

Emerging Subspecialties in Neurology: Neuro-oncology

A developing subspecialty with many opportunities

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NEURO-ONCOLOGY: EXCITING OPPORTUNITIES Neuro-oncology is a unique, developing neurologic subspecialty that combines many aspects of neurology with those of cancer biology. The neuro-oncologist is expert in both the diagnosis and management of primary brain tumors and neurologic complications of cancer. A career in neuro-oncology presents opportunities to utilize a multidisciplinary team approach and the application of cutting-edge technology toward patient treatment while providing compassionate patient care.

Neuro-oncology can trace its modern origins to the 1970s, when the first therapeutic trials were begun. The treatment and management of primary brain tumors is now a rapidly evolving field. The World Health Organization recognizes approximately 100 different types of primary and secondary brain tumors.^{1,2} Glioblastoma, which is the most common and aggressive type of primary brain tumor, has an incidence of 4 to 5 cases per 100,000. For patients with glioblastoma, life expectancies are measured in months rather than years, with median survival after diagnosis of only 12 to 14 months. In the past, surgical resection and radiation therapy were the main treatment options offered to these patients. In the last several years, studies have shown that chemotherapy provides a significant clinical benefit for patients with malignant brain tumors.³ More recently, molecular markers that predict response to treatment are beginning to be identified in glioblastoma.⁴ Clinical trials that incorporate biologic endpoints and correlative studies are improving our understanding of the mechanisms of disease and tumor response to treatment. This greater knowledge will lead to the development of more effective agents and individualized treatments based on specific tumor profiles. In addition to glioblastoma, the neuro-oncologist manages less common tumors, including other types of glioma, germ cell tumors, meningiomas, medulloblastomas, and primary CNS lymphomas, and becomes familiar with the cancers' different biologic and molecular profiles, and treatment approaches. Despite the often poor prognosis of pa-

tients with brain and spinal tumors, long-term successes are possible. Patient care focuses not only on improving survival but also on preserving quality of life for these patients and providing support for their families.

The neuro-oncologist also specializes in the care of patients with challenging neurologic complications associated with systemic cancers. A common complication of systemic cancer is metastasis to the brain. It is the most common type of brain tumor, with up to 170,000 cases a year in the United States. The neuro-oncologist is proficient in the management of seizures, cerebral edema, stroke, peripheral nerve disorders, and demyelinating disease, which often present unique diagnostic dilemmas and require complex management decisions in patients with cancer. Altered mental status is a common reason for neurologic consultation, and hospitalized patients with cancer usually have multiple causes of delirium, which requires a detailed history and neurologic examination to determine the accurate diagnosis.⁵ Neuro-oncologists sharpen their skills in lesion localization by observing neurologic deficits in the presurgical and postsurgical setting. This acumen is also vitally important in identifying the early signs and symptoms of spinal and leptomeningeal metastasis. Radiation therapy and chemotherapy can produce a variety of complications involving the nervous system, including strokes, seizures, demyelination, and focal necrosis. The challenging and complex nature of patient care makes neuro-oncology an interesting and exciting subspecialty.

Neuro-oncologists play a unique role by coordinating the care of each patient in collaboration with a wide variety of specialists, including neurosurgeons, radiation oncologists, neuropathologists, psychiatrists, and rehabilitation physicians. In this role, the neuro-oncologist has broad knowledge of these other specialties and the role they play in patient management. In academic settings, tumor boards are a core teaching venue and foster camaraderie and collaboration between neuro-oncologists and other subspecialty groups in an effort to develop

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optimal treatment plans for individual patients. Additionally, neuro-oncologists work closely with medical oncologists in coordinating care of patients with systemic cancers and brain metastases. Advances in neuro-oncology will require teamwork among clinicians and clinical and translational research programs so that the expertise from the myriad of fields involved can be integrated into the development of cohesive patient-oriented treatment plans. Opportunities exist for neuro-oncologists to collaborate with other physicians on cooperative cancer group and multi-institutional clinical trials. Effective communication skills are essential in neuro-oncology, especially because this neurologic subspecialty includes the discussion of complex medical issues and terminal diagnoses.

ADVANCES IN NEURO-ONCOLOGY With the explosion of our understanding of the molecular biology of cancer, neuro-oncology offers numerous opportunities for clinician-scientists to participate in the development and clinical testing of novel molecularly targeted agents. Glioblastoma is likely a heterogeneous disease,⁶ and thus not all types should be treated uniformly. With the proper training, a neuro-oncologist can utilize tools from cellular and molecular biology to design and evaluate the next generation of clinical trials. In the future, neuro-oncologists will integrate newly identified molecular biomarkers into clinical trials in an effort to develop individualized patient treatments. Biologic agents targeting proangiogenic factors, such as the vascular endothelial growth factor, and kinases, such as Src, epidermal growth factor receptor, and PI3 kinase, are promising treatment options as adjuncts to cytotoxic chemotherapies. The future holds promise that one day the molecular profile of a patient's tumor may predict tumor response to therapy and guide management decisions. The Cancer Genome Atlas project (<http://cancergenome.nih.gov/>) is systematically exploring the genomic changes involved in selected human cancers including glioblastoma, and the information it provides on molecular derangements in glioblastoma may be used to discover new targets for therapy. Neuro-oncologists will spearhead the future integration of these molecular discoveries into clinical trials in the effort to develop more effective treatments for brain tumors.

Another rapidly developing area of focus in neuro-oncology is the use of noninvasive methods of detecting tumor proliferation, invasion, and angiogenesis within the brain. Dynamic contrast-enhanced MRI, which can assess aspects of the tumor vasculature, and PET, which can be used to evaluate tumor proliferation, hypoxia, and metabolism, are two of the many exciting advances in neuroradiology that

may help change the way in which patients with gliomas are treated in the future. Functional MRI studies such as blood oxygenation level-dependent MRI and intraoperative MRI allow the neurosurgeon to precisely excise brain tumors with minimal injury to normal brain tissue, helping to maximize surgical resection and patient outcome⁷ while simultaneously preventing devastating neurologic sequelae. In the future, neurogeneticists and epidemiologists will assist in the determination of a patient's pharmacogenetic profile to predict response to, and toxicity from, specific treatments. Neuro-oncology is based on a multidisciplinary approach that seeks to incorporate these novel technologies, making it an exciting and rapidly evolving field.

TRAINING OPPORTUNITIES IN NEURO-ONCOLOGY At the resident level, there are several ways to gain exposure to neuro-oncology. If a neuro-oncology service exists in the resident's neurology department, then one could easily spend time with that service. However, some neurology departments may not have such a service. The interested resident could do an away rotation at an outside institution with a neuro-oncology service. Alternatively, the American Academy of Neurology (AAN) offers the Consortium of Neurology Residents and Fellows Mentorship Program, which allows one-on-one guidance and counseling to trainees interested in subspecialties such as neuro-oncology (<http://www.aam.com/education/mentors/>).

Neuro-oncology offers multiple training opportunities for fellows to prepare for a career in either clinical practice or academic neuro-oncology. Pediatric and adult neurologists, as well as medical oncologists, may choose to subspecialize in neuro-oncology by completing various training programs. The Society for Neuro-oncology lists almost 300 neurology-trained, about 100 medical oncology-trained, and slightly greater than 100 pediatrics-trained physicians in its membership. One- and 2-year programs offer specialized training in the management of primary brain tumors, brain metastasis, and the neurologic complications of systemic cancers. Typically, in the first year of a 2-year program, the candidate is dedicated to clinical neuro-oncology training; however, in the second year, the candidate may pursue clinical or basic science research interests in conjunction with more independent patient care management training. Fellows also will become comfortable administering intrathecal chemotherapy via lumbar puncture or Ommaya reservoir and managing related complications. Core curriculum guidelines have been established by the United Council for Neurologic Subspecialties (UCNS), which recently established

an accreditation mechanism for neuro-oncology fellowship programs (<http://www.ucns.org>). The UCNS has also defined the eligibility criteria for subspecialty certification in neuro-oncology. Interested trainees can find listings of current fellowships on the AAN Web site (<http://www.aan.com>). Currently, more than 15 neuro-oncology training programs are listed in the AAN section on fellowship training programs (<http://www.aan.com/education/fellowships/index.cfm>), each offering one to four positions per year. Additional resources and information about the field of neuro-oncology can be found on the Society for Neuro-oncology Web site (<http://www.soc-neuro-onc.org>).

As with other neurology subspecialties, applicants should identify the training programs in neuro-oncology that are best suited to their particular interests. Some programs concentrate on preparing the fellow to practice clinical neuro-oncology, while others focus on training the fellow for a career in academics. Programs can provide specialized training in molecular and stem cell biology, novel targeted therapies, functional neuroimaging, biomarker development, and patient care research, which includes the areas of neurocognitive outcomes and quality of life. Other programs may provide additional training in pediatric oncology, radiation oncology, and palliative care. Combined training in multiple subspecialties will prepare the neuro-oncology trainee for the challenges frequently encountered in the field.

CAREER PROSPECTS IN NEURO-ONCOLOGY

Multiple career tracks are available to aspiring neuro-oncologists. Some neuro-oncologists choose a private clinical practice in a major metropolitan area, typically with some general or cancer neurology patients integrated into the practice. Given the relative rarity of primary brain tumors, neuro-oncology practice is not suited for rural areas. Many neuro-oncologists choose an academic setting because it provides a wide patient base, easy access to diverse CNS tumor subspecialties, and facile integration of clinical and translational as well as basic research. In addition to supporting basic research related to neuro-oncology, many academic centers provide numerous opportunities for neuro-oncologists to concentrate on clinical trial development and the translation of new ideas from the laboratory to the clinical setting. Opportunities exist to integrate electrophysiology expertise with a career in neuro-oncology. Intraoperative monitoring is frequently used in tumor surgeries of the brain and spine, and neuro-oncologists frequently utilize EEG and EMG/nerve conduction studies in the clinical evaluation and management of their patients. Additional procedures such as intrathecal administration of chemotherapy via lumbar puncture

and Ommaya reservoir are frequently performed in the clinic for patients with leptomeningeal metastasis. Finally, one could consider employment in the biotechnology or pharmaceutical industry. Although there are no readily available data on jobs in industry, many medical oncologists and neurologists have had successful careers in this setting. Currently, there is a need for formally trained neuro-oncologists across the country; for example, at the time of this writing, 15 academic job listings were posted on the Society for Neuro-oncology Web site.

DISCUSSION The future of neuro-oncology is promising and offers an exciting opportunity to advance the treatment of patients with brain tumors and neurologic complications of cancer. The goal to personalize cancer therapy based on an individual patient's tumor drives research into the genetic and epigenetic factors that are important to tumor cell growth and survival and those that predict treatment response. Newer agents targeting growth factor signaling, angiogenesis, and cell cycle pathways are expanding treatment options for patients with brain tumors. Neuro-oncology provides an excellent opportunity to work as a neurologist with an expertise in oncology. Because of the small number of neuro-oncologists in the nation, they are a close-knit, collegial group, with many employment opportunities available to them. Subspecialization in neuro-oncology allows the neurologist to treat challenging diseases affecting the nervous system while simultaneously expanding the boundaries and defining the future of a young field.

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