respectively. Tumor control of volume <1 cm<sup>3</sup>, 1≤<4 cm<sup>3</sup>, 4≤<10 cm<sup>3</sup> and 10≤<15 cm<sup>3</sup> group at 15 years were 98.9%, 93.8%, 81.1% and 77.2%, respectively. Transient expansion of solid and/or cystic part of tumors persisted much longer than 3-4 years in some cases. Four salvage surgery were needed between 10 and 20 years and 2 after 20 years. Five of 6 cases showed good regression of tumor for more than 10 years before regrowth were detected. Viable schwannoma was confirmed histologically in every case. Two cases of malignant transformation were confirmed at 101 and 46 months (0.3%). Other rare but serious complication related treatment include subarachnoid hemorrhage due to aneurysm formation and cerebral infarction due to occlusion of AICA.

**Conclusions** GKRS provide good long-term tumor control with few complications in most of the cases. Need for salvage surgery after GKRS should not be decided by volume and timing after GKRS alone. Prediction of the fate of the transient expansion is almost impossible. Therefore, if a patient remains asymptomatic or within acceptable aggravation of symptoms, continuing follow-up is strongly recommended. More than 10 years of good control after GKRS do not necessarily means eradication of viable schwannoma cells and do not warrant life-long control.

## Stereotactic radiosurgery for post-operative residual vestibular schwannomas: immediate irradiation versus at time of confirmed growth

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**Introduction** Occasionally, intentional partial removal of a vestibular schwannoma (VS) is performed. In such cases, the timing of stereotactic radiosurgery (SRS) for the residual tumor is potentially problematic, i.e., is immediate irradiation or a “wait and see” approach better? Little information is available allowing us to address this question.

We compared long-term outcomes of SRS for post-operative residual VS between two treatment strategies, immediate (group-B) and delayed (group-A, at time of confirmed enlargement) irradiation.

**Methods** Among 402 patients receiving Gamma Knife SRS for VSs between June 1991 and March 2015, 127 had undergone surgery for VSs. We excluded 21 patients (13 lost-to-follow-up and 9 lacking pre-SRS surgical information). Thus, 106, 46 group-A and 60 group-B, patients were studied. Respective median tumor volumes were 2.6 cc and 2.8 cc. The median prescribed dose was 12.0 Gy in both groups.

**Results** Median follow-up was 73 (range: 6–164) months in group-A and 63 (range: 3–192) months in group-B. Tumor volume control was obtained in 34 of the 44 (77%) group-A and 46 of the 55 (84%) group-B (p=0.4519) patients. A further procedure was required in four (9%)/group-A and four (7%) group-B (p=0.7220) patients. Post-operative cumulative clinical control rates for the two SRS strategies were 96%/ 92% at the 60th/120th post-SRS month in group-A and 95%/91% in group-B (p=0.8813) patients. After SRS, among the 45 group-A patients, two (4%) experienced facial pain while none developed facial nerve paresis. Among the 60 group-B patients, facial pain occurred in three (5%) and facial palsy in one. There were no significant differences in the incidences of these post-SRS complications between the two groups (both p=1.0000).

**Conclusions** Neither of these post-operative SRS strategies was superior or inferior to the other. SRS can reasonably be postponed until the time of confirmed enlargement of the residual tumor.

## Long term results of Gamma knife micro-radiosurgery for acoustic tumors in Neurofibromatosis type 2 patients: treatment policy, strategy, and clinical results for maintenance of serviceable hearing

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**Introduction** Gamma Knife surgery (GKS) should be considered a standard treatment option for small and medium-sized acoustic tumors with favor clinical results. However, the management of the cases with Neurofibromatosis type 2 (NF2) was hard, and the treatment indication of GKS for bilateral acoustic tumors had still discussed. In recent 20 years, we had unique treatment policy for acoustic tumors in NF2 patients that the side of serviceable hearing should be priority target to try to prevent hearing loss due to tumor progression.

**Methods** A total of 20 patients with 32 acoustic tumors underwent GKS. Among of them, we investigated hearing function in the 16 cases with serviceable hearing (Gardner & Robertson: 12 class 1 & 4 class 2), and their Koos classification: 7 stage I, 4 stage II, 2 stage III, and 3 stage IV. In all patients, before starting to create the dose planning on Gamma Plan, we perfectly visualized small bony structures; cochlea, horizontal bar, Bill's bar, facial notch, superior and inferior vestibular groove, and then tried to assign three nerve divisions of acoustic nerve as tumor origin; superior vestibular, inferior vestibular, and cochlea nerve in each. We should grasp the anatomical relationship based on 4 dimensional tumor pathology. They were treated with the use of high-resolution magnetic resonance imaging fused with bone image; creation of the highly precise conformal and selective multi-isocenter dose planning with small collimators, carefully sparing adjacent cranial nerves of any excessive irradiation, and created a wide 80 % isodose area within the tumor while applying an adequate marginal dose (mean 11.9 Gy) at the 50 % isodose line.

**Results** Among 13 patients who were followed 74.4 months in average (24-195 months) after treatment, the tumor control and shrinkage rates were 93.8 % and 43.8%, respectively. Preservation of serviceable hearing reached in 81.3 %, especially 91.7% in G&R class 1 cases. There was no major morbidity including facial nerve function.

**Conclusions** Due to contemporary technological and methodological achievements based on microanatomy, GKS provided most of patients with NF2 maintenance of serviceable hearing. This clinical results predicts that GKS can prevent hearing malfunction at the earliest stage of less axon damage due to nerve sheath tumor progression, and can recommend that the patient who has solitary acoustic tumor with serviceable hearing should be treated by GKS as early as possible to maintain hearing preservation.

## Long term effects of Gamma Knife radiosurgery for skull base meningiomas

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**Introduction** Stereotactic radiosurgery is now a treatment option for skull base benign meningiomas. Surgery of these lesions has been complicated and high recurrence is seen in residual tumors

**Methods** We have treated 1190 benign meningiomas between April 1998 and April 2021 of which 856 were skull base meningiomas. Total 482 were treated 10 years after treatment and 458 were analyzed. 51% tumors were in CP angle and cavernous sinus region.

**Results** Total 482 were treated 10 years after treatment and 458 were analyzed. 51% tumors were in CP angle and cavernous sinus region. Local tumor control rates were 86% and 90% at 10 years and 15 years, respectively. Tumors with volume <15cc and average prescribed dose 12.6 Gy dose at first 5 year showed 99% tumor control. Tumors >15cc average prescription 11.8Gy at first 5year showed control rate of 97%. In first 10 years and later over all control & reduction was 96 & 90% respectively. New Cranial nerve deficits about 5% among cavernous sinus region tumors. 45 cases had undesired results, second treatment on 51% of undesired result treated for extension of original and 20% on treated tumor. 13 tumors increase but remained untreated. Unusual high edema seen in parietal parasagittal region tumors.

**Conclusions** Stereotactic radiosurgery was effective treatment method for local control of skull base meningiomas, especially for small or postoperative residual tumors. Correct combination of microsurgery and radiosurgery leads to excellent local control.

## Long-term outcomes of stereotactic radiosurgery for skull base tumors involving the cavernous sinus

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**Introduction** Stereotactic radiosurgery (SRS) is an effective and less invasive therapeutic option for cavernous sinus (CS) tumors. However, its long-term effectiveness efficacy and neurological outcomes remain to be demonstrated. We aimed to examine the long-term outcomes of SRS for CS tumors.

**Methods** Overall, 127 patients with benign CS tumors, including 91 with meningioma, 14 with trigeminal schwannoma (TS), 14 with non-functioning pituitary adenoma (PA), and 8 with cavernous hemangioma (CH), treated with SRS at our institution from 1990 to 2018, were included. Tumor control and functional preservation/recovery were evaluated in detail.

**Results** The mean post-SRS follow-up period was 102 months. The progression-free survivals (PFSs) were 97% at 5 years, 90% at 10 years, and 88% at 15 years for the entire cohort; 96% at 5 years and 87% at 10 years for meningiomas; and 100% at 10 years for the other tumors. No significant difference was observed among the tumor types (log-rank test; meningioma vs. TS,  $p = 0.232$ , meningioma vs. PA,  $p = 0.297$ , meningioma vs. CH,  $p = 0.277$ ). Improvement in cranial nerve (CN) function was observed in 35 (27%) patients. TSs tended to show CN improvements more often than meningiomas did (total improvements, 62% vs. 23%;  $p = 0.004$ , eye movement function, 100% vs. 20%;  $p = 0.002$ ). Deterioration or new development of CN deficits was observed in 11 (9%) patients.

**Conclusions** SRS provides durable tumor control and contributes to sufficient preservation of CN function.

## Long-term risks of hemorrhage and adverse radiation effects of stereotactic radiosurgery for brain arteriovenous malformations

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**Introduction** The information about long-term risks of hemorrhage and late adverse radiation effects (AREs) after stereotactic radiosurgery for brain arteriovenous malformations (AVMs) is lacking. This study investigated the annual hemorrhage rates, nidus obliteration rates, late ARE rates, and their associating factors in AVM patients treated with gamma knife surgery (GKS).

**Methods** We examined 1327 AVM patients treated with GKS. The Spetzler-Martin grade was I in 329 patients (25%), II in 423 (32%), III in 479 (37%), and IV/V in 96 (7%). The median treatment volume was 2.5 cm<sup>3</sup>, and the median marginal dose was 20 Gy.

**Results** The median follow-up period was 57 months. The five- and 10-year nidus obliteration rates were 64% and 83%, respectively. Smaller treatment volume ( $p < 0.001$ ), Spetzler-Martin grades I – III ( $p = 0.002$ ), and no pre-GKS embolization ( $p = 0.003$ ) significantly associated with nidus obliteration. The five- and 10-year cumulative hemorrhage rates were 7% and 10%, respectively. Larger treatment volume significantly associated with AVM rupture ( $p = 0.001$ ). The annual hemorrhage rate was 1.6% for the first five years post-GKS, which decreased to 0.5% thereafter. During the follow-up period, 42 symptomatic cyst formations/chronic encapsulated hematomas (CFs/CEHs, 3%) and three radiation-induced tumors (RITs, 0.2%) were observed. The 10- and 15-year cumulative ARE rates were 4.2% and 10.6%, respectively. Larger treatment volume ( $p = 0.001$ ), the use of more isocenters ( $P = 0.01$ ), and women ( $p = 0.02$ ) significantly associated with the development of late AREs.

**Conclusions** GKS is associated with reduced hemorrhage risk and high nidus obliteration rates in AVM patients. The incidence of late AREs tended to increase over time. The most common ARE was CF/CEH, which can be safely removed; however, careful attention should be paid to the long-term development of fatal RITs.

## Multimodal treatment for ruptured arteriovenous malformations at our institution with three modalities

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**Introduction** Ruptured brain arteriovenous malformations (AVMs) have an increased risk of rebleeding within one year. Our institution aims for curative treatment with multimodalities, including direct surgery, interventional radiology (IVR), and gamma knife radiosurgery (GKS). We reviewed therapeutic strategies and outcomes of ruptured AVMs at our institution.

**Methods** Of the AVMs treated at our institution from April 2002 to September 2022, 183 AVMs with bleeding within one year were included in this study. We retrospectively reviewed their treatments and outcomes with medical records. Ruptured AVMs initially treated with IVRs or direct surgeries at other hospitals were excluded. As a basic protocol for ruptured AVMs, direct surgery was the first choice, except for eloquent areas and deep lesions treated with GKS.

**Results** 97 AVMs (53%) were Spetzler-Martin (SM) grade 1–2, and follow-up periods were  $73 \pm 62$  months. Direct surgery was performed in 82 AVMs (45%) and GKS in 89 AVMs (49%). IVR was combined with direct surgery in 46 AVMs (25%) and GKS in 13 AVMs (7%), respectively. Direct surgery was significantly more common in Grades 1–2 (direct surgery, 63%; GKS, 34%,  $p < 0.01$ ), and GKS was more common in Grades 3–5 (direct surgery, 24%; GKS, 66%,  $p < 0.01$ ). 17 AVMs (9.3%) had rebleeding during follow-up (15 AVMs after GKS and 2 patients with medical therapy only). Durations between the primary treatment and rebleeding was  $22 \pm 23$  months. Final modified Rankin scale (mRS) 0–2 was more common in AVMs with the interventional therapies (interventional therapies, 147 AVMs, 86%; medical treatment only, 3 AVMs, 25%,  $p < 0.01$ ), whereas worsening to final mRS 3–6 was fewer (interventional therapies, 22 AVMs, 13%; medical treatment only, 8 patients, 67%,  $p < 0.01$ ). The obliteration rate was 95.1% in the direct surgery and 60.3% in AVMs followed more than three years.

**Conclusions** The development of rebleeding in patients with ruptured AVMs exacerbate their life and functional prognoses. Aggressive therapeutic intervention with multimodalities aiming for high embolization rate can potentially prevent rebleeding and achieve a good functional prognosis.

# General Session

## Abstracts





## Long-term outcomes of Gamma Knife radiosurgery for central neurocytoma

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**Introduction** Central neurocytomas (CNs) are rare, benign WHO grade II tumors with the majority found in the intraventricular location. We analyzed the long-term results of primary and adjuvant GKRS for CNs.

**Methods** We performed a retrospective analysis on patients diagnosed with CNs and treated with either primary or adjuvant GKRS from 1998 to 2017 to ensure a follow-up period greater than 5 years. Recurrences were defined as greater than 20% volume increase compared with the previous MR images. Tumor volumes were measured manually using the volumetric method. Outcomes such as progression-free survival, local control rate, residual tumor size, functional status, complications and mortality were evaluated. Tumor volume ratios were calculated as the ratio of follow up tumor volume to initial tumor volume and plotted against time to extrapolate the annual volume change rate.

**Results** A total of forty-seven patients were enrolled in this study between 1998 and 2017. The mean age was 34.2 years (range 11-62). Male to female ratio was 27:20. 29 patients (61.7%) were treated with primary GKRS 18 patients (38.3) underwent adjuvant GKRS following surgical resection. The mean clinical and radiological follow-up in months was 127.8. The most common presenting symptoms were headache, nausea or vomiting seen in 23 patients (48.9%). Mean GKRS dose was 15.57 (range 6-20Gy). Local tumor control was achieved in thirty-six patients (76.6%) and eleven patients (23.4%) experienced recurrence. 8 patients had in-field recurrence (17.0%) and 3 had out-of-field recurrences (6.4%). Primary GKRS group had greater local tumor control rate compared with the adjuvant GKRS group (86.2 vs. 61.1,  $p = 0.048$ ).

**Conclusions** Gamma knife radiosurgery is a safe and effective option as a primary and adjuvant treatment for CN.

## AG1-2

## Central neurocytoma with hemorrhage during Gamma Knife surgery: Case reports and review of the literature

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**Introduction** We evaluated 19 central neurocytomas (CN) at Seoul National University Bundang Hospital that underwent Gammaknife surgery (GKS) between 2009 and 2021. We reviewed 6 cases of neurocytoma with intraventricular hemorrhage (IVH), which is uncommon in central neurocytoma. CN is a highly vascularized and well-circumscribed tumor located in lateral ventricle; usually arise from the neuronal cells of septum pallucidum, fornix, or subependymal plate of lateral or third ventricle. Conventional treatment of CN is complete resection of tumor, usually leading to cure and long-term survival.

**Methods** We divided the groups of CN into primary and secondary applications of GKS; ten patients underwent GKS at the beginning, whereas nine patients received GKS following craniotomy and tumor excision. The patients consisted of 12 males and 7 females with intraventricular lesions. The median age was 37.6 years (range: 21-64) and the median tumor volume at GKS was  $7.2 \pm 8.7\text{cc}$  (0.31-38.67). Initial tumor volume was  $24.0 \pm 25.9\text{cc}$  (2.48-79.11) and marginal dose (Gy) was  $15.8 \pm 2.5$  (13-24). Progression free survival [PFS](month) was  $46.3 \pm 37.8$  (5.47-126.7) and the recurrence ratio was 21% with the average PFS was 27.7month.

**Results** Six intraventricular hemorrhages (IVH) occurred; three patients before initial GKS and the other three patients after GKS. Due to the fact that only one of these patients underwent a tumor biopsy prior to GKS, we were unable to investigate the immuno-histochemical backgrounds of IVH but may presume neuroradiological differences based on MR images. Six cases exhibited honeycomb-like morphology with multiseptated lobules, and their initial mean tumor volume was 21.1cc. Only one patient underwent GKS after surgery.

**Conclusions** Incidence of CNs with bleeding has been underestimated, previously misdiagnosed as oligodendrogliomas or cavernous malformations. Thus, when intraventricular mass with IVH is found, it is recommended to perform a tumor biopsy with suspicion of the possibility of CN. The specific etiology of CN bleeding is unknown; however, it may be due to increased vascularity and hemodynamic stress resulting from arteriovenous shunting, venous obstruction by tumor encasement, and weak tumor arteries. And it is also related with etiologic variables such as cardiovascular disease, thrombocytopenia, and in our study, a patient who gave birth 3 months before to IVH.

## Stereotactic radiosurgery for orbital cavernous hemangiomas: a single-center experience over a 22-year period

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**Introduction** Orbital cavernous hemangioma (OCH) is a common orbital lesion in Asian adults. Surgery is the most common treatment, but severe complications such as major bleeding and injury to surrounding neurovascular structures are not infrequent. Among the stereotactic radiosurgery modalities, Gamma Knife radiosurgery (GKRS) has been known for its precise delivery of high-dose radiation to targets within the skull and orbit, but the safety and clinical effectiveness of single-session GKRS treatment for OCHs remain unknown.

**Methods** Patients who presented with an OCH between September 1999 and May 2022 and were treated with single-session GKRS were included in this single-center cohort study.

**Results** There were 23 patients (7 males and 16 females) in this study. The median margin dose was 12 Gy (range 11–13 Gy). The median clinical and radiological follow-ups were 45 months (range 5–190 months) and 45 months (range 6–190 months), respectively. Nine (69.2%) of 13 patients with visual acuity impairment had improvement in best corrected visual acuity. Of the 8 patients with visual field defects, 5 patients (62.5%) had complete resolution. Tumor regression was observed in 22 patients (95.7%). The mean relative reduction in tumor volume was  $82.6\% \pm 23.7\%$ . The relative reductions in tumor volume were 33%, 49%, 72%, 84%, and 89% at 6, 12, 24, 36, and 48 months, respectively. Adverse effects of radiation were not observed.

**Conclusions** GKRS appears to be safe and efficacious for treating OCHs over long-term follow-up. The treatment is associated with a high rate of regression in OCHs and remarkable improvement in both visual acuity and visual field deficits.

## Reasonable timing to treat vestibular schwannomas with gamma knife surgery: serial observation of untreated small tumors and remnants after surgery

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**Introduction** Although gamma knife surgery (GKS) has been an established treatment option for vestibular schwannomas (VSs), there is no consensus regarding the treatment timing and the indication for postoperative residual tumor. In this study, tumor growth was analyzed by measuring the volume of untreated small VSs and postoperative residual tumors. The GKS intervention timing for VSs was discussed.

**Methods** From a VSs database collected at our hospital since 2010, 53 untreated VSs (Koos grade 1–2) and 44 patients with residual tumors <1 mL after surgical resection were included. Tumor growth was measured by volumetry on MRI images and a >20% difference was defined as a change in tumor volume. The Kaplan–Meier method was used to analyze the risk factors for tumor growth in untreated tumors and residual tumor growth frequency after surgery.

**Results** Untreated small VSs demonstrated tumor growth 61.2% at 5 years. Cerebellopontine angle (CPA) extension and sway velocity (SV) with eyes open of posturography were related to tumor growth. The tumor growth-free survival of patients with CPA extension and intracanalicular tumor at 2 years were 37.3% and 76.4%, respectively. Tumor growth free survival of patients with high and low SV at 2 years was 30.8% and 68.9%, respectively. The Cox hazard model demonstrated a significant risk for future tumor growth at high SV. Postoperative residual tumors <1 mL demonstrated 30% tumor growth at 5 years. Postoperative residual tumors grew significantly less than untreated VSs matched by tumor volume. The tumor volume was reduced in 9% of patients with residual tumors.

**Conclusions** In untreated VSs, the tumor growth risks were tumor size and tumors with balance abnormalities. Patients with disequilibrium should be under regular follow-up MRI to detect tumor growth. Early intervention might be appropriate for these patients. On the other hand, postoperative small residual tumors grew less frequently than those with natural history and in some cases, shrunk, suggesting that follow-up is appropriate. However regular MRI follow-up is also mandatory.

## Gamma Knife radiosurgery treatment results for older (age of $\geq 75$ ) patients with vestibular schwannoma

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**Objective** This study aims to compare the results of Gamma Knife Radiosurgery (GKS) for vestibular schwannoma (VS) in older patients aged 75 years or older with those of patients younger than 75 years old.

**Methods** A total of 723 consecutive patients with unilateral VS who underwent GKS at two institutions over 23 years were included in this study. We analyzed tumor control, overall survival, transient expansion, hydrocephalus, and facial nerve dysfunction by comparing 80 patients in the older group and 643 patients in the younger group.

**Results** The older group had more women, larger tumor volumes, and lower prescribed doses. The median overall survival time after GKS was significantly shorter in the older group. (10-year survival rate, 69.4% vs. 89.4%,  $p < 0.0001$ ) Cumulative 5- and 10- year incidence of tumor control failure tended to be higher in the older group (7.2% and 9.5%, respectively) than in the younger group (3.8% and 5.9%, respectively,  $p = 0.06$ ). The incidence of hydrocephalus was significantly higher in the older group compared to the younger group (16.4% vs. 5.0% at 5 years,  $p = 0.0001$ ). There were no significant differences in duration of transient expansion or incidence of facial nerve dysfunction.

**Conclusions** The indication of GKS should be made carefully for VS patients aged  $\geq 75$ , since older patients have a shorter life expectancy, relatively poor tumor control, and higher incidence of hydrocephalus.

## Long-lasting transient volume expansion of sporadic vestibular schwannomas after stereotactic radiosurgery: Is it tumor progression?

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**Introduction** Transient volume expansion (TVE) of vestibular schwannomas (VSs) is a well-known phenomenon, and it subsequently regresses usually within the first two years after stereotactic radiosurgery (SRS). In this study, we analyzed how much TVE occurs and how it changes after SRS for sporadic VSs.

**Methods** We performed a retrospective study of patients with VS treated with SRS during 2009–2018. One hundred eighty-eight patients had at least 24 months of clinical and radiographic follow-up and were included. Volume expansion was defined as a volume increase at any time with a loss of central contrast enhancement after SRS.

**Results** The mean tumor volume at SRS was  $2.7 \text{ cm}^3$  (range 0.01–20.7  $\text{cm}^3$ ). The mean marginal dose to the tumor was 12.4 Gy (range 6.0–15.0 Gy). The mean follow-up period was 78.7 (28.0–148.0) months. The overall tumor control rate was 92.0 %. After SRS, 155 (82.4%) of patients demonstrated volume expansion. The median time of volume expansion was 6 (2.0–37.0) months after SRS. In 105 (67.7%) among patients with post-radiosurgery tumor volume expansion, the tumor subsequently regressed within the first 24 months after SRS. However, in fifty-five (35.5%) patients, the tumor was still enlarged even after 24 months after SRS compared to the initial tumor volume. Among them with volume expansion even after 24 months after SRS, thirty-eight (69.1%) patients finally had tumor shrinkage at 45.7 (range 25.0–100.0) months after development of TVE. Tumor regression after TVE was identified in 11 (20.0%) patients after 3 years, 2 (3.6%) patients after 4 years, 6 (10.9%) patients after 5 years, and 3 (5.5%) patients after 6 years after TVE development. However, seventeen (30.9%) patients did not show a resolution of the increased tumor volume until the last follow-up period (30–141 months).

Among 55 patients with tumor volume expansion over 24 months after SRS, forty-nine (89.1 %) had not had any neurological symptoms related with tumor volume expansion, while 6 (10.9%) patients experienced additional surgery for tumor progression.

**Conclusions** TVE after SRS for VSs usually occurs and regressed within the first 24 months after SRS. However, in approximately one-third of patients, TVE seems to be delayed after 24 months after SRS, and in some patients even after 6 years. Thus, additional treatment for VSs with volume expansion after SRS should be decided cautiously considering this phenomenon of the long-lasting TVE, especially in patients with no neurological symptoms related with tumor volume expansion.

## Using the deformity index of vital structures to predict outcome of patients with large vestibular schwannomas after Gamma Knife radiosurgery

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**Introduction** Microsurgery is the mainstay of treatment for large vestibular schwannomas (VS), but the benefits of radiosurgery remain incompletely defined. Here, we aim to use automated volumetric analysis software to quantify the degree of brain stem deformity and other tumor characteristics, and then use such information to predict long-term outcomes of patients with large VS following GKRS.

**Methods** Between 2003 and 2020, 39 patients with large VS (volume >8 cc) undergoing GKRS with a margin dose of 10-12 Gy were with available MRI data and complete medical records. With 3-dimension (3D) MRI, we reconstructed the tumor, brainstem, and cerebellum to evaluate the extent of deformity of these vital structures for predicting the long-term outcome of patients.

**Results** Their mean tumor volume was  $13.9 \pm 6.1$  cc, and their mean follow-up after GKRS was  $86.7 \pm 65.3$  months. Favorable clinical outcome was observed in 26 (66.7%) patients, while 13 (33.3%) patients had treatment failure. Patients with small tumor volumes, low vital structure deformity indice (TV/BSV+CerV / and TV+EV/BSV+CerV), and long distance of tumor to the central line were more likely to have favorable clinical outcome after GKRS: specifically, Good vs Poor:  $12.3 \pm 5.3$  cc vs  $17.1 \pm 6.6$  cc ( $p < 0.01$ ),  $0.1 \pm 0.1$  vs  $0.2 \pm 0.1$  /  $0.12 \pm 0.06$  vs  $0.20 \pm 0.09$  ( $p < 0.01$  /  $p < 0.001$ ),  $4.5 \pm 3.8$  mm vs  $-0.2 \pm 3.5$  mm ( $p < 0.001$ ). Significant prognostic value was found with the following: tumor shrinkage ratio >50% ( $p < 0.01$ ), CV ( $p < 0.01$ ), CV/TV ( $p < 0.05$ ), TV/CerV ( $p < 0.05$ ), TV+EV/BSV+CerV ( $p < 0.05$ ) and the distance of tumor to the central line ( $p < 0.05$ ). In cox regression, favorable clinical outcome was highly correlated with the Charlson comorbidity index and cochlear dosage (both  $p < 0.05$ ). In multivariant analysis, tumor regression was highly correlated with the CV/TV ratio ( $p < 0.001$ ).

**Conclusions** The brainstem deformity ratio is likely a useful index to assess the clinical and tumor regression outcomes. Clinical outcomes are multifactorial and include factors such as image alterations, medical status, and cochlear function. We found that tumor regression was highly correlated with the ratio of cystic components, thereby indicating tumor characteristics contributed to tumor regression.

## Quantification of tumor response of cystic vestibular schwannoma to Gamma Knife radiosurgery by using artificial intelligence

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**Introduction** Gamma Knife radiosurgery (GKRS) is a common treatment modality for vestibular schwannoma (VS). The ability to predict treatment response is important in patient counseling and decision-making. The authors developed an algorithm that can automatically segment and differentiate cystic and solid tumor components of VS. They also investigated associations between the quantified radiological features of each component and tumor response after GKRS.

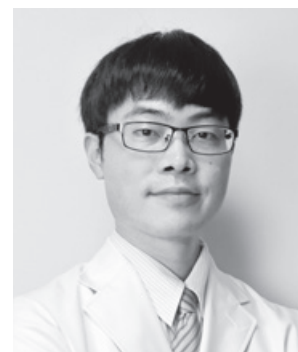
**Methods** This is a retrospective study comprising 323 patients with VS treated with GKRS. After preprocessing and generation of pretreatment T2-weighted (T2W)/T1-weighted with contrast (T1WC) images, the authors segmented VSs into cystic and solid components by using fuzzy C-means clustering. Quantitative radiological features of the entire tumor and its cystic and solid components were extracted. Linear regression models were implemented to correlate clinical variables and radiological features with the specific growth rate (SGR) of VS after GKRS.

**Results** A multivariable linear regression model of radiological features of the entire tumor demonstrated that a higher tumor mean signal intensity (SI) on T2W/T1WC images ( $p < 0.001$ ) was associated with a lower SGR after GKRS. Similarly, a multivariable linear regression model using radiological features of cystic and solid tumor components demonstrated that a higher solid component mean SI ( $p = 0.039$ ) and a higher cystic component mean SI ( $p = 0.004$ ) on T2W/T1WC images were associated with a lower SGR after GKRS. A larger cystic component proportion ( $p = 0.085$ ) was associated with a trend toward a lower SGR after GKRS.

**Conclusions** Radiological features of VSs on pretreatment MRI that were quantified using fuzzy C-means were associated with tumor response after GKRS. Tumors with a higher tumor mean SI, a higher solid component mean SI, and a higher cystic component mean SI on T2W/T1WC images were more likely to regress in volume after GKRS. Those with a larger cystic component proportion also trended toward regression after GKRS. Further refinement of the algorithm may allow direct prediction of tumor response.



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#### 【Award】

1. Travel grant award, the World Federation of Neuroradiological Societies, 2019
2. First prize for Paper of the year, Neuroradiological Society of Taiwan, 2019
3. Bronze medal for best oral presentation, Asian-Oceanian Society of Neuroradiology, 2021
4. Outstanding teacher, National Yang Ming Chiao Tung University, 2022

#### 【Publications】

1. Hu YS, Lin CJ, Wu HM, et al. Lateral sinus dural arteriovenous fistulas: sinovenous outflow restriction outweighs cortical venous reflux as a parameter associated with hemorrhage. *Radiology*. 2017 Nov; 285 (2): 528-535. SCI IF=29.146; Rank: 0.7% (1/136)
2. Hu YS, Guo WY, Lee IH, et al. Prolonged cerebral circulation time is more associated with symptomatic carotid stenosis than stenosis degree or collateral circulation. *J Neurointerv Surg*. 2018 May; 10 (5): 476-480. SCI IF=8.581; Rank: 7.1% (1/14)
3. Hu YS, Lee CC, Guo WY, et al. Trigeminal nerve atrophy predicts pain recurrence after Gamma Knife stereotactic radiosurgery for classical trigeminal neuralgia. *Neurosurgery*. 2019 Apr; 84 (4): 927-934. SCI IF=5.315; Rank: 12.3% (26/211)
4. Hu YS, Guo WY, Lin CJ, et al. Magnetic resonance imaging as a single diagnostic tool for verifying radiosurgery outcomes of cavernous sinus dural arteriovenous fistula. *Eur J Radiol*. 2020 Apr; 125: 108866. SCI IF=4.531; Rank: 31.6% (43/136)
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6. Hu YS, Lee CC, Wu HM, et al. Stagnant venous outflow in ruptured arteriovenous malformations revealed by delayed quantitative digital subtraction angiography. *Eur J Radiol*. 2021 Jan; 134: 109455. SCI IF=4.531; Rank: 31.6% (43/136)
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## Brain arteriovenous malformations and dural arteriovenous fistulas: risk evaluations and radiosurgical outcome prediction

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The brain arteriovenous malformations (BAVMs) account for 4% to 33% of intracranial hemorrhages, and are associated with a 50% neurological morbidity rate and a 12% mortality rate. Annual hemorrhage rates for BAVMs vary from 1% to 33%, depending on the clinical and anatomical features. Interventions for BAVMs carry different complication risks. Therefore, individualized risk assessment is crucial for physicians to determine the optimal treatment. Quantitative digital subtraction angiography (QDSA) techniques have been developed to objectively reflect hemodynamic changes associated with disease severity and therapeutic effects. In QDSA measurements, a venous stasis index, defined as the inflow gradient divided by the absolute value of the outflow gradient, shows the stagnant degree of BAVM venous drainage. A larger venous stasis index is an objective sign related to BAVM hemorrhage with a comparable diagnostic performance to exclusive deep drainage in angioarchitectural analysis. The QDSA measurements for drainage veins are more reliable than those for feeding arteries. QDSA reflects stagnant venous drainage in association with BAVM hemorrhage, but should be performed at least 1 month after BAVM hemorrhage to minimize the hemodynamic confounders. Gamma Knife radiosurgery (GKRS) is an effective and minimally invasive treatment option for patients with BAVMs. GKRS achieves complete obliteration in 65% to 82% of BAVMs after a latency period of 2 to 3 years. BAVMs with a larger stasis index may predict obliteration after GKRS. In addition to hemorrhage, radiation-induced changes (RICs) are major causes of neurological deficits for patients with BAVMs after GKRS. RICs, seen as increased perinidal T2-weighted hyperintensity on MRI, are commonly observed within 2 years after GKRS. Large BAVMs and neoangiogenesis on DSA before GKRS and thrombus within nidus or drainage vein on follow-up MRI are associated with moderate to severe RICs in treatment-naïve patients with BAVMs. Symptomatic RICs are more likely to develop in basal ganglia or brainstem.

Dural arteriovenous fistulas (DAVFs) comprise approximately 10% to 15% of intracranial vascular malformations and most frequently occur in the cavernous sinus (CS) and lateral sinus (LS). DAVFs may behave either benignly or aggressively, according to their venous drainage patterns and locations. Cortical venous reflux (CVR) and venous ectasia have been considered to be of high risk of hemorrhage according to the two most commonly used classification schemes: Borden and Cognard. On the angiography of LSDAVF, the combined conduit score (CCS) is defined as the sum of the proximal and distal conduit scores based on the patency of sinovenous conduits distal (downstream) and proximal (upstream) to the DAVF, ranging from 0 (total occlusion) to 8 (full patency). Sinovenous outflow restriction (SOR), indicated as a CCS of  $\leq 2$ , had a stronger association with hemorrhage than CVR in LSDAVFs, because SOR may precipitate the buildup of high intracranial pressure by the DAVFs. GKRS can serve as a primary treatment for low-risk DAVFs or patients who are not amenable to endovascular therapy or microsurgery. Several studies have investigated the factors associated with DAVF obliteration after GKRS and some suggested that CS and non-CS DAVFs should be considered different entities. CSDAVFs with fewer venous drainage routes are more likely to be obliterated after GKRS. By contrast, LSDAVFs with a nearly patent outflow are more likely to achieve obliteration. Unenhanced MRI/ 3D TOF MRA at 1.5 T is a reliable follow-up imaging technique for demonstrating CSDAVF obliteration after GKRS with observed specificity of 100% and sensitivity of 84%. A restrictive change of outflow can be observed in some LSDAVFs after GKRS without associated symptoms. Follow-up imaging after GKRS revealed that patients with SOR had a lower LSDAVF obliteration rate. Angioarchitectural and QDSA analyses may assist with hemorrhage risk assessment and GKRS outcome prediction for patients with BAVMs and DAVFs.

## Gamma Knife radiosurgery for the clival epidural-osseous dural arteriovenous fistulas

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**Introduction** Clival epidural-osseous dural arteriovenous fistulas (DAVF) are often associated with large nidus, multiple arterial feeders, and complex venous drainage. We investigated the outcomes of a series of clival epidural-osseous DAVFs treated using GKS.

**Methods** Thirteen patients with clival epidural-osseous DAVF were treated using GKS in our institution between 1993 and 2015. The age at the time of GKS ranged from 38-76 years (median 55 years). Eight patients were defined as Cognard class I, four patients were class IIa, and one patient was class IIa+b. The median treatment volume was 17.6 cm<sup>3</sup> (range: 6.2–40.3 cm<sup>3</sup>). The median prescribed margin dose was 16.5 Gy (range: 15–18 Gy). Clinical and radiographic follow-ups were performed at 6-month intervals. Patient outcomes after GKS were categorized as: 1) complete improvement, 2) partial improvement 3) stationary, and 4) progression.

**Results** All 13 patients demonstrated symptomatic improvement, and 12 of 13 patients achieved complete obliteration and one patient had partial obliteration on catheter angiography. The median follow-up period was 26 months (range: 14–186 months). The median latency period from GKS to obliteration was 21 months (range: 8–186 months). There was no intracranial hemorrhage during the follow-up period, and no mortality was observed. One definite complication was observed following treatment, and two patients required repeat GKS treatment with eventual complete obliteration.

**Conclusions** GKS offers a safe and effective primary or adjuvant treatment modality for complex clival epidural-osseous DAVFs. All patients in this case series demonstrated symptomatic improvement, and almost all patients achieved complete obliteration.

## AG2-3

### Radiosurgical outcome of intracranial avms planned on DSA and MRI for Gamma Knife stereotactic radiosurgery versus MRI alone

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**Introduction** Gamma Knife radiosurgery (GKRS) is a standard treatment for arteriovenous malformations (AVMs). Digital subtraction Angiography (DSA) has been traditionally used to localize the nidus while planning GKRS, though it is an invasive procedure. However, few recent studies have described the use of MRI to localize the nidus in place of DSA. The aim of the current study is to compare the outcome when GKRS planning is done based on DSA and MRI or MRI alone.

**Methods** All patients with AVM who underwent Gamma Knife Radiosurgery from 1<sup>st</sup> January, 2011 to 30<sup>th</sup> June, 2018 were included in this retrospective study and divided based on following criteria:-

Group A – Patients in whom Gamma Knife treatment was planned on MRI and DSA together

Group B - Patients where the Gamma Knife treatment was planned on MRI alone

The obliteration of AVM as confirmed with DSA was recorded.

**Results** 224 patients were included in the study. Both the groups were comparable as per age gender, pre-Gamma Knife embolization and pre-GKT microsurgery status. However, the MRI alone group had a higher percentage of higher SM grade patients (p-value of 0.0072). There was no statistically significant difference between baseline AVM volume and marginal AVM dose between two groups.

It was found that at 2 years follow up, the obliteration rate was more in Group B i.e. 25% compared with 11.34% in Group A (p=0.06973). Similarly, the obliteration rates comparison at 3 years and 5 years were not significant between Groups A and B. In Group A, 97 patients out of 148 felt symptomatic improvement (65.5%) compared with 51 out of 76 patients in Group B (67.1%) (p=0.8953). Ten out of 148 patients (6.8%) had post GKT bleeding in Group A compared with 5 out of 76 patients (6.6%) in Group B (p=0.9597). Nine patients in Group A (6.08 %) and 1 patient in Group B (1.3 %) died due to post GKT bleed and sequelae (p=0.2792). In Group A, 39 out of 148 patients (26.35%) had ARE (Adverse Radiation Effects) compared with 26 out of 76 (34.21%) in Group B (p=0.2197).

**Conclusions** GKRS treatment of AVMs planned on MRI and DSA does not add statistically significant advantage over the AVMs planned on MRI alone. The comparative obliteration rates were either equal or non-significantly higher in the MRI alone group as compared to the combined MRI and DSA group at 2-year, 3-year and 5-year follow up. There was no significant difference between post radiation sequelae and adverse effects between the two groups.



## Usefulness of Elements workstation (Brainlab) in stereotactic radiosurgery/stereotactic radiotherapy treatment planning

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**Introduction** Ookuma hospital started Gamma Knife Icon stereotactic radiosurgery and stereotactic radiotherapy (SRS/SRT) in this past September (from Sep. 26th, 2022). Usefulness of Elements workstation (Brainlab, Munich) in treatment planning of GammaPlan-based Icon SRS/SRT.

**Methods** In one case of large meningioma, one of large pituitary adenoma, and four of cerebral arteriovenous malformation (AVM), contouring of targets and organs at risk (OARs) were performed initially on Elements workstation and then those object sets were transferred to GammaPlan workstation. Dose planning was continued on GammaPlan workstation. Finally on the treatment day, dose planning was optimized and finalized on the images fused to thermoplastic mask-based Icon stereotactic CBCT (cone-beam computed tomography) images.

**Results** In cases of large meningioma and large pituitary adenoma involving the optic pathways, contouring of targets and OARs were performed comfortably in details on Elements workstation, because multiple image series (CT and MRIs of T1WI, T2WI, heavy T2 images, 3D-gradient echo images, and so on) can be handled on it.

In cases of AVMs, 2D-angiograms can be fused with 3D-MRIs and CTs. Therefore, stereotactic angiography with invasive skull frame equipped with fiducial system is not needed. In addition, contouring of AVM nidus was performed comfortably in details on Elements workstation, because those image series, including multi-phase angiograms, can be easily handled.

**Conclusions** Elements workstation, in addition to GammaPlan, enables more precise and more comfortable treatment planning of Icon SRS/SRT, especially skull base tumors and AVMs.

## AG3-2

## Long term results of Gamma knife radiosurgery for essential trigeminal neuralgia: final clinical evaluation of the role and needs according to more than 100 patients with at least 10 years follow up

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**Introduction** Although the early and middle-term efficacy of Gamma Knife surgery (GKS) for medical refractory essential trigeminal neuralgia (eTGN) has been reported, long-term evaluations are very limited. Our institutional initial clinical results which investigated 130 patients with at least 3 years follow up, had already reported in 2011 as follows; 86% experienced pain attack cessation, and 56.7% were medication free. On the other hand, 23% ones suffered from facial numbness, and 12.5% complained very bothersome. We should continue the very strict patient eligibility to recommend GKS for the patients with eTGN taking account into the severe complication of very bothersome whose rate could not be accepted, patient emotion point of view. So, we tried to investigate patient data obtained at least 10 years' post-treatment and examined the significance of this treatment with new endpoints to elucidate the true role of GKS among the modern treatments for eTGN.

**Methods** Among 249 consecutive patients with eTGN treated with GKS (Retro-Gasserian target/4-mm single isocenter/90 Gy@100%) at our institution between 2003 and 2011, 103 patients who could be followed up for at least 10 years (mean, 174 [120-219] months) after GKS and whose data were amenable to accurate evaluation were included in this retrospective study. In this study, we aimed to accurately evaluate pain attacks using the conventional BNI-P as a clinical evaluation method for pain and Engel's classification to evaluate electric discharge based on pathophysiological characteristics. The BNI-N was used to evaluate complications (facial dysesthesia).

**Results** At the last follow-up, the rate of pain attack cessation (both BNI-P I-IIIa and Engel's class I) was achieved in 58.2% (60/103), instead of 82.5% (85/103) at the initial effect. Among of the patients with pain attack recurrence, twenty eight ones (65.8%) underwent additional treatment. On the other hand, the rate of significant complication (BNI-N II-IV) which was mainly facial dysesthesia was 24.3% (25/103), including 2.9% (3/103) with very bothersome (BNI-N IV).

**Conclusions** GKS for eTGN demonstrated favorable therapeutic effects with long-term follow-up. Serious complication was a strong concern in the early and middle-term follow-up, resolved spontaneously. Therefore, the clinical indications for GKS should be expanded to patients with eTGN according to the present long-term clinical results.

## Outcome of Gamma Knife thalamotomy and biologically effective dose (BED)

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**Introduction** The purpose of this study was to investigate the results following nucleus ventralis intermedius (VIM) Gamma Knife thalamotomy (GKT) for medically-refractory tremor. In addition, we analyzed the correlation between biologically effective dose (BED) and the clinical outcome.

**Methods** Twenty patients underwent GKT for disabling tremor that did not respond to medical treatment. All of them except one patient, received unilateral GKT, and one patient underwent staged bilateral GKT. Mean age was 71.5 years (range 59-76 years). Eight patients had serious underlying medical diseases. A maximum dose of 130 Gy was administered to the VIM, using a single 4-mm isocenter. The Fahn-Tolosa-Marin clinical tremor rating scale (TRS) was used before and after GKT to evaluate the severity of tremor and changes after treatment. The measurements before and after treatment were compared using paired T-tests.

We calculated BED using the formula reported in the previous literature and conducted a regression analysis of BED and TRS score.

**Results** There were 16 evaluable patients, with available TRS scores before and after GKT. The median follow-up period was 10 months (range 1-41 months) and four patients deceased during the follow-up period. The mean scores before and after GKT was  $3.13 \pm 0.62$  and  $2.38 \pm 1.09$  for action tremor ( $p = 0.041$ ),  $2.75 \pm 1.00$  and  $2.19 \pm 0.98$  for writing ( $p = 0.003$ ),  $2.88 \pm 1.20$  and  $2.13 \pm 1.36$  for drawing ( $p = 0.002$ ),  $2.69 \pm 1.20$  and  $1.94 \pm 1.34$  for water-pouring ( $p = 0.013$ ). Three patients (18.8%) exhibited improvements in all categories of TRS scores; eight (50.0%) in two or three categories; four (25.0%) only in one category. The results of the regression analysis of BED and TRS score revealed a moderate positive correlation only between BED and action tremor score ( $r = 0.51$ ,  $p = 0.045$ ).

**Conclusions** In this study, GKT brought substantial improvements in tremor for the patients in old age or with serious medical comorbidities. A statistically-meaningful correlation between BED and clinical outcome was observed only in action tremor category. Further systemic prospective study in a large population of patients is required to find an optimal BED in GKT.

## Dynamic radiation-induced imaging changes more than 20 years following Gamma Knife surgery

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This is a case report describing a patient who was treated with Gamma Knife surgery for eight brain metastases in 1994. The patient developed an asymptomatic cyst with minimal edema at the site of one of the treated tumors seven years later. The edema subsided and the cyst stabilized. However, the patient developed an increased frequency of epileptic activity 23 years after the treatment. A MRI examination revealed that a slight edema had developed at the site of the cyst. The symptoms subsided without treatment, and the edema was no longer to be seen at the images from a follow-up MRI examination one year later. This case report illustrates that radiation induced changes may appear more than 20 years after radiosurgery. Thus, the possibility of radiation induced changes should be kept in mind as a differential diagnosis when imaging changes are observed many years after radiosurgery.

## Adverse radiation effects (ARE): The major challenging complication after stereotactic radiosurgery on intracranial lesions

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**Introduction** As the rapid widely use of stereotactic radiosurgery (SRS) in treating intracranial lesions, adverse radiation effects (ARE) are becoming major problem after SRS. The diagnosis and management of ARE after SRS are challenging. It's sometimes hard to differentiate ARE from tumor progression. Combined multiple parametric imaging tools may enhance diagnostic accuracy. The management of ARE is also an issue. To date, there are still no widely accepted guidelines available. Besides traditional methods including steroids and surgery, the anti-VEGF mono antibody bevacizumab has been shown to be effective treatment of ARE. We shared our experience in dealing with ARE at our institution and reviewed the relative literatures of the current management for ARE.

**Methods** We retrospective analysis the patients who had ARE after receiving gamma knife radiosurgery (GKRS) from Dec 2017 to Dec 2021. ARE were diagnosed by serial MRIs, MR diffusion image, MRS and PET scan. The management of ARE included observation, corticosteroids, bevacizumab and surgical resection.

**Results** There were 62 of 595 patients (10.1%) had ARE after GKRS. The median onset of ARE was 7 months. 33 patients (53%) were symptomatic, including 23 patients with metastatic tumor, 3 patients with vascular disorders and 7 patients with other disease entities. Symptoms relieved on 14/33 patients treated with corticosteroid and 12/14 patients with bevacizumab. 6 of 14 patients (42%) who receiving bevacizumab recurred ARE after withdrawing the drugs. The multivariate analysis revealed prescription dose and radiation volume are independent risk factors of developing ARE.

**Conclusions** Our results suggested ARE is not uncommon in patients receiving GKRS with half of them are symptomatic. Bevacizumab is well worked in short term result though at least 40% of the patients will recur after discontinuing the drug. The prescription dose of the lesion as well as radiation volume play an important role in developing ARE.

## Ventralis oralis anterior (Voa) deep brain stimulation plus Gamma Knife thalamotomy in an elderly patient with essential tremor

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**Introduction** Deep brain stimulation (DBS) of the ventralis intermedius nucleus (Vim) provides a safe and effective therapy for medically refractory essential tremor (ET). However, DBS may be risky in elderly patients and those with ischemic brain lesions. Gamma Knife radiosurgery (GKS) is a minimally invasive procedure, but bilateral thalamotomy is dangerous.

**Methods** We report a case of ventralis oralis anterior nucleus (Voa) DBS for dominant hand tremor plus Voa GKS for nondominant hand tremor in a very elderly patient with medically intractable ET. An 83-year-old right-handed woman visited our hospital with a medically intractable ET. Because of the ischemic lesion in the right basal ganglia, we decided to perform left unilateral DBS instead of bilateral DBS. We chose Voa as the target for DBS because, clinically, her tremor was mainly confined to her hands, and Voa had better intraoperative microelectrode recording results than Vim.

**Results** After 2 years, her right-hand tremor remained in an improved state, but she still had severe tremor in her left hand. Therefore, we performed GKS targeting the right Voa. One year after surgery, the patient's hand tremor successfully improved without any complications.

**Conclusions** Salvage Voa GKS after unilateral Voa DBS is a valuable option for very elderly patients and patients with ischemic brain lesions. We suggest that Voa GKS thalamotomy is as useful and safe a surgical technique as Vim GKS for dystonic hand tremor. To the best of our knowledge, this is the first case report using salvage Voa as the only target for ET.

## Gamma knife radiosurgery multisession providing long term tumor control of skull base meningioma

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**Introduction:** To evaluate long-term outcomes of patients who have undergone stereotactic radiosurgery for cranial base meningiomas, the authors experience of 12-year experience with these cases with follow-up to more than 7 years.

**Methods:** Between November 2008 and December 2019, the consultant Gammaknife treated benign cranial base meningiomas in 119 patients using Multisession Gamma Knife radiosurgery. The tumor volumes ranged from 1.7 to 55.3 cm<sup>3</sup> (median 8.1 cm<sup>3</sup>), and the radiosurgery doses ranged from 18 to 25 Gy (median 20 Gy) to the tumor margin.

**Results:** The mean duration of follow-up was 72.1 months (range 20–122 months). Tumor volume decreased in 55 patients (52.7%), remained stable in 56 patients (47%), and increased (local failure) in 8 patients (6%). Fourteen patients experienced tumor recurrence outside the treatment field. The progression-free survival rate, including malignant transformation and outside recurrence, was 93% at 5 years and 83% at 10 years. Neurological status improved in 16 patients (15%). Permanent radiation injury occurred in 6 patients (6%).

**Conclusions:** Gamma Knife radiosurgery is a safe and effective treatment for cranial base meningiomas as demonstrated with a long-term follow-up period of > 7 years. Surgeons must be aware of the possibility of treatment failure, defined as local failure, marginal failure, and malignant transformation; however, this may be the natural course of meningiomas and not related to radiosurgery. Good tumor Control could be achieved for long term duration.

## AG4-1

### Efficient timer errors measurements for all three collimators in Gamma Knife (GK) ICON

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**Introduction** Gamma Knife ICON has three independent collimators in diameters of 4mm, 8mm, and 16mm, and therefore three on-off timer errors. This study used two methods to measure the timer errors, aiming to establish an efficient and accurate measurement method and compared the results.

**Methods** The conventional first method was manual with a PTW Semiflex chamber. The detector, inside a 16 cm diameter sphere solid water phantom, was positioned at the focal point of a GK. The two-exposure method (Orton 1972) was used to calculate the timer errors. It took average of 3 min to measure one data point. The novel second method used a PTW diamond detector which was connected to an electrometer with the time-series data logger function to log the shot times of 6 sec, 6 sec, and 9 sec for the collimators of 4mm, 8mm, and 16mm, respectively. Each collimator was measured for 10 times for statistics purpose. A sigmoid function was used to fit the data in the transit period. Triangle function was used to fit the 4mm collimator contribution in the 16mm collimator shot. The average time collecting the charges for all three collimators were less than 5 min and the data processing time was less than 0.5 min for an i7 pc.

**Results** With the manual method, the timer errors for 4mm and 8mm collimators were 0.054 sec, 0.095 sec and -0.056 sec, respectively. The 16mm timer errors was negative which had no physical meaning. The 4mm collimator was too large for the chamber, among other reasons. With the automatic method, the timer errors for 4mm, 8mm, and 16 mm were fitted as 0.26, 0.16, and 0.48 sec, respectively. All results were positive. The 8mm timer error was shorter than 4mm's, while 16 mm collimator had the largest timer error due to its longer distance from the Block position and the unavoidable 4mm collimator contribution.

**Conclusions** For timer error measurement of the GK Icon, the conventional manual method was not adequate. The novel automatic method using the time-series data logger function of an electrometer could obtain the results correctly and efficiently.

## Use an electrometer's time-series data logger function in Gamma Knife ICON QA

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**Introduction** This study applied the time-series data logger function of an electrometer in Gamma Knife ICON QA. The manual method to use the PTW Semiflex chamber to measure the dose rate, timer accuracy, timer linearity, timer error, and transit dose has at least three issues: 1) it is strictly inaccurate because the chamber volume is too large for the 4mm collimator by which the source sectors must pass twice for each 16 mm collimator on-off action; 2) its integrated dose method is not accurate enough to measure the low tenth of a sec time error for the 4 mm and 8 mm collimator; 3) it is time consuming and random error prone. All can be overcome by the method in post processing the differential data collected using the time-series data function of an electrometer.

**Methods** A PTW chamber, inside a 16 cm diameter sphere solid water phantom, was positioned at the focal point of a GK. The chamber was connected to an electrometer of time-series data logger function with its sampling rate at 0.5 sec. Only 16 mm collimator was measured in the monthly QA. The current-time data was logged for four shots of 0.5, 1, 5, and 10 minutes. A collimator size correction factor was applied to the unavoidable 4 mm collimator contributions. The charge was the integration of the current over time. The dose rate, timer accuracy, timer linearity, timer error, and transit dose were obtained from the dose- shot time linear fitting.

**Results** For monthly QA, the dose rate, timer accuracy, timer linearity, timer error, and transit dose were 3.13 Gy/min, 59.5 sec, 1.00, 0.02 sec, and 0.001 Gy, respectively. The data collection time was about the exposure time, and the data processing time was less than 1 min on an i7 pc.

**Conclusions** This study demonstrated that a time-series data logger function can be used to perform tasks accurately and efficiently in GK's monthly QA.

## AG4-3

## Use an electrometer's time-series data logger function to measure a beam profile

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**Introduction** This study was to establish a method to measure beam profiles (position series data) efficiently by using an electrometer's time-series data logging function. A beam profile measuring system executes two functions: position a detector using servo-trails and log charge using an electrometer. The functions can be played using Gamma Knife's patient position system and an electrometer of time-series data logging ability, respectively.

**Methods** The proposed method was illustrated by measuring a z-direction beam profile for the 4mm collimator of Gamma Knife (GK) ICON. The GK Daily QA Tool Plus detector was connected to an electrometer with the time-series data logger function, with its sampling rate at 0.5 sec. The data logger was turned on, then the detector was programed to dwell 6 sec at each of the 37 positions ranging from 91 mm to 109 mm with 0.5 mm step. A MATLAB algorithm identified the 37 data clusters, averaged each cluster to be 37 values which corresponded to the 37 positions in space, therefore obtained a beam profile. The method could replace the time-consuming and random error prone film dosimetry in GK annual QA.

**Results** A beam profile of 37 points over 18 mm range was obtained. Three profile features in FWHM, 20% -80% penumbra, and center were calculated using a spline interpolation method. The results of 5.01 mm, 2.50 mm, and 100.2 were within the tolerance comparing with the corresponding parameters in the reference data. The method was efficient that the data collection took less than 4 min and the data processing took less than 30 sec on an i7 PC.

**Conclusions** We have demonstrated that a relatively inexpensive electrometer of timeseries time-series logging can be used to measure a beam profile efficiently.

## Verification of the absorbed energy calculation procedure of the Leksell Gamma Plan

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**Introduction** Absorbed energy by a tumor is an integration of dose to each point in the tumor, related to DNA aberrations caused by radiation. Despite its importance, the accuracy of the treatment planning to calculate it has never been verified. In this study, absorbed energy by two vestibular schwannomas was calculated with Leksell Gamma Plan (LGP) and verified using 3D-printed tumor model scintillation detectors in skull phantoms.

**Methods** The MR images of two patients containing tumors were exported to a 3D-slicing program in DICOM-RT format. The hollow skull phantoms were built by 3D printing according to each patient's skull image and filled with water. Tumor model scintillators (TMS) formed in the shape of the tumors were 3D-printed using self-developed scintillating plastic resin. The TMS outputs were measured in nine fields at the center of the solid water phantom and normalized to Monte Carlo simulation values. A TMS detector was inserted into the tumor location inside the skull phantom, and CBCT images were obtained. Treatment plans were made to irradiate the TMS using the TMR10 algorithm. 12.5Gy and 13Gy were prescribed to 50% isodose for each TMS. Irradiation was carried out in the same manner as the patient. The energy absorbed by TMS was measured and compared with LGP values.

**Results** The volume of the TMS was 0.722cm<sup>3</sup> and 0.216cm<sup>3</sup>. The mean adjusted R-square value of linear fitting of the calibration data was 0.9996 +/- 0.0020. The absorbed energy calculated by LGP was 14.24 +/- 2.44 mJ and 4.62 +/- 0.70 mJ, respectively. The corresponding measured energy was 14.29 +/- 0.11 mJ and 4.65 +/- 0.03 mJ.

**Conclusions** The absorbed energy by a TMS calculated by the TMR10 algorithm of the LGP agreed with measured values with differences less than 0.7%. It is necessary to verify the convolution algorithm using inhomogeneous anthropomorphic phantoms.

## Error analysis of probe measurements in extend treatment procedures

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**Introduction** The Gamma Knife (GK) is an advanced radiation treatment, stereotactic radiosurgery, for adults and children with small to medium brain tumors measuring up to 3 cm in diameter, abnormal blood vessel formations called arteriovenous malformations, epilepsy, trigeminal neuralgia, a nerve condition that causes chronic pain, and other neurological conditions. Since its invention, patients with serious disorders can be treated with this noninvasive procedure in one day with no overnight hospital stay.

The Philippine Gamma Knife Center (PGKC), launched in 1998 at the Cardinal Santos Medical Center, is the first and only center in Manila that uses a Leksell Gamma Knife to treat brain disorders. The initial GK machine acquired was the *Model B*. In 2014, PGKC acquired the *Perfexion* model, which offers the most precise treatment using robotic couch with improved patient comfort. Today, more than 3,000 patients have been treated in the center using this state-of-the-art equipment.

In 2016, two years upon acquisition of *Perfexion*, PGKC started using the *eXtend System* for multi-session treatments, called fractionated treatments, for larger lesions or those in more sensitive locations.

**Methods** The probe measurement data will be extracted from all the 57 patients who have undergone fractionated treatment employing the *eXtend System* treatment at the PGKC facility starting February 2016. Errors will be computed mathematically and then will be compared to errors generated by the machine. The author will identify the sources of error and make recommendations to minimize errors.

**Results** On progress.

**Conclusions** On progress.



## Hemorrhage risk of unruptured brain arteriovenous malformation after Gamma Knife radiosurgery: Significance of vascular compactness

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**Introduction** The goal of the study was to investigate whether morphology (i.e. compact/ diffuse) of brain arteriovenous malformations (bAVMs) correlates with the incidence of hemorrhagic events in patients with unruptured bAVMs after receiving Gamma Knife Radiosurgery (GKRS).

**Methods** This study retrospectively included 262 adult patients with unruptured bAVMs receiving upfront GKRS from double-institutions. Hemorrhagic events were defined as bleeding signs on computed tomography (CT) or magnetic resonance images (MRI). The morphology of bAVMs was evaluated using fully automated segmentation, which calculated the proportion of vessel, brain tissue, and cerebrospinal fluid in bAVMs on T2-weighted MRI. Compactness index, defined as the ratio of vessel to brain tissue, categorized the bAVMs into compact and diffuse types based on the optimal cutoff. Cox proportional hazard model was used to identify the independent factors for post-GKRS hemorrhage.

**Results** The median clinical and imaging follow-ups were 62.1 and 42.9 months. Post-GKRS hemorrhage occurred in 14 (5.3%) patients with 2 bAVMs bleeding twice, resulting in an annual bleeding risk of 0.9%. Multivariable analysis revealed that bAVM morphology (compact versus diffuse), bAVM volume and prescribed margin dose were significant predictors for post-GKRS hemorrhage. Among the diffuse bAVMs, the post-GKRS hemorrhage rate was higher for larger bAVMs (2.2 versus 13.5 versus 26.3 hemorrhage per 1000 person-years in bAVM volume <15 cm<sup>3</sup> versus 15-30 cm<sup>3</sup> versus >30 cm<sup>3</sup>; p=0.044). There was no significant difference between hemorrhage rates of each volume group within compact bAVMs. The hemorrhage rate after GKRS was higher in Spetzler-Martin grade IV-V bAVMs compared with grade I-III nidi (22.3 versus 4.1 hemorrhages per 1000 person-years; p = 0.001). The elevated post-GKRS hemorrhage risk in Spetzler-Martin grade IV-V bAVMs mainly originated from the diffuse bAVMs rather than the compact subgroup (35.2 versus 4.8 hemorrhages per 1000 person-years; p = 0.022).

**Conclusions** Compact and smaller bAVMs, with higher prescribed margin dose harbor lower risks of post-GKRS hemorrhage. The hemorrhage rate after GKRS was increased in the diffuse and large (>30 cm<sup>3</sup>) bAVMs and in the diffuse type Spetzler-Martin IV-V bAVMs to a level higher than 2.2% annually. This finding could help guide patient selection of GKRS management for the unruptured bAVMs.

## Gamma Knife radiosurgery for brain arteriovenous malformations: a 15-year single center experience in Southern Vietnam

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**Introduction** This study aims to identify the obliteration outcome, complications, and predictors in GKRS treatment for BAVM at a tertiary center in a developing country for 15 years.

**Methods** We retrospectively reviewed clinical and GKRS procedures of patients who received GKRS from October 2006 to December 2020 at Cho Ray Hospital, Vietnam. The patient data was classified into two cohorts. Cohort 1 and cohort 2 included patients who underwent GKRS from 2006 to 2011 and from 2011 to 2020, respectively. Exclusion criteria included patients with less than 24 months follow-up without obliteration, or AVM-related hemorrhage during this period.

**Results** 870 patients were included in the final analysis. Patients in cohort 1 had significantly smaller AVMs ( $8.4 \pm 11.6$  vs.  $11.2 \pm 12.8$  cm<sup>3</sup>,  $p < 0.001$ ) and were less frequently located in eloquent locations (46.6 vs. 65.5%,  $p < 0.001$ ) than in cohort 2. Mean AVM margin dose was  $20.4 \pm 3.2$  (range: 14-26) Gy. Mean follow-up time was  $49.6 \pm 22.6$  months (range: 5.9-102.6). The overall AVM obliteration rate was 66.6%. Cohort 1 had a significantly higher rate of complete obliteration than cohort 2 (81.0 vs. 55.1%,  $P < 0.001$ ). The post-GKRS annual hemorrhage risk was 1.0%. Significant radiosurgery-induced brain edema and radiosurgery-induced cyst formation was reported in  $n=24$  (2.6%) and  $n=4$  (0.5%), respectively. Using multivariate analysis, we identified obliteration predictors as prior AVM hemorrhage (HR= 1.430, 95% CI: 1.182-1.729), higher margin dose (HR=1.136, 95% CI: 1.086-1.188), eloquent location (HR= 0.765, 95%CI: 0.647-0.905), and higher AVM volume (HR=0.982, 95% CI: 0.968-0.997).

**Conclusions** GKRS is a safe and effective treatment for BAVM. Lack of prior AVM hemorrhage, eloquent location, and higher AVM were unfavorable predictors for post-GKRS obliterations.

## AG5-3

## Comparison of the outcomes after Gamma Knife radiosurgery for arteriovenous malformations in pediatric and adult patients

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**Introduction** The aim of this study is to compare the outcomes after Gamma Knife radiosurgery (GKRS) for arteriovenous malformations (AVM) in pediatric and adult patients with case-control study.

**Methods** A retrospective analysis was performed on AVM patients who underwent GKRS at our hospital from 1991 to 2021. Patients were classified into pediatric (<18 years) and adult ( $\geq 18$  years) cohorts and matched in a 1:1 ratio using propensity scores. The complete obliteration rate after GKRS and the incidence of adverse events, including symptomatic bleeding, in both groups were compared and analyzed.

**Results** Of a total of 848 patients who were eligible for inclusion in this study, 158 were selected for each of the matched cohorts. The mean nidus volume was 5.1 cm<sup>3</sup> for the pediatric group and 5.3 cm<sup>3</sup> for the adult group ( $p=0.777$ ), the mean prescribed dose was 20.8 Gy and 20.9 Gy ( $p=0.870$ ), and the mean observation period was 13.7 years and 14.1 years ( $p=0.591$ ). Cumulative complete obliteration rates at 3/5/10/15/20 years after GKRS were 57.1/67.4/78.5/79.8/81.3% in the pediatric group and 44.8/63.4/75.9/78.2/78.2% in the adult group, respectively, with no significant difference between them ( $p=0.136$ ). Cumulative adverse event rates at 3/5/10/15/20 years after GKRS were 3.8/4.6/11.4/19.3/19.3% in the pediatric group and 5.1/7.2/11.9/16.6/17.8% in the adult group. Annual incidence was slightly higher in pediatric group (1.2% vs 1.0%), but there was no statistically significantly different ( $p = 0.466$ ).

**Conclusions** The outcomes after GKRS for comparable AVMs in pediatric and adult patients were not found to be apparent different. GKRS is a reasonable treatment option for pediatric AVM patients as well as adult patients.



## A case of spontaneous obliteration of medium-sized unruptured cerebral arteriovenous malformation accompanied by reduced activity of protein S

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**Introduction** Spontaneous obliteration of cerebral arteriovenous malformations (AVMs) is rare, and most of them are triggered by intracranial hemorrhage from the AVMs. Meanwhile, protein S is a coenzyme of protein C that exhibits coagulation inhibitory action, and its decreased activity may lead to various types of thrombosis including sinus thrombosis. Here, we report a case of medium-sized unruptured AVM with spontaneous obliteration accompanied by reduced activity of protein S.

**Case** A 32-year-old female had loss-of-consciousness seizures and headaches since she was 17 years old. As a result of cerebral angiography and magnetic resonance (MR) imaging, she was diagnosed with a right fronto-parietal AVM (Spetzler-Martin Grade IV/2+1+1) and flow-related aneurysm of the anterior cerebral artery, and was referred to our center for gamma knife radiosurgery (GKS). At the patient's wish, GKS was not performed immediately, and so MR imaging follow-up was continued. Follow-up MR imaging after 7 months revealed stenosis of the deep drainer and a high intensity area on fluid-attenuated inversion recovery (FLAIR) around the nidus. The nidus was not detectable on MR angiography obtained after 3 years and 8 months, and cerebral angiography 7 years and 3 months later showed obliteration of the AVM and shrinkage of the anterior cerebral artery aneurysm. Along with this, the high intensity areas on FLAIR also began to contract. Blood tests were performed to investigate the etiology of the spontaneous obliteration and found that protein S activity was reduced (51.9%; the normal range was 63.5-149.0%).

**Conclusions** Spontaneous obliteration of medium-sized AVMs without hemorrhage is extremely rare. In this case, the decreased activity of protein S may have contributed to the thrombosis. If an enlarged high intensity area on FLAIR is observed during MR imaging follow-up of AVM, it is advisable to continue more careful evaluation because of the possibility of rapid hemodynamic changes in the AVM.

## AG6-1

## Improved prognosis for NSCLC patients with wildtype/mutant EGFR and brain metastases following stereotactic radiosurgery and immune/targeted therapy

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**Introduction** Advances in targeted therapy has improved the survival of non-small cell lung cancer (NSCLC) with mutant EGFR but evidence for those with brain metastases (BMs) was inconclusive while prognosis of those with wildtype EGFR remained poor. We examined the differential effect of stereotactic radiosurgery (SRS) and tyrosine kinase inhibitor (TKI) or immune checkpoint inhibitor (ICI) on NSCLC patients with mutant EGFR or wildtype EGFR, respectively.

**Methods** NSCLC patients with BMs who underwent SRS and/or TKI or ICI therapy were recruited. Overall survival (OS) and intracranial progression free survival (iPFS) following SRS were estimated using Kaplan-Meier methods. Hazard ratios for risk factors were estimated using Cox regression models.

**Results** For mutant EGFR, the median OS for combined SRS and TKI vs TKI alone vs SRS alone were 35.1 vs. 24.3 vs. 20.8 months, respectively, while the median iPFS were 20.0 vs. 13.8 vs. 11.8 months, respectively. For wildtype EGFR, the median OS for combined SRS and ICI vs. ICI alone vs. SRS alone were 28.1 vs. 17.3 vs. 15.6 months, respectively, while the median iPFS were 28.1 vs. 17.3 vs. 12.8 months, respectively. EGFR co-mutation (double or multiple mutations) was associated with poor OS and iPFS. Multivariable analysis showed that good performance status was associated with superior intracranial tumor control while extracranial metastases was associated with poorer survival.

**Conclusions** In NSCLC patients with mutant EGFR and BMs, combined SRS and TKI resulted in superior intracranial tumor control and survival and should be considered a standard-of-care treatment. For those with wildtype EGFR, there was evidence for improved intracranial tumor control with combined SRS and ICI while survival appeared to be better with this combined modality.

## Can we alleviate the radiation treatment for brain metastasis in the lung cancer patient with EGFR mutation in the era of targeted therapy?

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Whether combined radiation and tyrosine kinase inhibitor (TKI) therapy in non-small cell lung cancer (NSCLC) patients with brain metastases (BMs) and epidermal growth factor receptor (EGFR) mutations confers additional benefits over TKI therapy alone remains controversial. To compare outcomes between combined TKI and stereotactic radiosurgery (SRS) therapy versus TKI therapy alone in NSCLC patients with BMs and EGFR mutations, 280 patients were selected and categorized into two groups, TKI therapy alone (group I, n= 90) and combined therapy (group II, n=190). Cumulative tumor control rates were higher in group II compared to group I (79.8% vs. 31.2% at 36 months, p<0.0001). Cumulative overall survival (OS) rates were comparable between groups I and II (43.8% vs. 59.4% at 36 months, p=0.3203). Independent predictors of tumor control were older age, fewer number of BMs, lack of extracranial metastasis, and combined SRS and TKI therapy. Independent predictors of overall survival were fewer number of BMs and a higher Karnofsky Performance Status (KPS) score. Although OS rate did not differ between TKI therapy with and without SRS, the addition of SRS to TKI therapy resulted in improvement of intracranial tumor control. The lack of effect on survival rate with the addition of SRS may be attributable to extracranial disease progression. The addition of SRS to TKI therapy is recommended for intracranial disease control in NSCLC patients with BMs and EGFR mutations. Potential benefits may include prevention of neurological deficits and seizures. Future prospective studies may help clarify the clinical outcome benefits of SRS in these patients.

## AG6-3

## VEGFR-TKI treatment for radiation-induced brain injury after gamma knife radiosurgery for brain metastases from renal cell carcinomas

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**Introduction** Antiangiogenic vascular endothelial growth factor receptor tyrosine kinase inhibitors (VEGFR-TKIs) play an essential role in systemic therapy for renal cell carcinoma (RCC). Given the known anti-edematous effect of bevacizumab, an antiangiogenic antibody targeting VEGF, VEGFR-TKIs should exert therapeutic effects on radiation-induced brain injury after stereotactic radiosurgery. This preliminary study aimed to investigate the therapeutic effect of VEGFR-TKI against radiation-induced brain injury.

**Methods** Magnetic resonance images (MRIs) for six patients treated with VEGFR-TKIs who had been diagnosed with radiation-induced brain injury following gamma knife radiosurgery (GKRS) were retrospectively reviewed.

**Results** The median brain edema volume (BEV) and tumor mass volume (TMV) in the pre-TKI period were 57.6 mL (range: 39.4–188.2) and 3.2 mL (range: 1.0–4.6), respectively. Axitinib, pazopanib (followed by cabozantinib), and sunitinib were administered in four, one, and one cases, respectively. The median BEV and TMV in the post-TKI period were 4.8 mL (range: 1.5–27.8) and 1.6 mL (range: 0.4–3.6), respectively, over 2–14 weeks. The median rates of reduction in BEV and TMV were 90.8% (range: 51.9–97.6%) and 57.2% (range: 20.0–68.6%), respectively. Post-TKI values for BEV (p=0.027) and TMV (p=0.008) were significantly lower than pre-TKI values. Changes in volume were correlated with TKI use.

**Conclusions** The current study is the first to demonstrate the therapeutic effects of VEGFR-TKIs on radiation-induced brain injury in patients with brain metastases from RCC treated via GKRS.

## Effectiveness of immune checkpoint inhibitors in combination with stereotactic radiosurgery for patients with brain metastases from lung cancer: a propensity score-matched analysis

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**Introduction** Stereotactic radiosurgery (SRS) is the mainstay for treating brain metastases (BM) from lung cancer (LC). In recent years, immune checkpoint inhibitors (ICI) have been applied to metastatic LC and have contributed to improved outcomes. The authors investigated whether SRS with concurrent ICI for LC BM prolongs overall survival (OS) and improves intracranial disease control, and whether there are any safety concerns.

**Methods** Patients who underwent SRS for LC BM in our institution between January 2015 and December 2021 were included. Concurrent use of ICI was defined as no more than 3 months between SRS and ICI administration. The two treatment groups which had a similar likelihood of receiving concurrent ICI were generated by a propensity score matching (PSM) (match ratio 1:1) based on 12 potential prognostic covariates. Patient survival and control of intracranial disease were compared between the groups with and without concurrent ICI (ICI+SRS vs. SRS) by time-dependent analyses taking into account competing events.

**Results** In total, 585 LC BM patients (494 NCSCl and 91 SCLC) were eligible. Of those, 91 patients (16%) received concurrent ICI. Two patient groups of 87 patients (ICI+SRS group and SRS group) were generated by PSM. The 1-year survival rates of the ICI+SRS and SRS groups after the initial SRS were 65% and 46%, the median survival times 16.9 and 10.0 months, respectively (HR: 0.62 95% CI: 0.43–0.90,  $P=0.012$ ). The 1-year cumulative neurological mortality rates were 9% and 15%, respectively (HR: 0.40 95% CI: 0.18–0.87,  $P=0.021$ ). The 1-year local failure rates were 10% and 13% (HR: 0.68 95% CI: 0.29–1.6,  $P=0.38$ ) and the 1-year distant recurrence rates were both 44% (HR: 0.99 95% CI: 0.64–1.5,  $P=0.95$ ). CTCAE grade 4 toxicity (intratumoral hemorrhage immediately after SRS) occurred in 1 SRS group patient. CTCAE grade 2/3 toxicity was observed in 3 patients in the ICI-SRS group and 5 in the SRS group.

**Conclusions** The present study found that SRS with concurrent ICI for LC BM patients provided prolonged survival and lower neurological mortality rate. Intracranial disease control was similar between groups, with no apparent increase in treatment-related adverse events.

## Gamma Knife radiosurgery for surgical cavity of brain metastases: factor analysis and gene consideration

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**Introduction** Although surgical resection may remove the brain metastasis gross totally, the viable metastasis may exist in surgical cavity since the nature of malignancy. The presence of these viable tumors may cause marginal recurrence and influence of local tumor control. Stereotactic radiosurgery (SRS) provide a good local control for brain metastasis in the past decades, however, the radiation to the surgical cavity for preventing recurrence is a novel idea and the efficacy and safety are still debatable. This paper presents a retrospective analysis for local tumor control and complications following surgical resection and postoperative stereotactic radiosurgery (SRS) for brain metastases. We also investigated the influence of gene mutations on the efficacy of Gamma Knife radiosurgery (GKRS).

**Methods** This study included 97 patients (103 brain metastases) who underwent GKRS treatment and for whom surgical type, original tumor, gene mutation status, demographics, performance status, and tumor characteristics were available. Radiological images were obtained at 3 months after GKRS and at 3 month intervals thereafter. Kaplan-Meier plots and Cox regression analysis were used to correlate the clinical features to tumor control and overall survival.

**Results** The tumor control rates and overall 12-month survival rates were 75.0% and 89.6%, respectively. Tumor control rates in the radiation group versus the non-radiation group were 83.1% vs. 57.7% at 12-months and 66.1% vs. 50.5% at 24-months. During the 2-year follow-up period after SRS, the intracranial response rate in the post craniotomy radiation group was higher than that in the non-radiation group ( $p=0.027$ ). Cox regression multivariate analysis identified post craniotomy radiation as predictor of tumor control ( $p=0.035$ ).

**Conclusions** The current study demonstrated that, SRS for surgical cavity can provide better local tumor control, however, SRS for surgical cavity cannot provide better overall survival.

## Gamma knife radiosurgery for metastatic brain tumors from ovarian cancer (JLGK1801)

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**Introduction** Ovarian cancer (OC) has a low frequency of brain metastasis, and the prognosis for patients with brain metastasis is extremely poor. However, the frequency of brain metastasis is on the increase due to recent improvements in diagnostic imaging techniques and the introduction of molecular-targeted drugs. This study, led by the Japanese Leksell Gamma Knife Society (JLGK), was a retrospective observational study of the outcomes of patients treated with gamma knife radiosurgery (GKRS) for brain metastases from OC (JLGK1801 study).

**Methods** 118 patients with 566 brain metastases from OC who underwent GKRS at 10 GKRS centers in Japan were retrospectively reviewed.

**Results** The median overall time (OS) after GKRS was 18.1 months, 78.2% at 6 months, and 65.6% at 12 months. Factors significantly affecting OS were control of the primary tumor and the number of brain metastases. The incidence of neurological death was 3.2% at 6 months and 4.6% at 12 months in 10 patients with meningeal carcinomatosis. The incidence of neurological deterioration was 7.2% at 6 months and 13.5% at 12 months, and the incidence of new intracranial lesions was 20.6% at 6 months and 40.2% at 12 months. The local tumor control (LTC) rates at 6 and 12 months after GKRS were 97.6% and 95.2%. Factors significantly affecting LTC were peritumoral edema at GKRS, tumor volume, and prescribed dose. Comparison of 313 lesions in 69 patients with confirmed histopathological diagnosis of OC in two groups (161 lesions in 37 patients with serous adenocarcinoma and 152 lesions in 32 patients with other histological types) showed that patients with serous adenocarcinoma had significantly longer OS and higher LTC after GKRS.

**Conclusions** GKRS for brain metastases from OC was relatively safe and showed satisfactory results in terms of OS and LTC after irradiation. Serous adenocarcinoma showed significantly longer survival and higher local control than other histologic types.

## Volume prediction for large brain metastases after hypofractionated gamma knife radiosurgery through artificial neural network

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The effectiveness of single-session gamma knife radiosurgery (GKRS) for small metastatic brain tumors has been proven, but hypofractionated GKRS (hfGKRS) for large brain metastases (BM) from the linear quadratic (LQ) model is uncertain. The purpose of this study was to investigate volume changes large BM after hfGKRS from the LQ model and predict volume changes using artificial neural network (ANN). We retrospectively investigated the clinical findings of 28 patients who underwent hfGKRS with large BM (diameter >3 cm or volume >10 cc). A total of 44 tumors were extracted from 28 patients with features. We randomly divided 30 large brain tumors as training set and 14 large brain tumors as test set. To predict the volume changes after hfGKRS, we used ANN models (single-layer perceptron (SLP) and multi-layer perceptron (MLP)). The volume reduction was 96% after hfGKRS for large BM from the LQ model. ANN model predicted volume changes with 70% and 80% accuracy for SLP and MLP, respectively. Even in large BM, hfGKRS from the LQ model could be a good treatment option. Additionally, the MLP model could predict volume changes with 80% accuracy after hfGKRS for large BM.

## Natural history of lung squamous cell brain metastases in patients treated with radiosurgery: a thirty-year experience at a Tertiary Medical Center

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**Introduction** In this study we report our 30-year experience in stereotactic radiosurgery (SRS) treatment of lung squamous cell carcinoma (LUSC) brain metastases (BMs). It will serve to provide detailed longitudinal outcomes and predictors of efficacy in treating LUSC-BMs with SRS.

**Method** We retrospectively reviewed 51 patients and 109 tumors treated with SRS at our center between 1993–2022. Patient demographics, PDL1 genotype, immunotherapy use and mortality cause were recorded. Radiological and clinical outcomes were followed at 1-3-month intervals post-SRS. Cox-regression analysis and Kaplan-Meier survival curves were performed in statistical analysis.

**Results** We included 37 male and 14 female patients (median age 62.7 years at BM diagnosis). Median overall survival (OS) time was 6.9 months, 6-month OS rate was 62.1%, and Karnofsky performance scale (KPS) was the only independent predictor. Median time for local control maintenance was 7.6 months, 6-month local control rate was 69.1%, with TKI as the only independent predictor. Median time to distant failure was 5.3 months, 6-month distant failure rate was 48.9%, and factors with significant impact included gender ( $p < 0.001$ ), presence of extracranial metastases ( $p < 0.001$ ), use of immunotherapy ( $p < 0.001$ ), PDL1 genotype ( $p = 0.034$ ), and total intracranial metastases number ( $p = 0.002$ ). However, no definitive benefits of immunotherapy were identified in patients with higher PDL1 mutational tumors.

**Conclusions** In this study we defined the natural history of disease progression and outcomes in SRS-treated LUSC-BM patients. We also identified predictors of OS and tumor control among these patients. The findings of this study will serve as a guide when counseling these patients for SRS.

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## Large cystic brain metastases are treatable without drainage by hypofractionated or staged radiosurgery

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**Introduction** Hypofractionated stereotactic radiotherapy and staged-radiosurgery are useful for the treatment of large metastatic brain tumors. If the tumor is cystic, drainage is effective for early symptom relief and reduction of total radiation dose, but the risks of wound infection and meningeal dissemination are not neglectable. In this study, we retrospectively summarized our experiences of large cystic metastases which were treated by Gamma Knife radiosurgery without drainage.

**Methods** Fourteen patients with cystic metastatic brain tumors with a maximum diameter of 30 mm or more were treated at our institution during the period between 2019 and 2021. Mean age was 71.1 years (42-92 years; median 72 years), KPSs were 60-100%, primary tumors were lung cancer in 8 cases, breast cancer in 4 cases, and others in 2 cases. In 11 cases, drainage was avoided intentionally. Three cases were referral cases in which drainage had been performed, but sufficient cyst reduction was not obtained. The average maximum diameter was 37 mm (30-44 mm), 5-10 hypofractionated irradiation was performed in 3 cases, 2-3 staged-radiosurgery was performed in 11 cases, and the dose was 24-35 Gy.

**Results** Asymptomatic patients (7 cases) did not deteriorate after treatment, and symptomatic patients (7 cases) improved in motor paralysis and cerebellar ataxia. During the follow-up period (10.6 months on average), there were no local recurrences and the tumor volume decreased to 31.2% on average. There was no exacerbation of brain edema or meningeal dissemination.

**Discussion** The idea of reducing the size to 3 cm or less by drainage surgery is mostly for early improvement of the symptoms. In cystic tumors, however, there is less risk of post-irradiation edema compared to solid tumors, and the reduction in tumor size after treatment were likely a favorable impression. From the viewpoint of potential risks of bleeding, infection, and meningeal dissemination, avoiding drainage surgery seems to be feasible.

**Conclusions** Avoiding cyst drainage and performing fractionated or staged treatment seems to result in acceptable outcome in large cystic metastatic brain tumors.

## Fractionated Gamma Knife radiosurgery after cyst aspiration for large cystic brain metastases: case series and literature review

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**Introduction** Tumor cyst aspiration followed by Gamma Knife radiosurgery (GKRS) for large cystic brain metastases is a reasonable and effective management strategy. However, even with aspiration, the target lesion tends to exceed the dimensions of an ideal target for stereotactic radiosurgery. In this case, the local tumor control rate and the risk of complication might be a critical challenge. This study is aimed to investigate whether fractionated GKRS (f-GKRS) could solve these problems.

**Methods** Between May 2018 and April 2021, eight consecutive patients with nine lesions were treated with f-GKRS in five or ten sessions after cyst aspiration. The aspiration was repeated as needed throughout the treatment course to maintain the cyst size and shape. The patient characteristics, radiologic tumor response, and clinical course were reviewed using medical records.

**Results** The mean follow-up duration was 10.2 (2-28) months. The mean pre-GKRS volume and maximum diameter were 16.7 (5-55.8) mL and 39.0 (31-79) mm, respectively. The mean tumor volume reduction achieved by aspiration was 55.4%. The tumor volume decreased for all lesions, and symptoms were alleviated in all patients. The median overall survival was 10.0 months, and the estimated 1-year survival rate was 41.7% (95% CI: 10.9-70.8%). The local tumor control rate was 100%. No irradiation-related adverse events were observed.

**Conclusions** f-GKRS for aspirated cystic brain metastasis is a safe, effective, and less invasive management option for large cystic brain metastases.



## Usefulness of Gamma Knife stereotactic radiotherapy for repeat brain metastasis in the choroid plexus from renal cell carcinoma: a case report

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**Introduction** Metastases to brain choroid plexus are rare but occur in renal cell carcinoma or thyroid carcinoma patients. A case of renal cell carcinoma metastasis to the choroid plexus at Lusk foramen is presented.

**Case presentation** A 74-year-old female developed clear cell carcinoma in the right kidney and right nephrectomy was performed. A half year later multiple brain metastases in the right Lusk choroid plexus (5.4 ml) and in the right occipital lobe (0.01 ml) were developed. Both were successfully treated by Gamma Knife stereotactic radiosurgery (26 Gy in 2 fractions and 20 Gy in single fraction respectively). One year later another metastasis to the right lateral ventricle choroid plexus developed. It was also successfully treated Gamma Knife stereotactic radiosurgery again.

## Gamma Knife radiosurgery: A safe and effective treatment for brain metastases in pregnancy

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**Introduction** Brain metastases during pregnancy poses complex conundrum in management. Gamma Knife (GK) stereotactic radiosurgery (SRS) offers valuable option to clinicians in this scenario.

**Methods** We describe the safety and effectiveness of GK SRS in treating solitary cerebellar metastasis in a woman with recurrent breast cancer at third trimester of pregnancy. Dosimetry readings during trial run and actual treatment were recorded and follow-up MRI was performed after one month.

**Results** A 42-year-old woman presented with dizziness and unsteady gait during her third pregnancy at 28 weeks of gestation. She is a known case of triple negative breast carcinoma with local recurrence in 2021 and had completed second line chemotherapy 10-months ago. Upon presentation, she was fully conscious with neurological examination showing right cerebellar signs. MRI brain showed solitary right cerebellar enhancing mass, 2x2.7x2.1cm with perilesional edema and hemosiderin rim likely represent hemorrhagic metastasis. Chest radiograph depicted multiple cannon ball lesions. Obstetrical assessment revealed singleton fetus with gestation appropriate growth parameters and an estimated fetal weight of 1kg. Following multidisciplinary discussion, she agreed for urgent single session SRS to the brain metastasis with 2 cycles of 3-weekly paclitaxel chemotherapy. This will be followed by planned delivery of the fetus at term before subsequent palliative treatment. During the frame-based GK SRS, a trial run with dosimeters placed on phantom showed radiation exposure way below 100mSv tolerance. Actual treatment was performed at 16Gy of 50% isodose in 24 shots over 39.7 minutes beam on time. The treatment plan showed 98% coverage, 89% selectivity and gradient index 2.98. Dosimeters placed near uterine fundus and suprapubic region (consistent with concomitant ultrasound localization of fetal head) recorded 2.83mSv and 0.27mSv respectively. She successfully completed SRS treatment without complications. A repeat MRI after 4 weeks showed marked reduction of lesion size to 0.8x1x0.8cm. She was reassured for safe vaginal delivery planned at 36 weeks.

**Conclusions** GK SRS is safe and effective in treating pregnant patients with brain metastases. It allows concurrent chemotherapy, eliminates anesthetic risk while giving time to achieve adequate gestational age and fetal weight before birth. It improves quality of life and fetal outcome with lower perinatal risk and maternal morbidity.

## Gamma Knife Surgery for twenty or more brain metastases - a pilot and feasibility study

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**Introduction** One of the factors deciding whether Whole Brain Radiation Therapy (WBRT) or Gamma Knife Surgery (GKS) should be recommended for patients with multiple brain metastases (BM) has historically been the number of intracerebral lesions. The generally accepted upper limit for GKS has increased over the years from 3-4 to around ten at present.

**Methods** Our hypothesis in this prospective feasibility study was that also patients with  $\geq 20$  BM may benefit from GKS. The limitations using GKS for patients with numerous metastases are the long treatment times, the integral radiation dose to the brain and the clinical impact of the potential micro-metastases that are left untreated when using GKS instead of WBRT. Furthermore, the survival time must be sufficiently long for a sufficient number of patients to justify GKS.

**Results** We have now treated 61 patients with  $\geq 20$  BM, and we have complete follow up on all but two of them. None of the patients aborted the treatment in spite of the sometimes very long treatment times. A significant, but transient, radiation induced complication developed after one month in one patient. The survival time was more than six months for 2/3, more than one year for 1/2 and more than two years for 1/4 of the patients. The ECOG value was the only parameter predicting survival time ( $P < 0.01$ ). Half of the patients developed distal recurrences within six months following GKS, most being managed with repeat GKS or systemic treatment. The likelihood for salvage WBRT within six months following GKS was  $< 10\%$ , suggesting that micro-metastases are of limited clinical importance.

**Conclusions** GKS is indicated for selected patients in good clinical condition with 20 or more brain metastases.

## Multi-session radiosurgery for numerous small brain metastases

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**Introduction** Treatment of multiple brain metastases more than 10 is challenging and has been controversial. Whole brain radiotherapy (WBRT) is generally believed to be the first treatment choice. However, this is not always adequate because of the inconsistent effects and combined adverse effects such as dementia which may be resulted afterward. In order to escape from mental deterioration, WBRT has to be replaced by the other treatment methods like radiosurgery. We have performed such a treatment for numerous small brain metastases by Gamma Knife stereotactic radiosurgery (GKS).

**Methods** Twelve cases of numerous (more than 30) brain metastases were treated by GKS retrospectively during a period from July, 2016 to June, 2021. They were seven males and five females with the mean age of 63.4 years. All of them were with lung cancers. Mean total session number was 5.42 times, ranging 2 to 17. Each tumor was treated with the margin dose between 14 to 20 Gy. The tumor number treated in whole sessions was ranged from 31 to 144 (mean, 70.8).

**Results** Almost all the irradiated tumors either disappeared or shrank at the patient's death or at the last follow-up, though new metastatic tumors were subsequently developed in some cases which required an additional treatment with GKS. At the last follow-up (3 to 51 months after GKS), nine cases were alive and well and three were dead. As adverse effects, two cases demonstrated seizures by radiation brain injury and another showed a gait disturbance. No apparent mental deterioration was observed during follow-up.

**Conclusions** Local tumor control without any severe side effects including mental deterioration was achieved, which seemed to be consistent with radiosurgery in cases with 10 or less brain metastases. Radiosurgery for numerous small brain metastases may be preferable rather than WBRT.



## Leukoencephalopathy in patients with brain metastases who received radiosurgery with or without whole brain radiotherapy

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**Introduction** Whole brain radiation therapy (WBRT) for brain metastases (BMs) is a common cause of radiation-induced leukoencephalopathy; however the safety of alternative stereotactic radiosurgery (SRS) remains unclear. This study examined the incidence of leukoencephalopathy in patients treated with SRS alone versus WBRT plus SRS for BMs with a focus on the relationship between prognostic factors and leukoencephalopathy.

**Methods** Analysis was performed between 2002 and 2021. The total enrollment was 993 patients with the distribution: WBRT plus SRS (n=291) and SRS only (n=702). Leukoencephalopathy was graded from 0 to 3 for changes in white matter indicated by the MRI after WBRT or SRS. Patient characteristics and SRS dosimetric parameters were reviewed to identify factors that contributed to the incidence of leukoencephalopathy or overall survival.

**Results** The incidence of leukoencephalopathy was consistently higher in WBRT plus SRS group than in SRS alone group ( $p < 0.001$ ). Leukoencephalopathy was also associated with a larger total tumor volume ( $\geq 28\text{cm}^3$ ;  $p = 0.028$ ) and age ( $> 77$  years;  $p = 0.025$ ). Nonetheless, the SRS integral dose to skull in the subgroup of WBRT plus SRS treatment was not demonstrated significance in development of leukoencephalopathy ( $p = 0.986$  for integral dose 1-2J,  $p = 0.776$  for integral dose  $> 2$ J).

**Conclusions** This study revealed that SRS is safe for oligo-BMs in terms of leukoencephalopathy development. Patient age and total tumor volume were identified as important factors in assessing the development of leukoencephalopathy. The additional of SRS (even at an integral dose  $> 2$ J) did not increase the incidence of leukoencephalopathy.

## AG8-4

### Whole-brain radiotherapy vs. Localized radiotherapy after resection of brain metastases in the era of targeted therapy: a retrospective Study

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Whether targeted therapy (TT) and radiotherapy impact survival after resection of brain metastases (BM) is unknown. The purpose of this study was to analyze the factors affecting overall survival (OS), local control (LC), distant control (DC), and leptomeningeal metastases (LMM) in patients who had undergone resection of BM. We retrospectively analyzed 124 consecutive patients who had undergone resection of BM between 2004 and 2020. Patient information about age, sex, Karnofsky Performance Scale (KPS), origin of cancer, synchronicity, tumor size, status of primary cancer, use of TT, extent of resection, and postoperative radiotherapy was collected. Radiation therapy was categorized into whole-brain radiotherapy (WBRT), localized radiotherapy (local brain radiotherapy or stereotactic radiosurgery (LBRT/SRS)), and no radiation. We identified factors that affect OS, LC, DC, and LMM. In multivariable analysis, significant factors for OS were higher KPS score ( $\geq 90$ ) (HR 0.53,  $p = 0.011$ ), use of TT (HR 0.43,  $p = 0.001$ ), controlled primary disease (HR 0.63,  $p = 0.047$ ), and single BM (HR 0.55,  $p = 0.016$ ). Significant factors for LC were gross total resection (HR 0.29,  $p = 0.014$ ) and origin of cancer ( $p = 0.041$ ). Both WBRT and LBRT/SRS showed superior LC than no radiation (HR 0.32,  $p = 0.034$  and HR 0.38,  $p = 0.018$ , respectively). Significant factors for DC were use of TT (HR 0.54,  $p = 0.022$ ) and single BM (HR 0.47,  $p = 0.004$ ). Reduced incidence of LMM was associated with use of TT (HR 0.42,  $p = 0.038$ ), synchronicity (HR 0.25,  $p = 0.028$ ), and controlled primary cancer (HR 0.44,  $p = 0.047$ ). TT was associated with prolonged OS, improved DC, and reduced LMM in resected BM patients. WBRT and LBRT/SRS showed similar benefits on LC. Considering the extended survival of cancer patients and the long-term effect of WBRT on cognitive function, LBRT/SRS appears to be a good option after resection of BM.

## Treatment results of post-stereotactic radiosurgical recurrence in patients with brain metastases

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**Introduction** There is little information on treatment results of post-stereotactic radiosurgical (SRS) recurrence in brain metastasis (BM) patients. We aimed to reappraise this issue.

**Methods** This IRB-approved retrospective cohort study was based on our prospectively-accumulated database including 3892 consecutive patients undergoing gamma knife (GK) SRS performed for BMs during the 1998-2022 period. We selected 72 BM patients who underwent some treatment (Tx) for local recurrence and in whom MR imaging was performed at least once after Tx for this study (female; 47, male; 25, mean age 66 (range; 30-77) years.

**Results** As of August, 2022, no further recurrence has occurred during median post-Tx observation period of 15.4 (IQR: 8.9-29.0) months. Post-Tx median survival time (MST, months) which, therefore, was same as further recurrence-free survival time was 23.8 (95% CI: 17.9-51.3). Regarding Tx, SRS was performed in 56 patients, surgical removal in 15 and erlotinib administration in the other one. Post-Tx MSTs did not differ between the two patient groups, i.e., having SRS (21.5, 95% CI: 15.5-51.3) vs surgical removal (37.9, 95% CI: 9.3-na, p=0.58). Among 56 patients with SRS, 11 (19.6%) experienced SRS-related complications (RTOG grade 2 in 53 and grade 3 in the remaining three).

**Conclusions** Our results suggest that either SRS or surgical removal was very effective for post-SRS local recurrence while incidence of SRS-related complications was slightly higher than reported rates after single course of SRS.

## A new tool for assessing risks of systemic and neurologic death in brain metastasis patients undergoing Gamma Knife radiosurgery

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**Introduction** To optimize treatment intensity in Gamma Knife radiosurgery (GKS) for brain metastasis (BM) it is essential to independently assess risks for both systemic death (SD) and neurologic death (ND). Herein, we propose a new tool, the "SD-ND risk assessment".

**Methods** Four extracranial disease (ECD) factors for SD and 2 intracranial disease factors (ICD) for ND were obtained using the Fine and Gray proportional hazard model in 4530 consecutive BM cases treated with GKS during a 24-year period (1998-2021). There were 1853 lung-adenocarcinoma, 686 non-adeno/non-small cell lung, 427 small cell lung, 687 gastrointestinal tract, 568 breast, 127 urogenital and 182 other cancers. We defined the ECD score as followings, KPS score ( $\leq 70\%$ =0, 80-100%=1), control of primary tumor (active=0, controlled=1), extra-cranial metastases (yes=0, no=1) and prognostic biomarkers (no/unknown=0, yes=1). We classified SD risk into three groups, i.e., SD high-risk with total ECD score of 0 or 1, intermediate (Im, 2) and low (3 or 4). The ICD score was defined as MRI findings of nodular leptomeningeal dissemination (yes=0, no=1) and maximum BM diameter ( $>2.5\text{cm}$ =0,  $\leq 2.5\text{cm}$ =1). ND risk was divided into two groups, "ND high-risk" with total ICD score of 0 or 1 and "low" with those of 2. The 2 ND risk groups were incorporated into the 3 SD risk groups, e.g., SD-high & ND-low or SD-Im & ND high, as the "SD-ND risk assessment".

**Results** The one-year cumulative SD and ND incidences were 16.6% and 3.3% in the SD-low & ND-low (n=567), 20.4% and 8.8% in the SD-low & ND-high (n=382), 53.1% and 5.3% in the SD-Im & ND-low (n=946), 45.4% and 10.6% in the SD-Im & ND-high (n=764), 73.4% and 3.7% in the SD-high & ND-low (n=911), 70.8% and 13.3% in the SD-high & ND-high (n=960), respectively, risk groups. This SD-ND risk assessment was validated in lung, gastrointestinal tract and breast cancers.

**Conclusions** Our SD-ND risk assessment was found to be a very useful and robust tool for assessing both SD and ND risks and optimization of radiation treatment intensity in GKS-treated BM patients.

## Development of expanding hematoma and expanding cysts in AVMs after GKS

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**Introduction** Expanding cysts and hematomas are the most common late complications after gamma knife surgery (GKS) for arteriovenous malformations (AVMs) and still have debatable mechanism of formation. Therefore, the present study reviews a case series of 18 patients with expanding cysts or hematomas to evaluate the clinical, imaging, and pathologic aspects of the complications and to discuss the possible mechanisms for the formation of the late complications.

**Methods** Retrospective analysis was conducted on 1072 patients who underwent gamma knife surgery for brain AVM at Taipei Veterans General Hospital between 1993/3-2022/3. Clinical data, images, as well as pathology results were collected from the patients' medical records and analyzed.

**Results** Of the 989 patients who were followed-up for at least 5 years, 18 patients were found to have late cyst formation and expanding hematoma. 13 of 18 patients received craniotomy due to progression of their complications. Upon histological examinations, organizing hematoma with fresh and dated hemorrhage, fibrinoid necrosis of the vessels, gliosis of normal brain tissue, infiltration of hemosiderin-laden histiocytes, as well as extravascular protein leakage were all observed in either the expanding hematomas or brain tissues intervening AVMs in all specimens.

**Discussion** We propose that both delayed cysts and expanding hematomas arise from radiation induced vascular damage in brain tissues adjacent to the AVM. Radiation during GKS induced increased permeability of the vessels, chronic inflammation, brain parenchyma atrophy, and extravasation of red blood cells. Expanding hematoma forms from recurrent hemorrhage from the radiated vessels into the adjacent brain parenchyma whereas expanding cysts had recurrent hemorrhage in a cystic space.

**Conclusions** The current study reports 18 cases of expanding hematomas or cysts developed after GKS for AVM. 13 of them underwent craniotomy and histology examinations showed similar results. Hence, we propose that expanding hematomas and cysts have alike mechanism of recurrent hemorrhage from the radiated vessels.

## AG9-2

### Long-term results of gamma knife radiosurgery for pediatric arteriovenous malformations

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**Objective** We investigate the long-term outcome of gamma knife radiosurgery (GKS) for brain arteriovenous malformations (AVMs) in children ( $\leq 15$  years of age).

**Methods** Among pediatric AVM patients who underwent GKS from January 1994 to December 2021, we examine 100 lesions in 87 cases with follow-up of at least 6 months. The cases included 44 boys and 43 girls, median age 11 (range 4-15) years, and 53 (61%) had a history of hemorrhage prior to treatment. The regions included 68 (68%) cerebral lobes, 12 (12%) basal ganglia/thalamus, 8 (8%) corpus callosum, 5 (5%) cerebellum, 3 (3%) brainstem, etc. The Spetzler-Martin grade was II in 52 (52%), III in 25 (25%), and I in 15 (15%) patients, etc. The median lesion size was 1.5 ml (0.08-25.4 ml), and the median prescribed dose to the nidus margin was 20 Gy (range 10-25 Gy). The median follow-up period after initial treatment was 48 months (range 6-301 months).

**Results** The cumulative obliteration rates of nidus at 5, 10, and 15 years after treatment were 66, 70, and 79%, respectively. Hemorrhage after GKS was observed in 6 cases (7%), and the hemorrhage period ranged from 21 to 135 months after treatment. Four patients (4.6%) had enlarged nidus after GKS, and 13 patients (15%) underwent repeat GKS for residual nidus 41-207 months after the initial treatment. As for complications, 7 cases (8%) developed symptomatic radiation injury within 24 months after treatment and they were transient except for 1 case that was operated on. There were 2 cases of asymptomatic cyst formation and 3 cases of chronic encapsulated hematoma appearance between 60-144 months after treatment. No malignant tumors were observed.

**Conclusions** GKS is effective in pediatric AVMs even after long-term observation. The possibility of complications during long-term follow-up should be kept in mind.

## Effect of treatment of cerebral arteriovenous malformations (AVMs) on AVM-associated epilepsy

Etsuko Yamamoto Hattori, Hisae Mori, Taichi Ikedo, Koji Iihara, Hiroharu Kataoka

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**Background** About half of patients with arteriovenous malformations (AVMs) develop epilepsy. Although AVM-associated epilepsy is reported to improve with treatment of AVMs, treatment can induce seizures in some cases.

**Methods** 545 patients with AVM who underwent treatment decisions or interventions at our hospital between February 2002 and August 2022. Patients were classified into 3 groups: surgical resection, stereotactic radiotherapy, and conservative treatment, and the Engel classification and cumulative seizure rate were retrospectively evaluated.

**Results** 153 patients developed epilepsy during the course of the study (excluding patients who received only prophylaxis or had an unknown history of epilepsy treatment). The mean age was 32 years, 87 (56.9%) were male. Surgical resection was performed in 53 patients, stereotactic radiotherapy in 82 patients, and conservative treatment in 24 patients (some overlap). 42 patients (27.5%) had their first seizure after AVM treatment. 50 patients (32.7%) had Engel classification IVC; 23 patients by surgical resection, 29 patients by stereotactic radiotherapy (some overlap), with no difference by treatment ( $p = 0.322$ ). The 3-year seizure rate for supratentorial lesions was 30.8% for surgical resection, 17.1% for stereotactic radiotherapy, and 29.7% for conservative treatment ( $p = 0.002$ , Kaplan-Meier method).

**Discussion** About 33% of the patients had worsening seizure control after AVM treatment, possibly due to perioperative edema after surgical resection or transient edema after stereotactic radiotherapy. Stereotactic radiotherapy had the lowest cumulative seizure rate, which was thought to be due to the slower edema compared to surgical resection.

**Conclusions** AVM-associated epilepsy can be exacerbated by AVM treatment and requires attention to perioperative seizures.

## AG9-4

## Two cases of response to gamma knife radiosurgery for arteriovenous malformation complicated by Moyamoya disease

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**Introduction** Moyamoya disease (MMD) and cerebral arteriovenous malformation (AVM) rarely coexist.

We report two coexisting MMD and AVM cases that were effectively treated with gamma knife radiosurgery (GKRS).

**Case 1** A 46-year-old woman. MMD was diagnosed following intraventricular hemorrhage. She also had a cerebellar AVM (Spetzler-Martin grade 2) with the right superior cerebellar artery (SCA) as a feeder. We performed the right STA-MCA bypass for MMD. GKRS for AVM was performed one year after bypass surgery, and complete nidus occlusion was confirmed four years after GKRS.

**Case 2** A 22-year-old man. He was diagnosed with MMD, caused by ischemic infarction of the right occipital lobe. He underwent the right STA-MCA bypass; five years later, the progression of the contralateral lesion required the left STA-MCA bypass and encephalomyo-synangiosis (EMS).

MRA fifteen years after showed an aberrant vascular signal in the right frontal lobe, diagnosed the AVM, and GKRS was performed. Three years following the GKRS, the nidus is disappearing.

**Discussion** Taking measures to prevent AVM rupture in patients with MMD is critical because a ruptured AVM can result in death due to cerebral ischemia associated with elevated cerebral pressure.

In addition, treatment for MMD might involve further revascularization procedures.

Craniotomy of the AVM may result in graft injury and unanticipated indirect anastomosis; GKRS may be advantageous in minimizing these complications in AVMs in both disorders.

**Conclusions** GKRS successfully treated both of the highly unusual cases of AVM associated with MMD.

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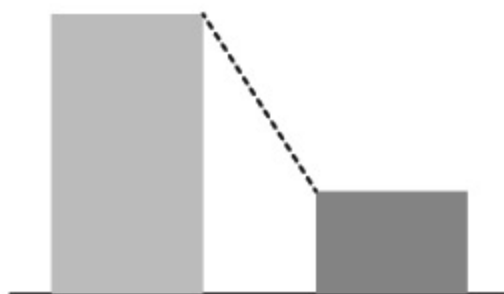
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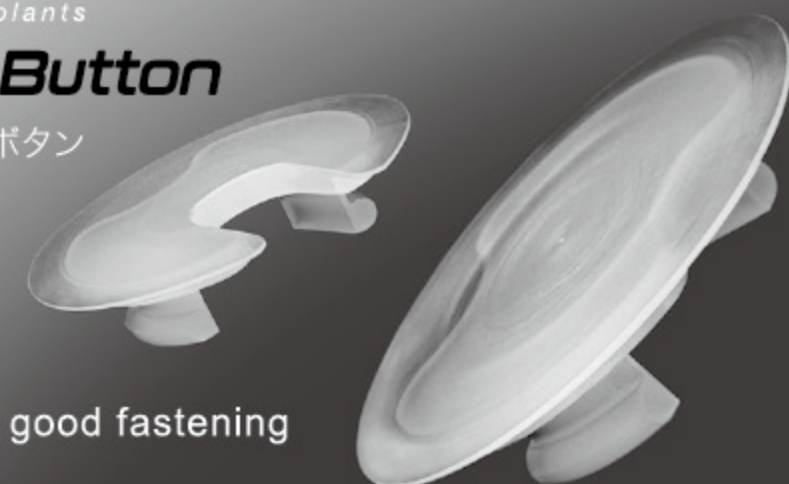
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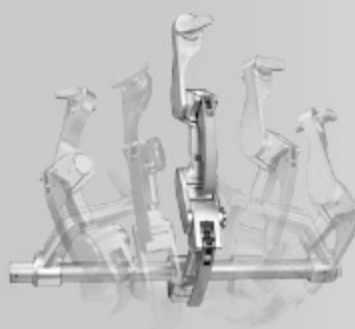
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