Horia Vulpe, MD, CM[‡§]
Akshay V. Save, BSc[‡¶]
Yuanguang Xu, PhD[‡]
Carl D. Elliston, MA[‡]
Matthew D. Garrett, MD, MM[‡]
Cheng-Chia Wu, MD, PhD[‡§]
Simon K. Cheng, MD, PhD[‡§‖]
Ashish H. Jani, MD[‡]
Jeffrey N. Bruce, MD[§¶]
Guy M. McKhann, MD[§¶]
Tony J. C. Wang, MD[*‡§¶]
Michael B. Sisti, MD[*‡§¶‖]

[‡]Department of Radiation Oncology, Columbia University Irving Medical Center, New York, New York; [§]Herbert Irving Comprehensive Cancer Center, NewYork-Presbyterian/Columbia University Irving Medical Center, New York, New York; [¶]Department of Neurological Surgery, Columbia University Irving Medical Center, New York, New York; [‖]Department of Otolaryngology/Head and Neck Surgery, Columbia University Irving Medical Center, New York, New York

[*]These authors contributed equally to this work.

Correspondence:
Tony J. C. Wang, MD,
Center for Radiosurgery,
Department of Radiation Oncology,
NewYork-Presbyterian/Columbia University Irving Medical Center,
622 West 168th Street, BNH B-11,
New York, NY 10032.
Email: tjw2117@cumc.columbia.edu

Received, August 14, 2018.
Accepted, February 25, 2019.

Frameless Stereotactic Radiosurgery on the Gamma Knife Icon: Early Experience From 100 Patients

BACKGROUND: The Gamma Knife (GK) Icon (Elekta AB) uses a cone-beam computed tomography (CBCT) scanner and an infrared camera system to support the delivery of frameless stereotactic radiosurgery (SRS). There are limited data on patients treated with frameless GK radiosurgery (GKRS).

OBJECTIVE: To describe the early experience, process, technical details, and short-term outcomes with frameless GKRS at our institution.

METHODS: We reviewed our patient selection and described the workflow in detail, including image acquisition, treatment planning, mask-based immobilization, stereotactic CBCT localization, registration, treatment, and intrafraction monitoring. Because of the short interval of follow-up, we provide crude rates of local control.

RESULTS: Data from 100 patients are reported. Median age is 67 yr old. 56 patients were treated definitively, 21 postoperatively, and 23 had salvage GKRS for recurrence after surgery. Forty-two patients had brain metastases, 26 meningiomas, 16 vestibular schwannomas, 9 high-grade gliomas, and 7 other histologies. Median doses to metastases were 20 Gy in 1 fraction (range: 14-21), 24 Gy in 3 fractions (range: 19.5-27), and 25 Gy in 5 fractions (range: 25-30 Gy). Thirteen patients underwent repeat SRS to the same area. Median treatment time was 17.7 min (range: 5.8-61.7). We found an improvement in our workflow and a greater number of patients eligible for GKRS because of the ability to fractionate treatments.

CONCLUSION: We report a large cohort of consecutive patients treated with frameless GKRS. We look forward to studies with longer follow-up to provide valuable data on clinical outcomes and to further our understanding of the radiobiology of hypofractionation in the brain.

KEY WORDS: Radiosurgery, Brain neoplasms, Radiotherapy

Neurosurgery 0:1–8, 2019 DOI:10.1093/neuros/nyz227 www.neurosurgery-online.com

Cobalt-60 stereotactic radiosurgery was first developed by the Swedish neurosurgeon Lars Leskell in the 1960s. This technique allows focused radiation treatments to be delivered with exquisite precision to benign and malignant lesions of the brain. For decades, the only immobilization device available has been the rigid stereotactic frame, which is fixed with pins onto the patient's skull to prevent motion during treatment. It also defines the stereotactic space in which gamma rays are collimated to their targets.

Advances in positioning and dosimetry have been integrated in newer models of what came to be known as the Gamma Knife (GK, Elekta Instruments AB, Stockholm, Sweden). Improving on the initial U and B models, the C model automated patient positioning and the GK Perfexion eliminated the need to change an external collimator helmet manually. Further improvements in treatment planning software facilitated contouring, planning, and treatment delivery.

ABBREVIATIONS: AVM, arteriovenous malformation; **CBCT,** cone-beam computed tomography; **CNS,** central nervous system; **CTDI,** CT dose index; **GBM,** glioblastoma multiforme; **GK,** Gamma Knife; **GKRS,** GK radiosurgery; **IFMM,** intrafraction motion management; **MRI,** magnetic resonance imaging; **SRS,** stereotactic radiosurgery; **VS,** vestibular schwannoma; **WBRT,** whole-brain RT

Neurosurgery Speaks! Audio abstracts available for this article at www.neurosurgery-online.com.

Despite these advancements, immobilization with the stereotactic Leskell G Frame has its drawbacks. The pins can be uncomfortable, and complications have been reported, including infections and persistent pain at the insertion site. The process of scheduling framed treatments can be laborious if delays are introduced. Finally, the invasive nature of the frame generally prevents multifraction treatments.

The Icon is the most recent model of the GK. It has been approved by the United States Food and Drug Administration in August 2015. The GK Icon incorporates an onboard cone-beam computed tomography (CBCT) scanner and an infrared intrafraction motion management (IFMM) system. These 2 additions allow a thermoplastic mask to be used for immobilization without the need for an invasive frame. Imaging and planning can be done in advance, treatments are streamlined, and the mask lends itself to multisession fractionated GK radiosurgery (GKRS). Indications and patient selection for fractionated GKRS are gradually evolving as we collectively gain more experience with this novel technology.

In this article, we describe our early experience, process, technical details, and short-term outcomes of 100 consecutive patients treated with frameless GKRS on the GK Icon at our institution.

METHODS

All patients provided written consent and were enrolled in an institutional ethics board-approved prospective observational trial at the time of initial consultation.

Patient Selection

The present series includes patients treated with frameless GKRS between April 2017 and February 2018.

At our institution, patients are selected for GKRS after a multidisciplinary discussion that typically includes a neurosurgeon, radiation oncologist, and neuro-oncologist. Patients are offered frameless GKRS except in the following clinical scenarios: (1) < 1 cm metastases and/or in eloquent areas such as the brainstem or motor/sensory cortex, (2) treatments that require prescription doses greater than 21 Gy, such as trigeminal neuralgia, essential tremor, or obsessive-compulsive disorder, and (3) patients who cannot reliably remain still in a thermoplastic mask after a thorough assessment by the physician.

Patients we consider for fractionated GKRS in 3 to 5 fractions include, but are not limited to, those with large brain metastases or cavities >2.5-3 cm, vestibular schwannomas (VS) near the cochlea, and previously irradiated patients with recurrent gliomas. The decision is made through a multidisciplinary team discussion.

Occasionally, the first fraction is treated framed and subsequent fractions frameless. This occurs most often when patients have both small metastases in sensitive areas and larger lesions not suitable for a single fraction. The framed fraction ensures maximal immobilization when targeting the small lesions while subsequent fractions are delivered to the larger targets. Finally, we use a mask in the rare cases when there is anticipated collision between the frame and the GK unit that cannot be eliminated with a change in gamma angle.

Imaging

All magnetic resonance imaging (MRI) intended for frameless GKRS planning are 1mm, thin-slice, volumetric, axial images acquired down to C3 vertebral body. We use T1 contrast-enhanced images for brain metastases and T1 contrast-enhanced and noncontrast T2 for VS, recurrent gliomas, and meningioma. Patients with arteriovenous malformations are also imaged with digital subtraction angiography and MR angiography for localization.

Generally, we acquire the MRI on the day of GKRS, or 2 to 3 d prior, for patients with brain metastases, glioblastoma multiformes (GBMs), and resected meningiomas. For slow-growing tumors such as VS or meningiomas, we occasionally preplan on MRIs acquired within 2 to 3 wk.

Treatment Planning

MRI images are imported into GammaPlan, and the scalp border is defined. Depending on the clinical case, the radiation oncologist or the neurosurgeon first delineates the targets and places initial shots. We use forward and inverse planning to achieve an optimized dose distribution. Both the radiation oncologist and the neurosurgeon verify and approve the final plan.

Immobilization

After planning is completed, we accompany the patient to the Icon GK suite, where we play music of their choice to reduce anxiety and improve the patient experience.[1] We soften a malleable hardening pillow and mold it onto the headrest. Patients are instructed to lie down as far up the couch in the Y-axis as possible, with shoulders near or touching the edge of the GK cradle, making sure they remain within the CBCT field of view. Their head rests comfortably on the pillow, which is now hardening.

To facilitate patient repositioning during multifraction treatments, we record the height of the couch after it has been adjusted for comfort (Z-axis). We also make a dent in the pillow at the top of the head to indicate the superior/inferior position (Y-axis) and draw a line on the pillow on each side at the level of the pinnae.

With the patient laying comfortably supine, we then mold a warmed thermoplastic mask over the patient's face, instructing them to keep the mouth slightly open for ease of breathing. We fold back a rim of the mask around the nasal aperture to prevent sharp uncomfortable edges after hardening. Slight pressure is applied over the chin and forehead to keep the mask snug (Figure 1).

We deploy the IFMM camera and place the circular reflective marker on the patient's nose for real-time intrafraction motion monitoring.

Simulation, Registration, and Treatment

Once the patient has been immobilized, the CBCT arm is lowered into position, and a reference CBCT is performed. Initially we used an energy of 90 kVp and a CT dose index (CTDI) of 6.3 mGy, but recently, we have found that a CTDI of 2.5 mGy provides comparable image quality for registration. This reference CBCT defines the baseline stereotactic space, akin to a Simulation CT on a conventional linear accelerator. The reference CBCT is registered with the planning MRI using Gamma Plan's registration algorithm. Once the MRI-CBCT registration is complete, the dose distribution is recalculated to adapt to the new patient geometry. We review the new distribution and make modifications to the plan if there are significant differences in dose to the target or the organs at risk. These can include changes to shot position,

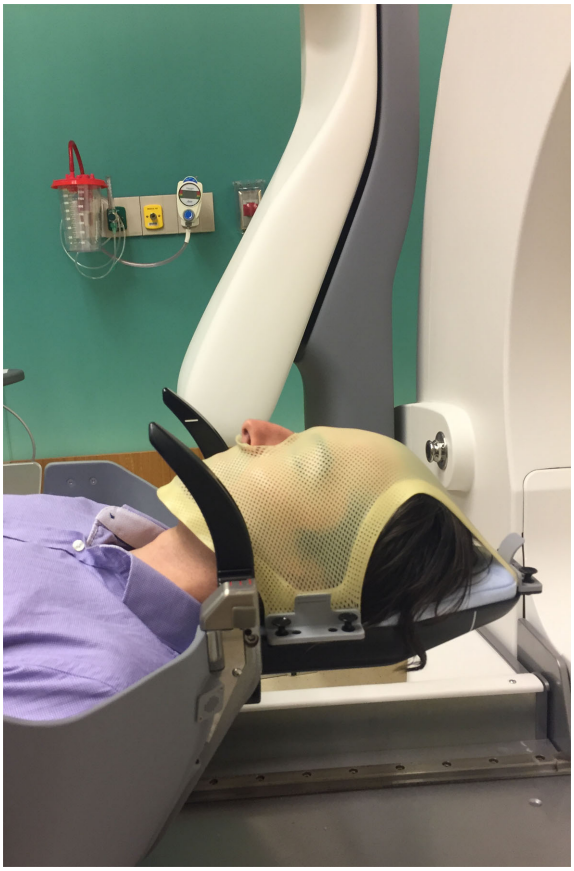

FIGURE 1. *Patient position in headrest and thermoplastic mask. The photograph pictured is used with consent.*

weight, adding/removing sector blocking, or adding/removing entire shots. During this time, the mask has hardened on the patient's face.

Once the new distribution is approved, a second CBCT is performed for pretreatment localization with CTDI of 2.5 mGy. It is registered to the reference CBCT. Shifts are usually small, as the patient has not moved off the table. The new adapted 3D distribution and dose–volume histograms are again reviewed and if satisfactory, the treatment is delivered. Subsequent multifraction treatments require only one pretreatment CBCT for localization. If patients can no longer fit comfortably in the mask on subsequent fractions because of mask shrinkage, occasionally, a new mask must be created. A new reference CBCT followed by a pretreatment localization CBCT can then be performed and the patient treated. On occasion, we perform a single-localization CBCT as would have been done with the previous mask.

Intrafraction Monitoring

Intrafraction monitoring with the IFMM is set to allow nasal tip motion of up to 1.5 to 3 mm during treatment. Deviation beyond the threshold for > 30 s automatically aborts radiation delivery, and a repeat CBCT is required before treatment can resume.

TABLE 1. Patient and Tumor Characteristics

Variable	n (%)
Patients	100
Age at treatment (years)	
Median	67
Range	26-91
Sex	
Men	37
Women	63
Pathology	
Metastasis, total	42
Metastasis, non-small cell lung cancer	18
Metastasis, breast	5
Metastasis, melanoma	3
Metastasis, other	16
Meningioma, total	26
Meningioma, not otherwise specified	16
Meningioma grade 1	3
Meningioma grade 2	6
Meningioma grade 3	1
GBM	7
Ependymoma	3
Vestibular schwannoma	16
Other	6

Follow-Up, Toxicity, and Recurrence

Patients are seen every day by the radiation oncologist and specialized nursing during their treatments (1-5 fractions) and receive a telephone call 1 d after completion to assess side effects. Following treatment, patients undergo regular physical examination and diagnostic imaging depending on the clinical scenario. Patients with brain metastases typically follow up with an MRI every 2 to 3 mo if they remain in good performance status. Crude rates of local relapse are presented here, but because of the short interval of follow-up, no actuarial calculation of local control rates was undertaken. Toxicity was graded with the Common Terminology Criteria for Adverse Events version 5 and assessed by meticulous chart review including interval imaging, admission records, and changes in medication. Toxicity was attributed to GKRS unless there was clear evidence of another cause, or demonstrated disease progression.

RESULTS

One hundred patients were treated with frameless GKRS in the study period from April 2017 to February 2018. Patient and tumor characteristics are presented in Table 1. Treatment details are presented in Tables 2 and 3.

Median age was 67 yr old. Fifty-six patients were treated definitively, 21 postoperatively, and 23 had salvage GKRS for recurrence after prior surgery. Nineteen patients received prior SRS treatments. Forty-two patients (42%) had a total of 96 brain metastases, 76 of which were intact and 19 treated to the postoperative cavity. The most common primary malignancy for metastases was non-small cell lung cancer (18 patients, 43%), followed by breast (5 patients, 12%) and melanoma (3 patients,

TABLE 2. Dose and Fractionation

	Definitive GKRS or salvage GKRS	Data
Metastases dose, median (range), Gy		
Median dose in 1 fraction/3 fractions/5 fractions		20 (14-21)/24 (19.5-27)/25 (25-30)
Meningioma dose, median (range), Gy		
Median dose in 1 fraction/3 fractions/5 fractions		14 (12-18)/22.5 (21-24)/25 (25-30)
Vestibular scwannoma dose, median (range), Gy		
Median dose in 1 fraction/3 fractions/5 fractions		12 (12)/19.5 (19.5)/25 (25)
Ependymoma dose, median (range), Gy		
Median dose in 1 fraction/3 fractions/5 fractions		18 (18-20)/-/25 (25)
High grade glioma dose (including GBM), median (range), Gy		
Median dose in 1 fraction/3 fractions/5 fractions		20 (18-20)/15 (15)/25 (25-30)
	Postoperative cavity GKRS	
Metastases, postoperative RT, n (%)		19 (20%)
Median dose in 1 fraction/3 fractions/5 fractions		16/24/25
Meningiomas, postoperative RT, n (%)		14 (54%)
Median dose in 1 fraction/3 fractions/5 fractions		14/21/30
	Repeat radiosurgery	
	Previous SRS dose/fractions, Gy	Re-GKRS dose/fractions, Gy
Metastases (n = 7)	16/1	18/1
	16/1	21/3
	18/1	24/3
	18/1	21/3
	20/1	18/1
	20/1	24/3
	30/5	30/5
Meningioma (n = 3)	14/1	25/8
	14/1	14/1
	14/1 (2011) 14/1 (2013)	14/1
Ependymoma (n = 1)	18/1/1	25/5
Hemangiopericytoma (n = 1)	18.75/1 to 65% IDL (1997) 14/1 to 60% IDL (2006) 14/1 to 505 IDL (2014)	25/5
AVM (n = 1)	15/1 (1999) 18/1 (2014)	25/5

7%). Two patients had small-cell lung cancer (1 metastasis and 5 metastases, respectively). Other malignancies included colon, prostate, pancreatic, peritoneal, thyroid, urothelial, esophageal, renal cell carcinoma, mesothelioma, and diffuse large B-cell lymphoma.

The most common nonmetastatic lesions were meningiomas (26 patients), vestibular schwannomas (16 patients), and high-grade gliomas (7 GBM, 1 anaplastic astrocytoma, and 1 high-grade glioma not otherwise specified). Other histologies included 3 ependymomas, 1 arteriovenous malformation (AVM) (treated to 25 Gy/5), 1 hemangiopericytoma (25 Gy/5), 1 central nervous system (CNS) lymphoma (25 Gy/5), 1 schwannoma (25 Gy/5), and a cerebral aneurysm (25 Gy/5).

Fifty percent of patients were treated in a single fraction, 19% in 3 daily fractions, and 31% in 5 daily fractions.

Ependymomas and high-grade gliomas all underwent prior surgery. Prior whole-brain RT (WBRT) was given to only 2 patients with metastases. Partial brain RT to doses between 54 and 60 Gy was given to 12 patients with ependymomas and high-grade gliomas. One patient with meningioma previously received 52.5 Gy/29 to the same treated lesion. Salvage WBRT after GKRS was given to 4 patients with brain metastases and 1 patient with CNS lymphoma. Average time between the last GKRS and salvage WBRT was 147 d (range 63-262 d). Median treatment time was 17.7 min (range 5.8-61.7).

Thirteen patients underwent repeat GKRS to a total of 14 lesions. There was complete overlap of the 50% isodose line in 13 lesions and >50% overlap in 1 lesion. There were 7 metastases, 3 meningiomas, 1 ependymoma, 1 hemangiopericytoma, 1 AVM, and 1 GBM. Three of 14 lesions underwent multiple previous SRS. One meningioma received 14 Gy/1 in 2011 and 14 Gy/1 again in 2013 on GK. We treated this lesion to 14 Gy/1 in 2017. One hemangiopericytoma received 18.75 Gy/1 to the 65% isodose line on a linear accelerator in 1997, followed by 14 Gy/1 to the 40% isodose line in 2006 on GK, and 14 Gy/1 to the 50% isodose line in 2014 also on GK. We re-treated this lesion to 25 Gy/5 in 2018. Finally, an AVM received 18 Gy/1 in 1999 on GK, followed by 15 Gy/1 in 2014 on GK. We re-treated this AVM to 25 Gy/5 in 2018. All other lesions were re-treated only once, and all re-treatment GKRS doses in this series were prescribed to the 50% isodose line. Details of these re-treatments are presented in Table 2.

TABLE 3. Treatment Planning and Dosimetric Data

Prescription isodose line, median (range), %	50 (50-70)
Target volume, median (range), cm^3	1.919 (0.008-65.145)
Target volume in 1 fraction, median (range), cm^3	0.237 (0.008-24.700)
Target volume in 3 fractions, median (range), cm^3	6.610 (0.036-33.570)
Target volume in 5 fractions, median (range), cm^3	5.094 (0.215-65.145)
Brainstem maximum point dose, mean, Gy	
In 1 fraction/3 fractions/5 fractions	11.7/16.4/21.3
Brainstem maximum dose to 0.1 cm^3, mean, Gy	
In 1 fraction/3 fractions/5 fractions	8.5/11.97/17.45
Optic chiasm maximum point dose, mean, Gy	
In 1 fraction/3 fractions/5 fractions	14.2/-/12.5
Optic chiasm maximum dose to 0.1 cm^3, Gy	
In 1 fraction/3 fractions/5 fractions	8.5/-/4.5
Optic nerve maximum point dose, Gy	
In 1 fraction/3 fractions/5 fractions	12.7/-/17.9
Optic nerve maximum dose to 0.1 cm^3	
In 1 fraction/3 fractions/5 fractions	11.1/-/12.1
Cochlea maximum point dose, mean, Gy	
In 1 fraction/3 fractions/5 fractions	5.6/-/13.1
Cochlea mean organ dose, mean, Gy	
In 1 fraction/3 fractions/5 fractions	3.9/-/7.6
Cochlea volume, mean, cm^3	0.052
Target coverage, % (range)	98.8 (85-100)
Selectivity, mean (range)	0.59 (0.1-0.95)
Gradient index, mean (range)	2.96 (2.42-4.06)
Treatment time for frameless treatments, median (range), minutes	17.7 (5.8 -61.7)
First fraction framed in fractionated course, n (%)	11 (11)

TABLE 4. Cone-Beam CT Data

Shifts between reference CBCT and first pretreatment CBCT, mean (range), mm			
Translational x, y, z	0.24 (0-2.37)	0.36 (0.01-1.73)	0.47 (0.00-2.78)
Rotational x, y, z	0.51 (0-4.03)	0.26 (0-1.62)	0.35 (0-4.37)
CBCT shifts for fractions 2-5, mean (range), mm			
Translational x, y, z	0.94 (0-6.05)	0.85 (0.01-4.75)	2.89 (0-24.76)
Rotational x, y, z	1.81 (0.02-8.06)	1.14 (0-7.38)	1.61 (0.01-11.18)
Patient with repeat CBCT during the same fraction n, %	31, 31%		

Initial shifts for the first pretreatment CBCT were small because patients remained immobilized in the thermoplastic mask. For multifraction regimens, subsequent CBCTs have slightly greater shifts for registration in the stereotactic space. Thirty-one patients had more than 1 localization CBCT (excluding the day 1 reference CBCT). We do not have the data on reasons for repeat CBCT but these commonly included motion of > 1.5 to 3 mm for > 30 s on the IFMM, patient asking for a break, or patients not tolerating the treatment position. CBCT data are presented in Table 4.

Fifty patients had a follow-up MRI in our records after completing GKRS. Median follow-up time was 104 d. Sixteen local recurrences were identified in 9 patients with metastases and 7 patients with high-grade gliomas (Figure 2). Crude mean time between GKRS and recurrence was 120 d (range 85-314 d).

Nineteen patients had documented side effects potentially attributable to GKRS or combination surgery and postoperative GKRS. Eight patients had grade 1 fatigue, 1 G1 nausea, 4 G1/2 headache, 3 G1/2 seizures, 1 G2 amnesia, 2 G2 muscle weakness, 1 G3 muscles weakness, 1 G3 cerebral edema, and 1 patient with G4 intracranial hemorrhage and G4 encephalitis.

DISCUSSION

To our knowledge, this is the first detailed report on a large number of patients treated with frameless GKRS on the Icon GK. In our experience, we found 2 major improvements with the advent of the GK Icon: (1) improved workflow and (2) increased number of patients eligible for GK treatment because of fractionation.

Workflow

Before the Icon, the GKRS process commonly started early in the morning when the neurosurgeon fixed the stereotactic frame. Patients went for MRI and/or CT imaging with the invasive frame in place, waited for contouring and planning to be completed, then received their treatment. Unanticipated disturbances in this process could lead to significant delays. Patient tardiness, neurosurgical emergencies, MRI unavailability, or any complications during frame placement could lead to delays for the patient, MRI machine, and GK suite. In some cases, patients may have wait with the invasive frame in place much longer than anticipated.

To improve this workflow, some institutions acquire a diagnostic MRI without the frame a few days before the procedure. This allows for preplanning and for a more predictable workflow. There is no need to hold an MRI slot on the day of treatment, only a CT scan is acquired with the frame in place. This CT is then fused to the preplanned MRI and contours checked for accuracy before proceeding.

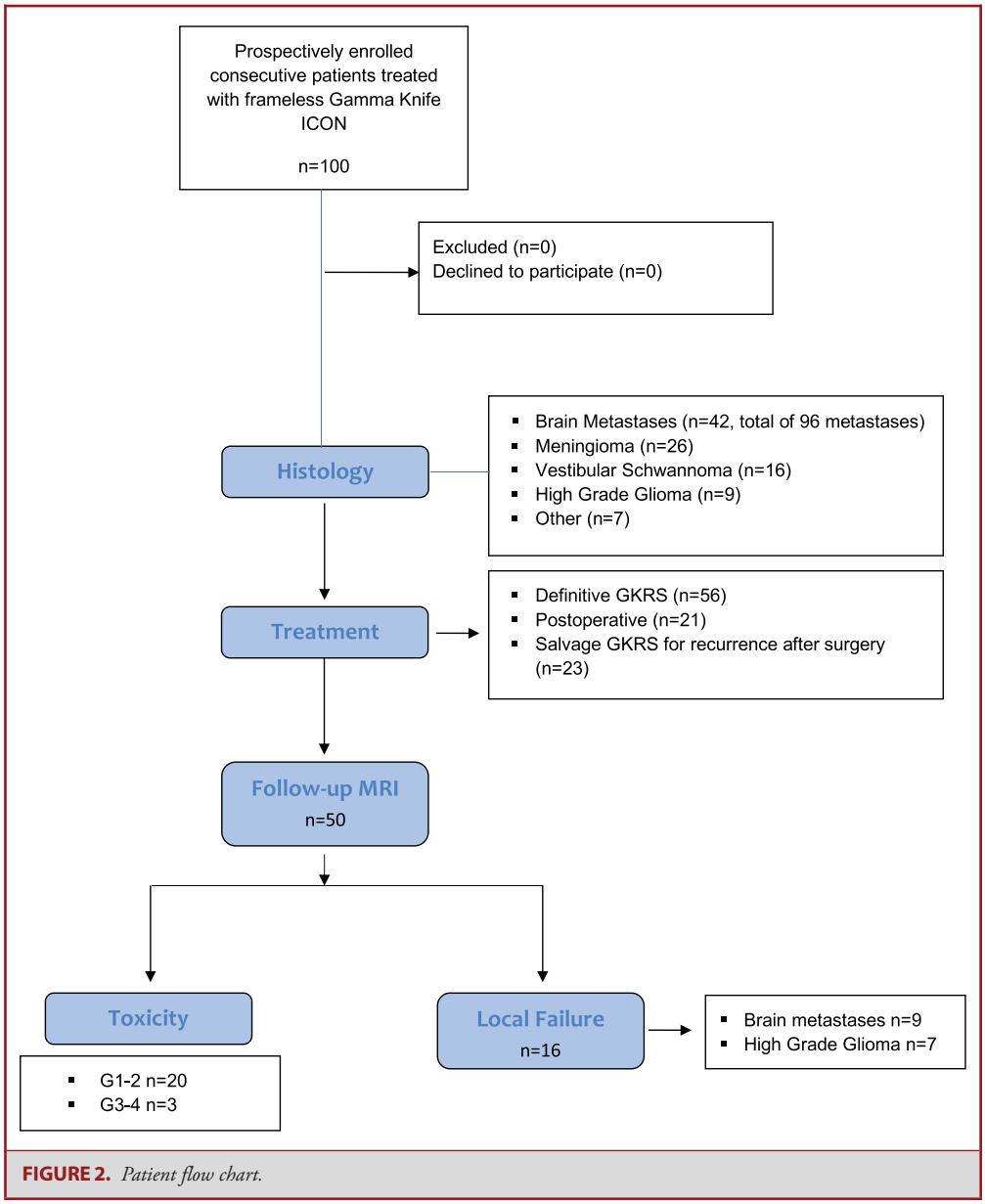

FIGURE 2. *Patient flow chart.*

With frameless Icon GKRS, patients have the choice of having the MRI before or on the day of treatment, with no significant change in workflow. Should a patient be late, they may comfortably wait for the next available imaging slot while another patient is being scanned. Scheduling appointments is easy when we remove the need to coordinate neurosurgical time for frame placement. Patient seen in clinic with slow growing, benign, tumors who already have an adequate MRI within a reasonable timeframe (eg, 2-3 wk) can be scheduled to start GK the following day. With this flexibility in scheduling, we have noticed improved workflow for the GK suite, as well as improved patient convenience and comfort.

Fractionation

Patients with large tumors who undergo single-fraction radiosurgery are known to be at higher risk of radiation necrosis.[2-4] For this reason, doses are generally reduced, which can decrease tumor control.[5] Delivering GK in multiple smaller doses exploits the radiobiological benefit of fractionation, with increased DNA repair in normal tissues compared to tumor cells. This is particularly valuable near critical organs like the brainstem, optic pathways, and cochlea. Fractionated cochlear dose constraints are easier to attain when treating in 5 fractions,[6,7] and tumor control rates for VS in 5 fractions have been recently reported to be excellent.[8] Similarly, we are able to treat very close to the

optic pathway while maintaining a tolerance in 5 fractions of 22.5 Gy, which is often easier to achieve than 8 Gy in a single fraction.[6] Patients with large lesions including large metastases, meningiomas, VS, recurrent gliomas, and resection cavities can now be treated in 3 to 5 fractions on the GK. These patients benefit from both the radiobiological advantage of fractionation and the dosimetric precision of a GKRS unit.

During a fractionated course, each localization CBCT is registered to the first stereotactic CBCT, and small translational shifts are corrected. Rotational shifts are not corrected given the absence of a 6 degree of freedom couch. The Gamma Plan software computes a new dose distribution before each fraction based on the new geometry, which is reviewed, and shots adjusted as needed. Most of the time, the differences are small because of the system's robustness to small rotations when 192 beams are focused at the isocenter around a spherical target.

We have noticed an increase in patients who are candidates for GKRS with this approach. Furthermore, single-fraction treatments can easily be converted to multifraction courses at the time of planning if the dose constraints to organs at risk cannot be met.

The Extend system (Elekta Instruments AB, Stockholm, Sweden) is another noninvasive repeat fixation device based on a vacuum-assisted mouthpiece. This technology is not available at our center but constitutes another solution for frameless GKRS that preceded the GK Icon, and patients eligible for fractionated Icon GKRS are also potential candidates for the Extend.

Patient Comfort and Safety

Complications of GKRS have been reported in the form of pin site infections, scarring, numbness, and pain. These can be minimized with careful attention to pin insertion site and local anesthetics, but not avoided altogether.[9,10] The thermoplastic mask is a noninvasive immobilization device that needs no anesthetic injections and no skin penetration for fixation. Randomized studies comparing the patient experience between the frame and the mask are unlikely to be completed. However, semistructured interviews and questionnaires reveal low rates of anxiety[11] and pain[12] related to the mask.

Treatment Accuracy

An important factor for treatment accuracy is the immobilization of patients in the stereotactic space. With a rigid frame, the assumption is that the patient's head is fixed relative to the frame, which defines the stereotactic space. Occasionally, frames have been known to slip,[13,14] though this is very rare. The Leskell G Frame has otherwise been consistently shown to maintain submillimeter positioning accuracy during treatments with shifts as low as 0.03 mm.[15-17]

The GK Icon defines the stereotactic space using a CBCT, immobilizes patients with a thermoplastic mask, and ensures they remain in the stereotactic space with real-time monitoring by an infrared camera (IFMM system). The mechanical stability of the CBCT unit itself has been shown to be submillimeter over a prolonged period of several months.[18] Coregistration with preplanning MRI and with pretreatment CBCTs was, in turn, determined to generate only submillimeter deviations.[19] The IFMM monitors intrafraction stability in the thermoplastic mask by tracking the patient's nose tip at a frequency of 20 Hz with 0.1 mm accuracy.[20] If the motion exceeds the prespecified threshold for a total of more than 30 s, the treatment is interrupted, and a new CBCT is required before restarting. Nose tip motion acts as a surrogate for changes in head geometry that can potentially alter the dose delivered to the target or organs at risks. We commonly use a nose tip threshold of 3 mm for most patients that we select for mask-based treatment. Early data show that intracranial target motion is on average about 50% that of nose tip motion.[21,22] In our experience, most commonly this motion is rotational when the patient's neck leans backward or forward. Small uncorrected rotational changes have been demonstrated to have a minor impact on dose on other radiosurgical units (non-GK) as long as they remain < 0.5 degrees,[23] which is also relevant when considering the small uncertainty introduced by the absence of a 6-degree couch. We do, however, opt for a frame-based treatment when additional precision is required.

CONCLUSION

We report the characteristics of patients, tumors, and treatments from a large cohort treated with frameless GKRS on the GK Icon to date. We find improvements in workflow and a greater number of patients eligible for GKRS because of the ability to fractionate treatments and to use noninvasive immobilization. We look forward to future studies with longer follow-up to provide valuable data on clinical outcomes and to further our understanding of the radiobiology of hypofractionation in the brain.

Disclosures

Dr Wang reports personal fees and non-financial support from AbbVie, personal fees from AstraZeneca, personal fees and non-financial support from Elekta, personal fees and non-financial support from Merck, personal fees from Doximity, personal fees from Wolters Kluwer, personal fees and non-financial support from Novocure, personal fees and non-financial support from RTOG Foundation, personal fees from Cancer Panels, outside the submitted work. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

1. O'Callaghan C, Sproston M, Wilkinson K, et al. Effect of self-selected music on adults' anxiety and subjective experiences during initial radiotherapy treatment: a randomised controlled trial and qualitative research. *J Med Imaging Radiat Oncol*. 2012;56(4):473-477.
2. Kohutek ZA, Yamada Y, Chan TA, et al. Long-term risk of radionecrosis and imaging changes after stereotactic radiosurgery for brain metastases. *J Neurooncol*. 2015;125(1):149-156.
3. Shaw E, Scott C, Souhami L, et al. Single dose radiosurgical treatment of recurrent previously irradiated primary brain tumors and brain metastases: final report of RTOG protocol 90-05. *Int J Radiat Oncol Biol Phys*. 2000;47(2):291-298.
4. Sneed PK, Mendez J, Vemer-van den Hoek JG, et al. Adverse radiation effect after stereotactic radiosurgery for brain metastases: incidence, time course, and risk factors. *J Neurosurg*. 2015;123(2):373-386.

5. Vogelbaum MA, Angelov L, Lee SY, Li L, Barnett GH, Suh JH. Local control of brain metastases by stereotactic radiosurgery in relation to dose to the tumor margin. *J Neurosurg*. 2006;104(6):907-912.
6. Hanna GG, Murray L, Patel R, et al. UK consensus on normal tissue dose constraints for stereotactic radiotherapy. *Clin Oncol*. 2018;30(1):5-14.
7. Timmerman RD. An overview of hypofractionation and introduction to this issue of seminars in radiation oncology. *Semin Radiat Oncol*. 2008;18(4):215-222.
8. Nguyen T, Duong C, Sheppard JP, et al. Hypo-fractionated stereotactic radiotherapy of five fractions with linear accelerator for vestibular schwannomas: a systematic review and meta-analysis. *Clin Neurol Neurosurg*. 2018;166:116-123.
9. Duenas SM, Pun J, Radwan HA, Akerman M, Schulder M. A randomized trial on the efficacy of topical anesthesia for pain reduction during frame placement for Gamma Knife radiosurgery. *Stereotact Funct Neurosurg*. 2016;94(4):259-264.
10. Wang DD, Lau D, Rolston JD, Englot DJ, Sneed PK, McDermott MW. Pain experience using conventional versus angled anterior posts during stereotactic head frame placement for radiosurgery. *J Clin Neurosci*. 2014;21(9):1538-1542.
11. Arino C, Stadelmaier N, Dupin C, Kantor G, Henriques de Figueiredo B. Thermoplastic mask in radiotherapy: a source of anxiety for the patient? *Cancer Radiother*. 2014;18(8):753-756.
12. Sharp L, Lewin F, Johansson H, Payne D, Gerhardsson A, Rutqvist LE. Randomized trial on two types of thermoplastic masks for patient immobilization during radiation therapy for head-and-neck cancer. *Int J Radiat Oncol Biol Phys*. 2005;61(1):250-256.
13. Otto K, Fallone BG. Frame slippage verification in stereotactic radiosurgery. *Int J Radiat Oncol Biol Phys*. 1998;41(1):199-205.
14. Ramakrishna N, Rosca F, Friesen S, Tezcanli E, Zygmanszki P, Hacker F. A clinical comparison of patient setup and intra-fraction motion using frame-based radiosurgery versus a frameless image-guided radiosurgery system for intracranial lesions. *Radiother Oncol*. 2010;95(1):109-115.
15. Karlsson B, Kalend A, Martinez R. Frame stability and anatomical QA in radiosurgery. *Acta Neurochir*. 2011;153(11):2265-2270.
16. Li W, Cho YB, Ansell S, et al. The use of cone beam computed tomography for image guided Gamma Knife stereotactic radiosurgery: initial clinical evaluation. *Int J Radiat Oncol Biol Phys*. 2016;96(1):214-220.
17. Rojas-Villabona A, Miszkiel K, Kitchen N, Jager R, Paddick I. Evaluation of the stability of the stereotactic Leksell Frame G in Gamma Knife radiosurgery. *J Appl Clin Med Phys*. 2016;17(3):75-89.
18. AlDahlawi I, Prasad D, Podgorsak MB. Evaluation of stability of stereotactic space defined by cone-beam CT for the Leksell Gamma Knife Icon. *J Appl Clin Med Phys*. 2017;18(3):67-72.
19. Chung HT, Kim JH, Kim JW, et al. Assessment of image co-registration accuracy for frameless gamma knife surgery. *PLoS One*. 2018;13(3):e0193809.
20. Elekta. *High Definition Motion Management - enabling stereotactic Gamma Knife® radiosurgery with non-rigid patient fixations*. White Paper. Available at: https://www.elekta.com/dam/jcr:0035e682-4893-432c-ab88-b1efbd76beeb/High-Definition-Motion-Management—enabling-stereotactic-Gamma-Knife_-radiosurgery-with-non-rigid-patient-fixations-white-paper.pdf. Accessed May 31, 2019.
21. Chung C, Li W, Bootsma G, et al. Clinical evaluation of a novel thermoplastic mask system with intrafraction motion monitoring using IR tracking and cone beam CT for Gamma Knife radiosurgery. *Int J Radiat Oncol Biol Phys*. 2014;90(1):S848.
22. Wright G, Harrold N, Hatfield P, Bownes P. Validity of the use of nose tip motion as a surrogate for intracranial motion in mask-fixated frameless Gamma Knife((R)) Icon therapy. *J Radiosurg SBRT*. 2017;4(4):289-301.
23. Gevaert T, Verellen D, Engels B, et al. Clinical evaluation of a robotic 6-degree of freedom treatment couch for frameless radiosurgery. *Int J Radiat Oncol Biol Phys*. 2012;83(1):467-474.

Neurosurgery Speaks! *Audio abstracts available for this article at www.neurosurgery-online.com.*