

What's New in My Specialty? New Developments in Neurosurgery and Neurology

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Assistant Professor of Neurosurgery, Neurooncology and Skull Base



Ogden Surgical-Medical Society
May 20, 2022

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DISCLOSURE

- Thieme Medical Publishing (royalties)



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MICHAEL KARSY, MD, PHD, MSC

- Undergraduate Neurosciences with Honors UCLA – 2006
- MD/PhD at NYMC – 2013
 - Dissertation “The Role of Tumor Suppressor p53 in the Regulation of Cancer Stem Cells of Glioblastoma Multiforme”
- MSc Bioengineering at University of Utah - 2016
- Residency University of Utah- 2013-2020
- Fellowship in Minimally Invasive and Open Skull Base at Thomas Jefferson University Hospital- 2021
- Research focus on translational neurooncology and targeted therapy, prognostic markers, and novel surgical techniques



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OUTLINE

- Updates in Neurooncology and Skull Base
 - Minimally invasive surgery with surgical technology
 - Integration of targeted therapy into patient care
 - Interdisciplinary management/clinical trials
 - Emerging technology: augmented reality, real-time imaging



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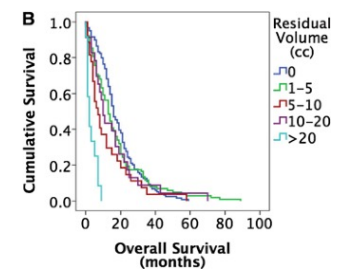
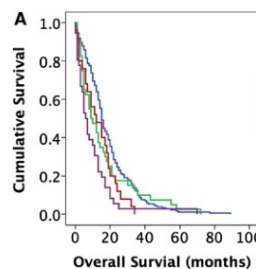
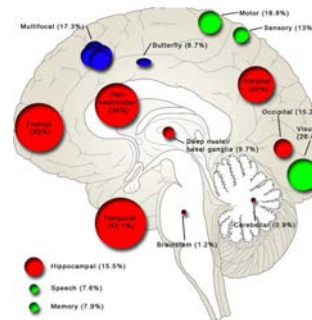
Minimally invasive surgery



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EXTENT OF RESECTION IMPROVES SURVIVAL

- N=330 patients with glioblastoma, 2006-2011
- Improving extent of resection remains important in improving survival
- Survival predictors: tumor volume, age, multifocal location, deep nuclei/basal ganglia



• Awad AW, Karsy M, Sanai N, Spetzler R, Zhang Y, Xu Y, Mahan MA Impact of removed tumor volume and location on patient outcome in glioblastoma. J Neurooncol. 2017 Oct;135(1):161-171

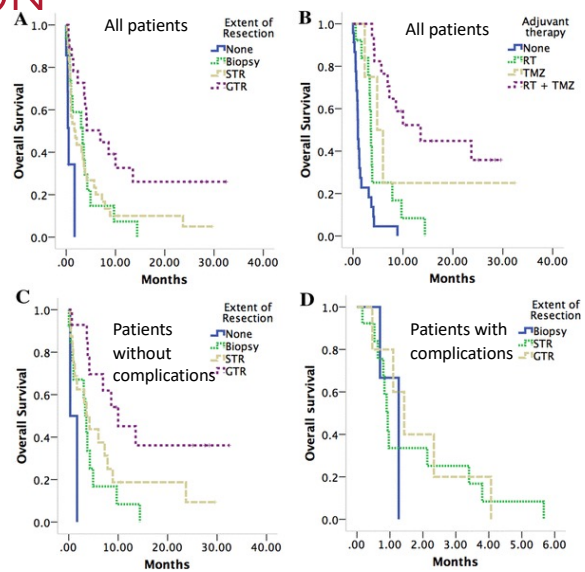
• Lacroix M, Abi-Said D, Fourney DR, Gokasian ZL, Shi W, DeMonte F, Lang FF, McCutcheon IE, Hassenbusch SJ, Holland E, Hess K, Michael C, Miller D, Sawaya R A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection, and survival. J Neurosurg. 2001 Aug;95(2):190-8.



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PATIENT COMPLICATION IMPAIRS SURVIVAL

- N=82 patients >75 years of age, 1995-2016
- Patient complication significantly impairs overall survival in elderly and young patients
- Minor complications reduce ability to complete adjuvant therapy



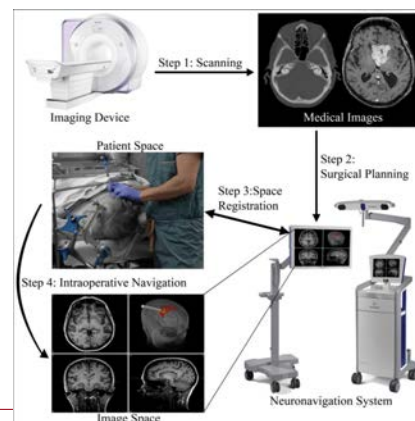
• Karsy M, Yoon N, Boettcher L, Jensen R, Shah L, MacDonald J, Menacho ST. Surgical treatment of glioblastoma in the elderly: the impact of complications. *J Neurooncol.* 2018 May;138(1):123-132



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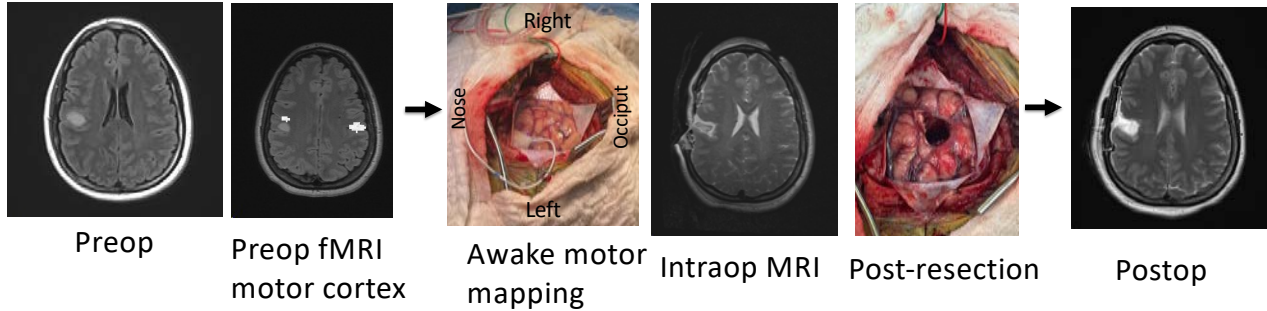
UPDATE: MINIMALLY INVASIVE RESECTION

- Improved technology for more accurate tumor localization and safer resection
 - Neuronavigation
 - Awake mapping
 - Intraoperative MRI
 - Functional MRI
 - Ultrasound
 - Tractography



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SURGICAL ADJUNCTS IN TUMOR RESECTION



- 34-year-old female presenting with new onset seizures
- WHO III IDHmut astrocytoma, EGFRlow, MGMT-unmeth, 1p19q intact, GFAP+, ATRX+, p53 80%, ki-67 10%

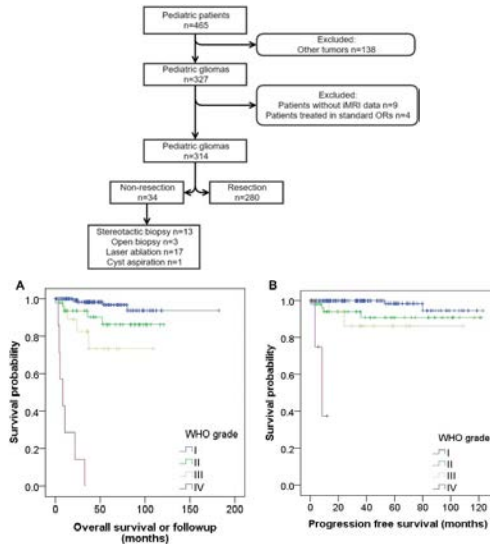
↓
Interdisciplinary tumor board
 -TMZ, RT
 -Clinical trial screening



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EXPANSION OF IMRI TO OTHER TYPES OF CASES

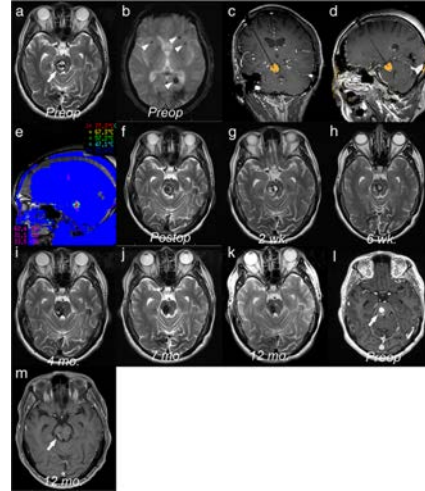
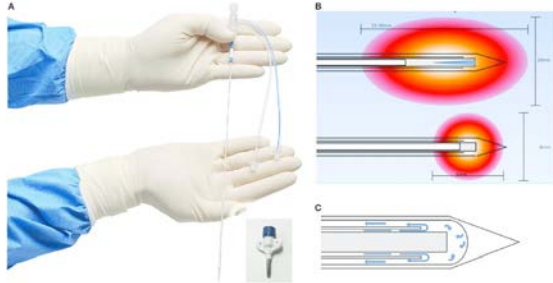
- N=314 pediatric patients, age 9.7 years, 2007-2019
- Multicenter registry
- 46.8% of patients underwent additional tumor resection after iMRI with most samples (87.9%) being positive



Karsy M, Akbari SH, Limbrick D, Leuthardt EC, Evans J, Smyth MD, Strahle J, Leonard J, Cheshier S, Brockmeyer DL, Bollo RJ, Kestle JR, Honeycutt J, Donahue DJ, Roberts RA, Hansen DR, Riva-Cambria J, Sutherland G, Gallagher C, Hader W, Stareveld Y, Hamilton M, Duhaime AC, Jensen RL, Chicoine MR. Evaluation of pediatric glioma outcomes using intraoperative MRI: a multicenter cohort study. *J Neurooncol.* 2019 Jun;143(2):271-280.

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UPDATE: LITT AND IMRI FOR LESION TREATMENT



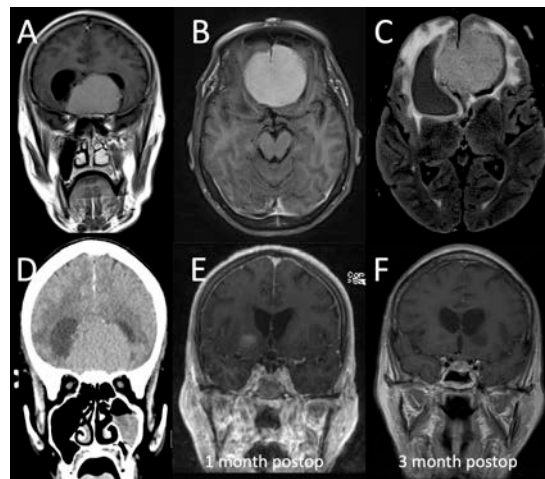
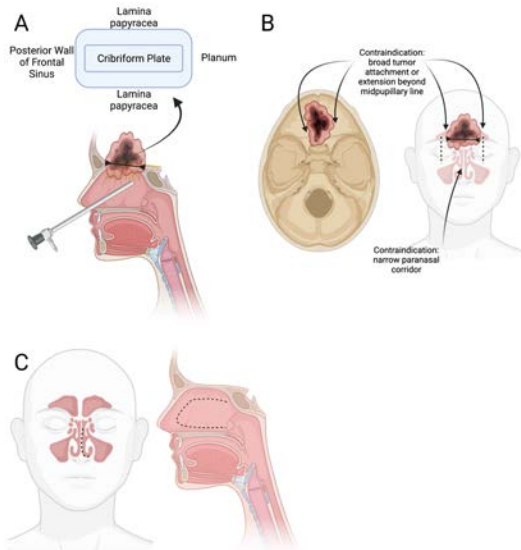
- n=2 cases, brainstem cavernous malformations, recurrent symptomatic hemorrhage, treatment with laser interstitial thermal therapy
- Improvement in symptoms and lesion involution over time



Nicholas T. Gamboa, Michael Karsy, Rajiv R. Iyer, Robert J. Bollo, Richard H. Schmidt *Acta Neurochirurgica* (2020) 162:1771–1775

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UPDATE: ENDOSCOPIC SKULL BASE

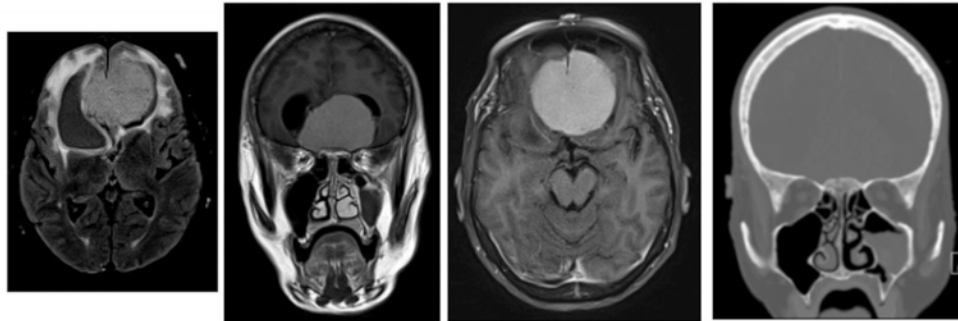


Cutler J, Henson JC, Alf J, Karsy M. How I Do It: Endonasal Transethmoidal, Transcribriform Approach for Resection of Giant Olfactory Groove Meningioma. *Acta Neurochir* accepted 2022

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ENDOSCOPIC SKULL BASE

68 year-old-female presents after a mechanical fall. Family reports several years of personality and memory changes.



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RAPID Research Consortium

“Enabling a Stellar Sellar Transformation”

To serve the **clinician-scientist** by...

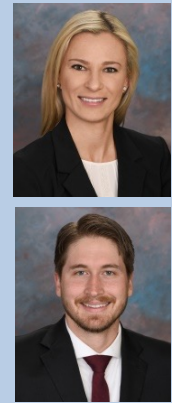
- 1) developing a platform for multicenter pituitary quality improvement efforts and clinical and translational research,
- 2) promoting collegiality and scholarship,
- 3) applying innovative solutions to the challenges of outcomes research.

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STEERING COMMITTEE



BCOC



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CURRENT STATE OF PITUITARY RESEARCH

- ❖ Pituitary tumors are orphan disease
- ❖ Pituitary research occurs in silos
- ❖ No collaborative platform for executing studies at scale
- ❖ No national surgery outcomes registry exists
- ❖ Translational research is challenging , in part because of lack of tumor samples and opportunities for multidisciplinary collaboration

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Targeted treatment



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UPDATE: INTEGRATION OF TRANSLATIONAL TREATMENTS INTO NEUROONCOLOGY

frontiers in Oncology

REVIEW
JOURNAL 23 February 2022
doi:10.3389/fonc.2022.774136

Frontiers in Bioscience
Landmark

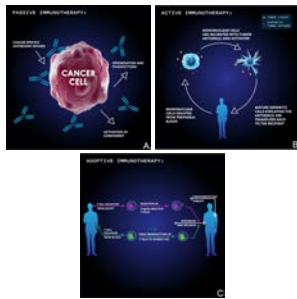
Front. Biosci. (Landmark Ed.) 2022, 27(4):136
https://doi.org/10.3389/fonc.2022.774136

Frontiers in Bioscience
Landmark

Front. Biosci. (Landmark Ed.) 2022, 27(3):177
https://doi.org/10.3389/fonc.2022.770377

Glioma Stem Cells as Immunotherapeutic Targets: Advancements and Challenges

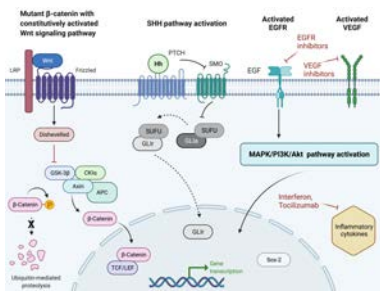
Keenan Piper^{1,2*}, Lisa DePaolige^{1,2*}, Michael Karsy¹ and Charles Cobbs^{1*}



Targeted Therapy in the Management of Modern Craniopharyngiomas

Maikerly Reyes¹, Mohammad Taghvaei¹, Siyuan Yu¹, Anish Sath¹, Sarah Collopy¹, Giyapuram N. Prashant¹, James J. Evans¹, Michael Karsy^{1,2*}

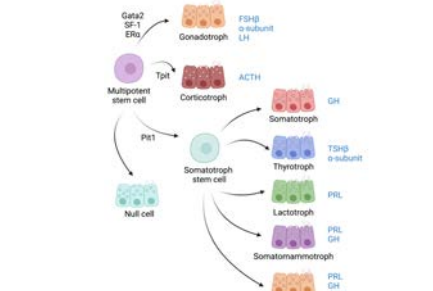
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Academic Editor: Graham Prevedel
Submitted: 20 November 2021 | Revised: 28 January 2022 | Accepted: 9 February 2022 | Published: 20 April 2022



A review of multiomics platforms in pituitary adenoma pathogenesis

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Academic Editor: Graham Prevedel
Submitted: 30 November 2021 | Revised: 31 January 2022 | Accepted: 10 February 2022 | Published: 4 March 2022



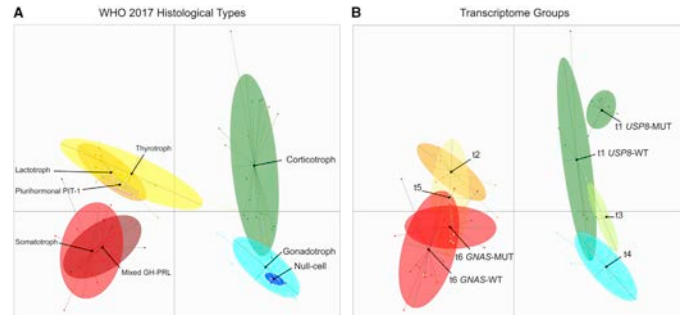
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UPDATE: TUMOR GENETICS IMPROVES UNDERSTANDING OF TUMOR BIOLOGY

- Integration of chromosomal analysis, microRNA, DNA methylation, and mRNA genomics to reclassify pituitary tumors in a way never done before

Pangenomic Classification of Pituitary Neuroendocrine Tumors

Mario Neou,^{1,2,3,16} Chiara Villa,^{1,2,3,4,5,16} Roberta Armignacco,^{1,2,3} Anne Jouinot,^{1,2,3} Marie-Laure Raffin-Sanson,^{6,7} Amandine Septhier,^{1,2,3} Franck Letourneur,^{1,2,3,8} Ségolène Dity,^{1,2,3} Marc Diedlisheim,⁹ Brigitte Izac,^{1,2,3,8} Cassandra Gaspar,^{1,2,3,10} Karine Perlemono,^{1,2,3} Victoria Verjus,^{1,2,3} Michèle Bernier,¹ Anne Boulin,¹¹ Jean-François Emile,¹² Xavier Bertagna,^{1,2,3,13} Florence Jaffrezic,¹⁴ Denis Laloe,¹⁴ Bertrand Baussart,¹⁵ Jérôme Bertherat,^{1,2,3,15,17} Stephan Gaillard,^{15,17} and Guillaume Assié^{1,2,3,15,17,18*}

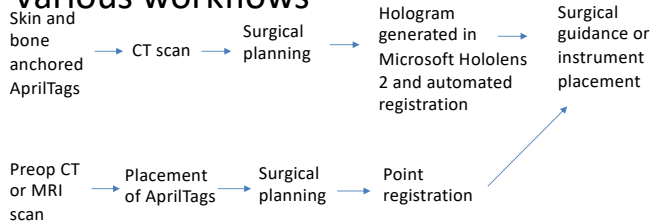


Emerging technologies

UPDATE: INTEGRATION OF AUGMENTED REALITY INTO THE SURGICAL OPERATING ROOM

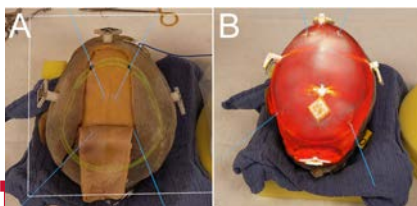
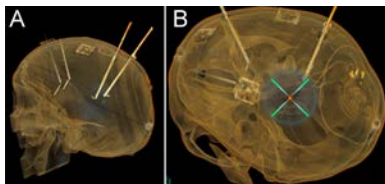


Various workflows



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AR-GUIDED EVD PLACEMENT

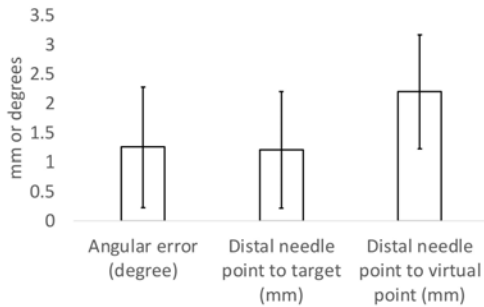


- Phantom model 1 – skull model, 0.5mm targets, CT measured accuracy
- Phantom model 2 – skull model, 1 mm targets, Axiem measured accuracy
- Cadaver model – ventricle target, Axiem measured accuracy



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AR-GUIDED EVD PLACEMENT

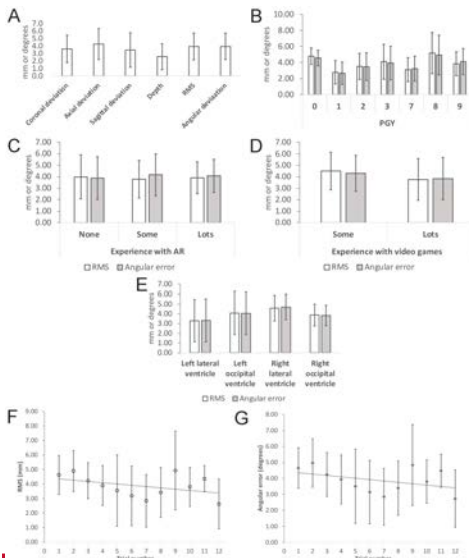


- Phantom model 1 – skull model, 0.5mm targets, CT measured accuracy
 - Mean error of 0.65 ± 0.61 mm from needle tip to target and angular error (γ) of $0.67 \pm 0.54^\circ$



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AR-GUIDED EVD PLACEMENT



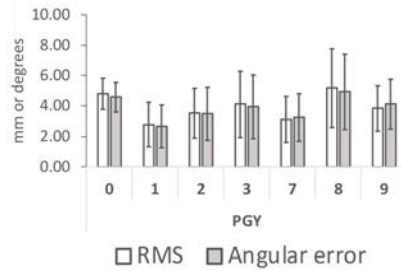
- Phantom model 2 – skull model, 1 mm targets, Axiem measured accuracy
 - A mean RMS of 3.9 ± 1.8 mm and γ of $3.95 \pm 1.78^\circ$
 - No difference in accuracy depending on PGY level, experience with AR, video games or EVD placements
 - Some improvement in accuracy over number of trials but not significant



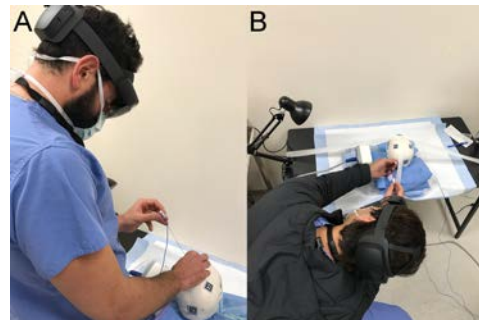
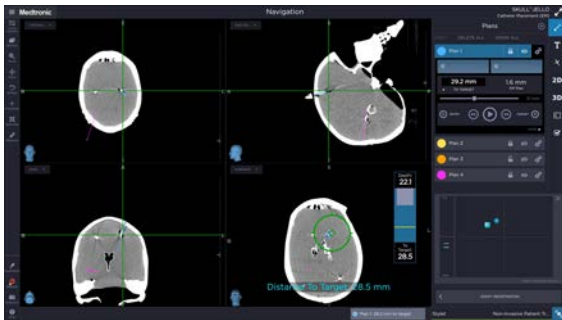
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AR TO IMPROVE PROCEDURAL ACCURACY

- Accuracy not impacted by previous resident experience, experience with AR, video games or EVDs



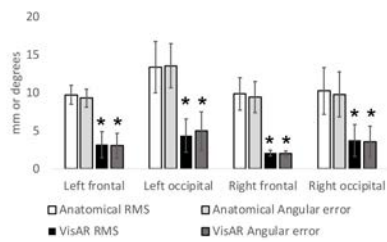
No significant difference in root mean square or angular error depending on experience level



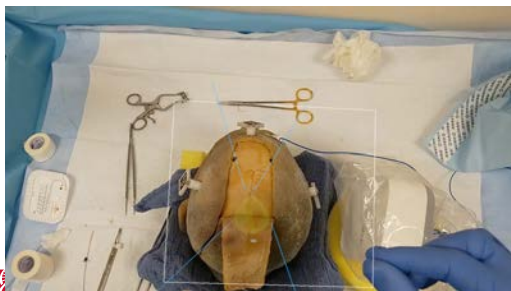
Two residents using AR for the first time

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AR-GUIDED EVD PLACEMENT



- Cadaver model – ventricle target, Axiem measured accuracy
- Significant improvement in accuracy with AR compared to anatomical trajectories



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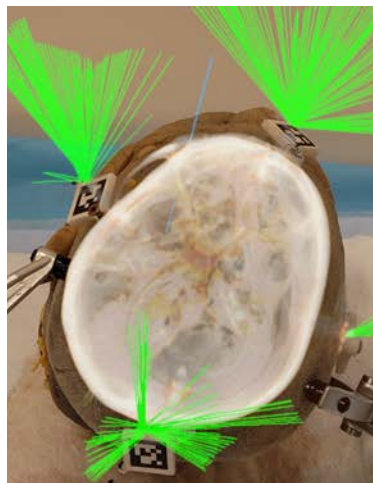
AR-GUIDED TRAJECTORIES FOR TRIGEMINAL NEURALGIA



In development

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AR-GUIDANCE FOR SKULL BASE APPROACHES



In development

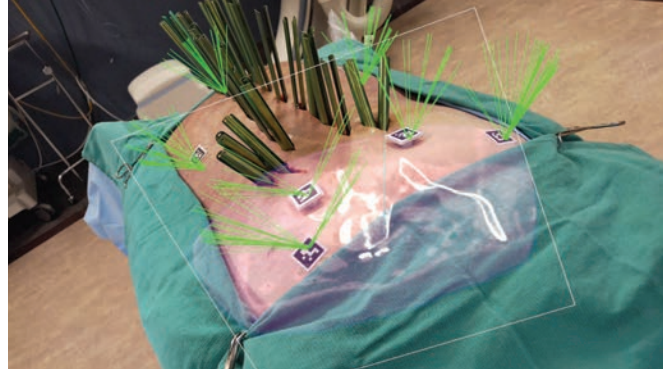
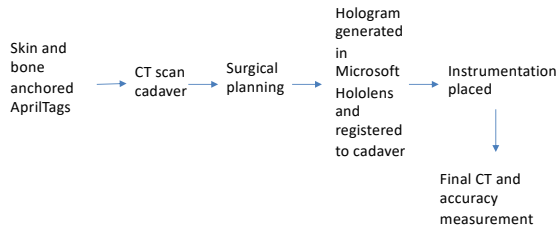
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Augmented Reality Spine Surgery Navigation

Increasing Pedicle Screw Insertion Accuracy for Both Open and Minimally Invasive Spine Surgeries

^{A02} Brent Felix, MD,^a Seyed Babak Kalatar, MD,^b Bradley Moatz, MD,^c Christoph Hofstetter, MD, PhD,^d Michael Karsy, MD, PhD,^e Ryan Parr, PhD,^f and Wendell Gibby, MD^{f,g,h}

- N=124 pedicle screw trajectories in 7 cadavers
- Multiple spine surgeons with various experience
- 96% GRS A or B accuracy



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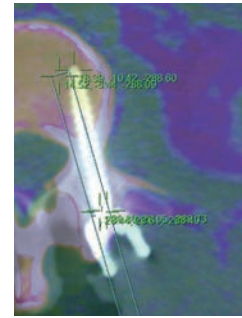
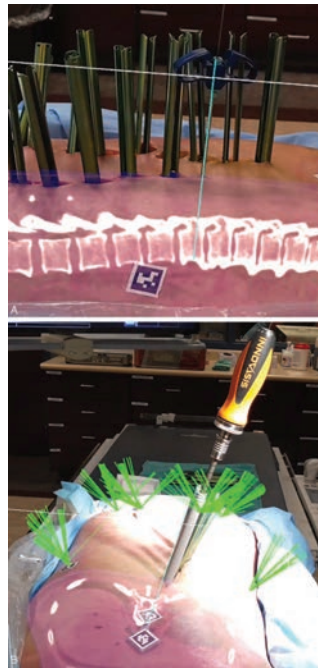
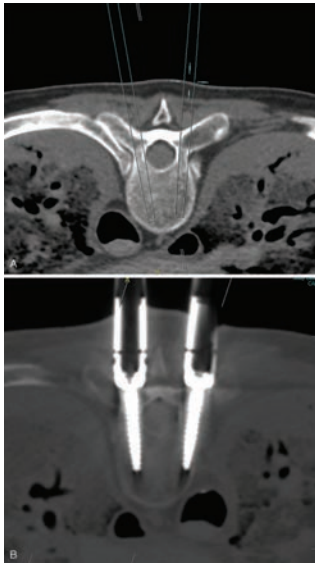


Figure 6. Fused images of preoperative CT scan with virtual pedicle placement (blue) and actual pedicle screw placement. Coordinate measurements overlain in green.

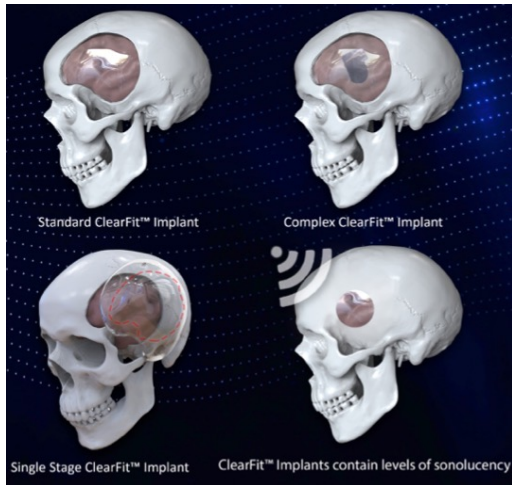
Grade	Breach, mm
A	No breach
B	0.0-2.0
C	2.1-4.0
D	4.1-6.0
E	>6.0

	GRS A	GRS B	GRS C	Totals	% Accuracy
Open	59	4	2	65	96.9
MISS	54	2	3	59	94.9
Combined	113	6	5	124	96.0%

GRS indicates Gertzbein-Robbins scale; MISS, minimally invasive spine surgery.

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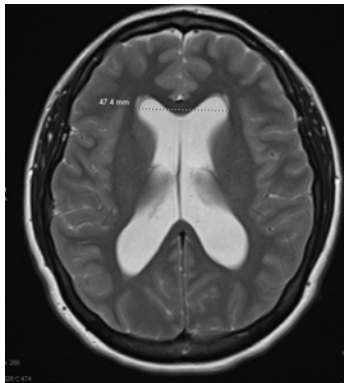
UPDATE: INTEGRATION OF NOVEL DEVICES IN THE OR



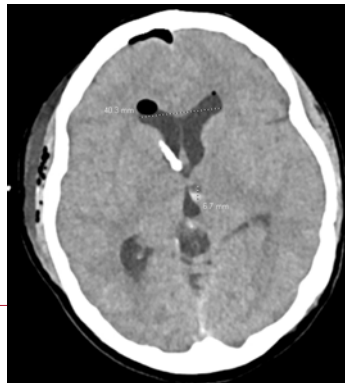
- Longevity ClearFit device, various cranioplasty or burr hole covers allowing ultrasound through the skull



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3/11/21
Preop

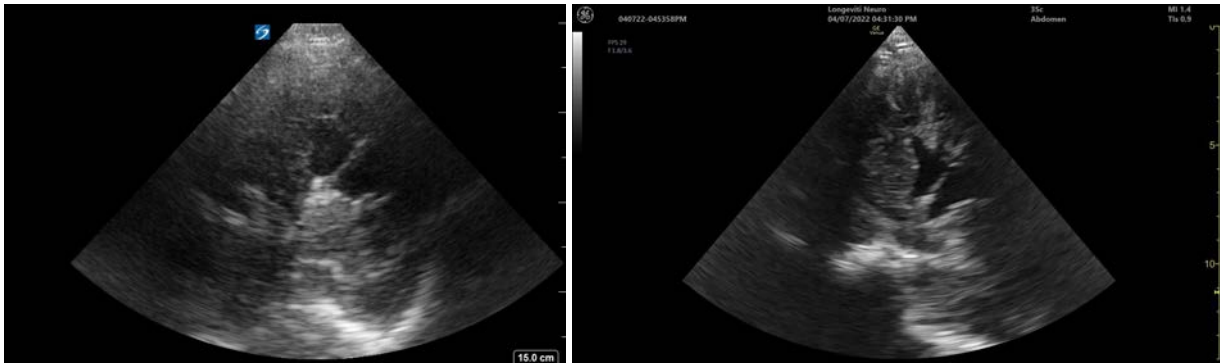


4/6/22
Postop 1
ETV and tectal tumor bx
Decreased ventricular size



4/7/22
Post op day2
Ultrasound tech
Decreased ventricular size

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4/7/22
Post op day2
Sonosite, Karsy
Decreased ventricular size

4/7/22
Post op day2
GE, David
Decreased ventricular size

4/22/22 Unable to insonate using Neurosurgery clinic
ultrasounds as correct probe not available

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INTEGRATING MULTIMODAL IMAGING INTO PATIENT CARE

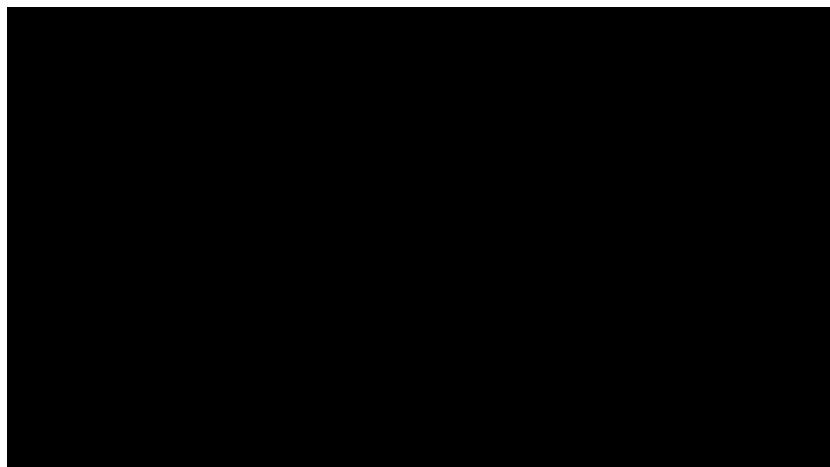


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INTEGRATING MULTIMODAL IMAGING INTO PATIENT CARE



AR-GUIDED INSTRUMENTATION PLACEMENT

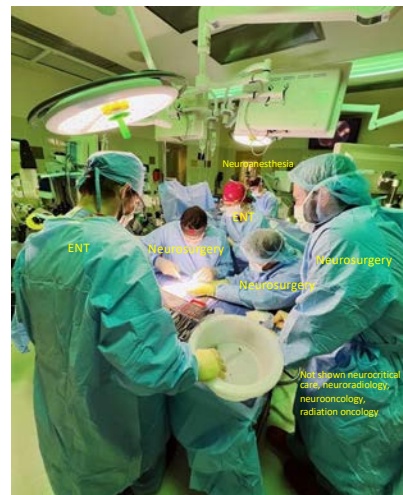
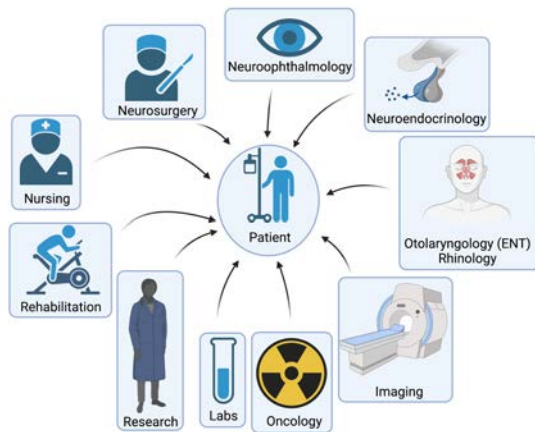


Interdisciplinary management



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CLINICAL NEUROSCIENCES CENTER - INTERDISCIPLINARY MANAGEMENT OF NEUROLOGICAL DISEASE



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CURRENT NEUROONCOLOGY CLINICAL TRIALS

- NCT03970447 - Glioblastoma Adaptive, Global, Innovative Learning Environment (GBM AGILE)
- NCT03776071 - Randomized, Double-Blind, Placebo-Controlled Phase III Study of Enzastaurin Added to Temozolomide During and Following Radiation Therapy in Newly Diagnosed Glioblastoma Patients Who Possess the Novel Genomic Biomarker DGM1
- NCT04421378 - A Phase I/II Study of Selinexor in Combination with Standard of Care (SoC) Therapy for Newly Diagnosed or Recurrent Glioblastoma
- NCT05023551 - Phase I Study of DSP-0390 in Patients with Recurrent High-Grade Glioma
- NCT04782609 - A Phase 1B Dose Escalation/Dose Expansion Study of Icapamespib (PU-AD) in Patients with Recurrent Malignant Glioma
- NCT03224767 - Phase II Trial of BRAF/MEK Inhibitors in Papillary Craniopharyngiomas
- NCT03604978 - Phase I/II Study of Nivolumab Plus or Minus Ipilimumab in Combination with Multi-Fraction Stereotactic Radiosurgery for Recurrent High-Grade Radiation-Relapsed Meningioma
- NCT02523014 - Phase II Trial of SMO/AKT/NF2 Inhibitors in Progressive Meningiomas with SMO/AKT/NF2 Mutations
- NCT03994796 - Genomically-Guided Treatment Trial in Brain Metastases
- NCT04114981 - Phase III Trial of Post-Surgical Single Fraction Stereotactic Radiosurgery (SRS) Compared with Fractionated SRS for Resected Metastatic Brain Disease
- NCT03550391 - A Phase III Trial of Stereotactic Radiosurgery Compared with Hippocampal-Avoidant Whole Brain Radiotherapy (HA-WBRT) plus Memantine for 5-15 Brain Metastases
- NCT04609046 - Phase I Trial of Methotrexate, Rituximab, Lenalidomide, and Nivolumab (Nivo-MR2) Induction Followed by Lenalidomide and Nivolumab Maintenance in Primary CNS Lymphoma
- NCT04947319 - Open-Label Phase II Study to Investigate the Efficacy, Safety, and Pharmacokinetics of Tirabrutinib in Patients with Primary Central Nervous System Lymphoma (PCNSL)



NEUROONCOLOGY TEAM



William Couldwell,
MD, PhD
Neurosurgery



Randy Jensen,
MD, PhD
Neurosurgery



Sarah T.
Menacho, MD
Neurosurgery



Michael Karsy, MD,
PhD, MSc
Neurosurgery



Jeremiah Alt, MD,
PhD
Otolaryngology -
Rhinology



Gretchen
Oakley, MD
Otolaryngology
- Rhinology



Richard Orlandi,
MD
Otolaryngology -
Rhinology



Richard Gurgel, MD
Otolaryngology -
Neurootology



Neil Patel, MD
Otolaryngology -
Neurootology



NEUROONCOLOGY TEAM



Howard Colman, MD, PhD
Neurooncology



Joe Mendez, MD
Neurooncology



Donald Cannon, MD
Radiation oncology



Lindsay Burt, MD
Radiation oncology



Christina DeCesaris, MD
Radiation oncology



Jason Hunt, MD, FACS
Otolaryngology – head and neck



Marcus Monroe, MD
Otolaryngology – head and neck



Richard Cannon, MD
Otolaryngology – head and neck



NEUROONCOLOGY TEAM



Alison Crum, MD
Neuro-Ophthalmology, Ophthalmology, Oculoplastic & Facial Plastic Surgery



Kathleen B. Digre, MD
Headache, Migraine, Neuro-Ophthalmology



Bradley J. Katz, MD, PhD
Neuro-Ophthalmology, Ophthalmology, Vasculitis



Meagan Seay, DO
Neuro-Ophthalmology, Ophthalmology



Massiell German, MD
Neuroendocrinology



Corrine Welt, MD
Neuroendocrinology



James Craven, MB, BCh, BAO, MSc
Neuroendocrinology



Jyotika Singh, DO
Headache, Neuro-Ophthalmology



Judith EA Warner, MD
Neuro-Ophthalmology, Neurology, Ophthalmology



Douglas Marx, MD
Oculoplastics

And many more...



UNIVERSITY OF UTAH - SKULL BASE TEAM

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