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Letter to the Editor

Exploring neurosurgical oncology in medical school

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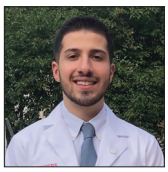

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Dear Editor,

We believe that neurosurgical oncology necessitates additional layers of preparation, given its multidisciplinary nature. Brain and spine tumor care is split into multiple steps involving different specialists at each, including diagnosis (encompassing neuroradiology, neuropathology, and neuro-oncology), technicality (neurosurgery and neuroanesthesiology), and treatment (neuro-oncology, radiation oncology, and palliative care). The complex nature of this workflow requires that the neurosurgical oncologist, often deemed to be the overseeing physician alongside the neuro-oncologist, "speak the language" of their physician colleagues. Such an approach would ensure the best possible patient outcomes based on the current treatment landscape.

Despite the importance of honing interdisciplinary expertise, neurosurgical oncologists often have difficulty pursuing such opportunities due to time constraints. A minimum of 11 years of medical education and training is required to become an attending neurosurgeon. Neurosurgical oncology typically entails the completion of additional training, such as in the form of a Ph.D. degree and/or fellowship in neuro-oncology. The 7-year residency prioritizes the mastery of surgical skills and provides exposure to some, but not all, aspects of neuro-oncology. As attending physicians, neurosurgeons continue to focus on sharpening operative skills.

Simply put, time away from the operating room hurts technical ability in neurosurgery. In comparison, the practice of oncology is often enhanced by time away from the clinic when spent on research and/or independent study of the literature. This provides an opportunity to improve patient outcomes through acquired knowledge of cutting-edge diagnostic and therapeutic strategies. Because the neurosurgical oncologist must achieve the same level of proficiency as a neuro-oncologist, one potential solution is to extend the timeline of oncology-focused education in reverse.

We propose that medical school presents the ideal time for the preparation of future neurosurgical oncologists. The broad-scope knowledge acquired in foundational topics along with physiology, pathology, and pharmacology provides a ripe opportunity to delve into the field. Furthermore, medical students are unable to develop their surgical adeptness at this stage. To achieve this objective, a set of clinical electives across relevant disciplines, including hematology/oncology, neurosurgery, neuropathology, neuroradiology, and radiation oncology, can be pursued by 3rd- and 4th-year medical students outside of the core curriculum at Rutgers New Jersey Medical School [Table 1]. These mechanisms not only count toward attaining the necessary academic credits for graduation but also make direct learning possible under the mentorship of physicians

from each of these subspecialties that encompass the diverse aspects of neurosurgical oncology.

In addition, inspired by the curriculum established for neuro-oncology fellows and the *World Health Organization Classification of Tumors of the Central Nervous System*, we recently organized extracurricular focused learning sessions that covered essential principles of neuro-oncology over 2 years under the direction of a neurosurgical oncologist [Table 2]. The objectives were four-fold: (i) to gain exposure to key aspects of neurosurgical oncology by regularly reading high-quality literature, (ii) to build a habit of effective discussion and presentation of scientific findings, (iii) to assemble a network of students and faculty members with a common interest in neurosurgical oncology, and (iv) to receive and share career guidance. Medical students in any year of study were eligible to participate. For each topic, we delved into various publications (*i.e.*, laboratory studies, clinical trials, clinical studies, and reviews), which together provided an overview of the approach to discovering tumor markers and targets, characterizing biological mechanisms, and evaluating treatments across various central and peripheral nervous system tumor types [Table 3]. Independent readings followed by these small-group meetings permitted guided discussions in the context of clinical neurosurgery. Although these focused learning sessions did not count toward any academic credit, they promoted in-depth exploration of relevant topics in neurosurgical oncology in addition to career guidance under the mentorship of an established neurosurgical oncologist.

Furthermore, we discovered that ongoing separate experiences in bench and clinical research created learning opportunities for one another. We also occasionally elected to have one participant, sometimes a guest physician from another field, to lead the discussion on a preferred topic.

Table 1: Clinical electives relevant to neurosurgical oncology that are available for registration by medical students at Rutgers New Jersey Medical School.

Clinical elective	Department	Year of medical training	Duration
Acting Internship in Neurological Surgery	Neurological Surgery	4	4 weeks
Hematology/Oncology	Medicine	3 or 4	2 or 4 weeks
Introduction to Neurological Surgery	Neurological Surgery	3	2 weeks
Introduction to Neuroradiology	Radiology	3 or 4	2 or 4 weeks
Neuropathology	Pathology	4	4 weeks
Radiation Oncology	Radiation Oncology	3 or 4	2 or 4 weeks

Table 2: Overview of themes covered in focused learning sessions on neurosurgical oncology at Rutgers New Jersey Medical School.

Theme	Description
Clinical trial design	Learn about clinical trial components and data analysis in addition to adaptive designs and master protocols.
Reproducibility and ethics in research	Learn about common issues related to lack of reproducibility in science along with its potential reasons and mechanisms for its prevention.
Professionalism in neurosurgery	Learn about expectations for a career in neurosurgery, including behavior at conference meetings.
Classification, grading, and neuropathology of tumors	Learn about criteria for characterizing tumors in the clinical setting.
Specific tumor types	Learn about various brain and spine tumors, including glioma, ependymoma, cranial and spinal meningioma, brain metastasis, lymphoma, pediatric low-grade glioma, medulloblastoma, and papillary craniopharyngioma.
Large-scale genomic studies	Learn about approaches to identify common mutational signatures of tumors (*e.g.*, exome sequencing, whole-genome sequencing).
Small-scale clinical series	Learn about clinical series with a small *n* describing outcomes for a certain treatment combination.
Radiation safety and radiobiology	Learn about contouring for radiation applied to tumor resection sites.
Advances in surgical techniques for tumor resection	Learn about recent technological advances that have facilitated safer and more effective tumor resection.
Neuro-oncology clinical trials	Learn about major precedent-setting clinical trials that have influenced the current treatment landscape.
Mechanisms of emerging pharmaceutical therapies	Examples include CAR-T cell therapy and novel tyrosine kinase inhibitors.
Interface between academia and industry	Learn about the evolution of findings in the laboratory setting to translational applications in the clinic.

Table 3: Articles discussed in focused learning sessions that span topics relevant to neurosurgical oncology.

Topic	Article(s)
Brain metastasis	• Achrol AS, *et al*. Brain metastases. Nat Rev Dis Primers. 2019;5(1):5. • Hsieh JJ, *et al*. Renal cell carcinoma. Nat Rev Dis Primers. 2017;3:17009. • Mills MN, *et al*. Management of brain metastases in breast cancer: a review of current practices and emerging treatments. Breast Cancer Res Treat. 2020;180(2):279-300. • Patchell RA, *et al*. A randomized trial of surgery in the treatment of single metastases to the brain. N Engl J Med. 1990;322(8):494-500. • Patchell RA, *et al*. Postoperative radiotherapy in the treatment of single metastases to the brain: a randomized trial. JAMA. 1998;280(17):1485-1489. • Sperduto PW, *et al*. Summary report on the graded prognostic assessment: an accurate and facile diagnosis-specific tool to estimate survival for patients with brain metastases. J Clin Oncol. 2012;30(4):419-425. • Sperduto PW, *et al*. Estimating survival in patients with lung cancer and brain metastases: an update of the graded prognostic assessment for lung cancer using molecular markers (Lung-molGPA). JAMA Oncol. 2017;3(6):827-831. • Tawbi HA, *et al*. Combined nivolumab and ipilimumab in melanoma metastatic to the brain. N Engl J Med. 2018;379(8):722-730. • Turajlic S, Larkin J. Immunotherapy for melanoma metastatic to the brain. N Engl J Med. 2018;379(8):789-790.
Central nervous system lymphatic vessels	• Louveau A, *et al*. Structural and functional features of central nervous system lymphatic vessels. Nature. 2015;523(7560):337-341.
Clinical trial design	• Bhatt DL, Mehta C. Adaptive designs for clinical trials. N Engl J Med. 2016;375(1):65-74. • Mauri L, D'Agostino RB Sr. Challenges in the design and interpretation of noninferiority trials. N Engl J Med. 2017;377(14):1357-1367. • Pfeffer MA, McMurray JJ. Lessons in uncertainty and humility - clinical trials involving hypertension. N Engl J Med. 2016;375(18):1756-1766. • Pocock SJ, Stone GW. The primary outcome fails – what next? N Engl J Med. 2016;375(9):861-870. • Woodcock J, LaVange LM. Master protocols to study multiple therapies, multiple diseases, or both. N Engl J Med. 2017;377(1):62-70.
Cranial and spinal meningioma	• Ojemann RG. Management of cranial and spinal meningiomas (honored guest presentation). Clin Neurosurg. 1993;40:321-383.
Ependymal tumors	• Ellison DW, *et al*. cIMPACT-NOW update 7: advancing the molecular classification of ependymal tumors. Brain Pathol. 2020;30(5):863-866. • Pajtler KW, *et al*. Molecular classification of ependymal tumors across all CNS compartments, histopathological grades, and age groups. Cancer Cell. 2015;27(5):728-743.
Glioma	• Alexander BM, *et al*. Adaptive global innovative learning environment for glioblastoma: GBM AGILE. Clin Cancer Res. 2018;24(4):737-743. • Alexander BM, *et al*. Individualized screening trial of Innovative Glioblastoma Therapy (INSIGhT): a Bayesian adaptive platform trial to develop precision medicines for patients with glioblastoma. JCO Precis Oncol. 2019;3:PO.18.00071. • Bagley SJ, *et al*. CAR T-cell therapy for glioblastoma: recent clinical advances and future challenges. Neuro Oncol. 2018;20(11):1429-1438. • Dang L, *et al*. Cancer-associated IDH1 mutations produce 2-hydroxyglutarate. Nature. 2009;462(7274):739-744. • June CH, Sadelain M. Chimeric antigen receptor therapy. N Engl J Med. 2018;379(1):64-73. • Parsons DW, *et al*. An integrated genomic analysis of human glioblastoma multiforme. Science. 2008;321(5897):1807-1812. • Stupp R, *et al*. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med. 2005;352(10):987-996. • Stupp R, *et al*. Maintenance therapy with tumor-treating fields plus temozolomide versus temozolomide alone for glioblastoma: a randomized clinical trial. JAMA. 2015;314(23):2535-2543. • Stupp R, *et al*. Effect of tumor-treating fields plus maintenance temozolomide versus maintenance temozolomide alone on survival in patients with glioblastoma: a randomized clinical trial. JAMA. 2017;318(23):2306-2316. • Sturm D, *et al*. Hotspot mutations in H3F3A and IDH1 define distinct epigenetic and biological subgroups of glioblastoma. Cancer Cell. 2012 Oct 16;22(4):425-437. • Tesileanu CMS, *et al*. Temozolomide and radiotherapy versus radiotherapy alone in patients with glioblastoma, IDH-wildtype: *post hoc* analysis of the EORTC randomized phase III CATNON trial. Clin Cancer Res. 2022 Jun 13;28(12):2527-2535.

(Contd...)

Table 3: *(Continued)*.

Topic	Article(s)
	• Van den Bent MJ, *et al*. Adjuvant and concurrent temozolomide for 1p/19q non-co-deleted anaplastic glioma (CATNON; EORTC study 26053-22054): Second interim analysis of a randomized, open-label, phase 3 study. Lancet Oncol. 2021;22(6):813-823. • Verhaak RG, *et al*. Integrated genomic analysis identifies clinically relevant subtypes of glioblastoma characterized by abnormalities in PDGFRA, IDH1, EGFR, and NF1. Cancer Cell. 2010;17(1):98-110. • Yan H, *et al*. IDH1 and IDH2 mutations in gliomas. N Engl J Med. 2009;360(8):765-773.
Glioma surgery	• Cohen-Gadol A. High-grade glioma. Neurosurgical Atlas. https://www.neurosurgicalatlas.com/volumes/brain-tumors/supratentorial-and-posterior-fossa-tumors/high-grade-glioma • Hervey-Jumper SL, Berger MS. Insular glioma surgery: an evolution of thought and practice. J Neurosurg. 2019;130(1):9-16. • Kruser TJ, *et al*. NRG brain tumor specialists consensus guidelines for glioblastoma contouring. J Neurooncol. 2019;143(1):157-166. • Sanai N, Mirzadeh Z, Berger MS. Functional outcome after language mapping for glioma resection. N Engl J Med. 2008;358(1):18-27.
Intracranial meningioma	• Brastianos PK, *et al*. Genomic sequencing of meningiomas identifies oncogenic SMO and AKT1 mutations. Nat Genet. 2013;45(3):285-289. • Clark VE, *et al*. Genomic analysis of non-NF2 meningiomas reveals mutations in TRAF7, KLF4, AKT1, and SMO. Science. 2013;339(6123):1077-1080. • Simpson D. The recurrence of intracranial meningiomas after surgical treatment. J Neurol Neurosurg Psychiatry. 1957;20(1):22-39.
Medulloblastoma	• Kool M, *et al*. Genome sequencing of SHH medulloblastoma predicts genotype-related response to smoothened inhibition. Cancer Cell. 2014;25(3):393-405. • Northcott PA, *et al*. Subgroup-specific structural variation across 1,000 medulloblastoma genomes. Nature. 2012;488(7409):49-56.
Mutational signatures in human cancer	• Alexandrov LB, *et al*. Signatures of mutational processes in human cancer. Nature. 2013;500(7463):415-421. • Alexandrov LB, *et al*. The repertoire of mutational signatures in human cancer. Nature. 2020;578(7793):94-101.
Nervous system tumor classification and grading	• Capper D, *et al*. DNA methylation-based classification of central nervous system tumors. Nature. 2018;555(7697):469-474. • Louis DN, *et al*. International Society of Neuropathology--Haarlem consensus guidelines for nervous system tumor classification and grading. Brain Pathol. 2014;24(5):429-435.
Next-generation sequencing	• Chaisson MJP, *et al*. Multi-platform discovery of haplotype-resolved structural variation in human genomes. Nat Commun. 2019;10(1):1784.
Papillary craniopharyngioma	• Brastianos PK, *et al*. Exome sequencing identifies BRAF mutations in papillary craniopharyngiomas. Nat Genet. 2014;46(2):161-165.
Pediatric glioblastoma	• Schwartzentruber J, *et al*. Driver mutations in histone H3.3 and chromatin remodeling genes in pediatric glioblastoma. Nature. 2012;482(7384):226-231.
Pediatric low-grade glioma	• Bandopadhayay P, *et al*. MYB-QKI rearrangements in angiocentric glioma drive tumorigenicity through a tripartite mechanism. Nat Genet. 2016;48(3):273-282.
Professionalism	• Air EL, *et al*. Developing a professionalism and harassment policy for organized neurosurgery. Neurosurgery. 2021;88(5):1038-1039.
Reproducibility in pre-clinical research	• Baker M. 1500 scientists lift the lid on reproducibility. Nature. 2016;533(7604):452-4. • Ioannidis JP. Acknowledging and overcoming nonreproducibility in basic and preclinical research. JAMA. 2017;317(10):1019-1020.
Resistance to B-RAF(V600E) inhibition	• Luebker SA, Koepsell SA. Diverse mechanisms of BRAF inhibitor resistance in melanoma identified in clinical and preclinical studies. Front Oncol. 2019;9:268. • Nazarian R, *et al*. Melanomas acquire resistance to B-RAF(V600E) inhibition by RTK or N-RAS upregulation. Nature. 2010;468(7326):973-977.
Schwannoma	• Agnihotri S, *et al*. The genomic landscape of schwannoma. Nat Genet. 2016;48(11):1339-1348.
SWI/SNF chromatin remodeling	• Kadoch C, Crabtree GR. Mammalian SWI/SNF chromatin remodeling complexes and cancer: Mechanistic insights gained from human genomics. Sci Adv. 2015;1(5):e1500447. • Wang X, *et al*. SMARCB1-mediated SWI/SNF complex function is essential for enhancer regulation. Nat Genet. 2017;49(2):289-295.

Such a model of learning was anecdotally successful in facilitating an apprehension of neurosurgical oncology and related specialties.

To the best of our knowledge, a similar approach to prepare neurosurgical oncologists beginning in medical school has not been implemented elsewhere. There is precedent for such a curriculum, given that neuro-oncology fellows do not necessarily focus on technical skills and are given dedicated time for research and independent learning. Habits developed early in the timeline of a neurosurgical oncologist will pave the way for a productive career. In addition, interactions with different physicians at an early stage, whether through tumor boards or conference meetings hosted by professional organizations, such as the American Association for Cancer Research, American Association of Neurological Surgeons, American Society for Radiation Oncology, American Society of Clinical Oncology, Congress of Neurological Surgeons, and Society for Neuro-Oncology, can further facilitate interdisciplinary learning. Such an initiative may also be effective for neurosurgery residents, though careful planning around their intensive schedules is essential for its successful execution. We believe that a comparable strategy can be implemented at other medical schools for the training of future neurosurgical oncologists.

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Ethical approval

Not applicable.

Declaration of patient consent

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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