The Family Center for Neurofibromatosis Clinical and Research Report
TABLE OF CONTENTS

Letter from the Director ................................................................. 3

Clinic History .............................................................................. 4

Our Mission ................................................................................. 6

Clinicians at the Center ............................................................... 7

Education .................................................................................... 9

Research Highlights ................................................................... 10

Current Areas of Research .......................................................... 11

Our Multidisciplinary Model of NF Care ....................................... 17

   The Massachusetts General Hospital Team ............................. 18

   The Massachusetts Eye and Ear Infirmary Team .................... 33

Publications ................................................................................. 37
At The Family Center for Neurofibromatosis, we provide comprehensive care for adults and children with all forms of NF. Our history of ground-breaking research and outstanding patient care could not have been achieved without our multidisciplinary team of dedicated NF experts. Our commitment to clinical management and research continues to allow us to provide specialized care using both novel therapies and proven techniques.

As we look forward, I am pleased to report on our advances in care through clinical research, which would not be possible without the pioneering efforts of our clinicians and researchers. Current research explores all aspects of NF, from the molecular biology of tumors to the psychological aspects of having NF.

The goal of this report is to highlight our clinical and research mission, introduce the members of our team, and recognize research accomplishments and publications.
The Family Center for Neurofibromatosis at MGH was founded in 1982 by Dr. Robert Martuza. The clinic was one of the first in the world to recognize the unique, multidisciplinary problems that NF patients and their family face—and the vital role that a dedicated clinic could play in the research community. The NF team is comprised of both clinicians and researchers at Massachusetts General and Massachusetts Eye and Ear Infirmary.

Massachusetts General is the oldest and largest teaching hospital of Harvard Medical School. Since its beginning in 1811, Mass General has been committed to advancing clinical care through pioneering research and education. Today, Mass General has the largest hospital-based research program in the United States, allowing scientists and health care professionals to translate clinical research into new and better treatments.

Massachusetts Eye and Ear Infirmary was founded in 1824 and became associated with Harvard Medical School in 1866. Throughout its history, the Mass Eye and Ear Infirmary has placed a strong emphasis on the pursuit of knowledge. As a result of this commitment, clinicians and researchers at Mass Eye and Ear Infirmary have advanced patient-care by discovering new drugs, perfecting new techniques, and identifying disease-causing genes.
MGH is a founding member of the Harvard Medical School Center for NF and Allied Disorders. The CNfAD facilitates interdisciplinary approaches to research and promotes cooperative clinical studies between Harvard Medical School affiliated institutions as it aims to bridge the gap between clinical and basic scientists to gain the synergies that result from directly relating studies of humans with those in experimental models.

The CNfAD is directed by Dr. James Gusella, a molecular geneticist whose research over the last 30 years has focused on both neurodegenerative and neurodevelopmental disorders including neurofibromatosis types 1 and 2, schwannomatosis, and related disorders, such as tuberous sclerosis and von Hippel Lindau disease.

Learn more about CNFAD at http://www.cnfad.org/
OUR MISSION

Clinical:

- Provide comprehensive medical care for patients with neurofibromatosis and schwannomatosis
- Emphasize a family-centered approach that focuses on continuity of care from birth to adulthood
- Care for patients and families affected by all forms of neurofibromatosis, including NF1, NF2, and schwannomatosis

Research:

- Advance the understanding of neurofibromatosis and schwannomatosis through innovative clinical and basic science research.
- Identify new medical treatments for neurofibromatosis and schwannomatosis by designing and running clinical trials

Education:

- Train health care professionals about the medical, psychological, and social aspects of neurofibromatosis and schwannomatosis.
- Educate the next generation of health care providers to care for patients and families affected by neurofibromatosis and schwannomatosis.

Advocacy:

- Raise awareness about neurofibromatosis and schwannomatosis in society and within the health care community
- Assist patients and families navigate the health care system in order to ensure they receive the appropriate medical care
Scott Plotkin, MD, PhD

Dr. Plotkin is Director of The Family Center for Neurofibromatosis and Associate Professor of Neurology at Harvard Medical School. His primary research interest is developing clinical trials for patients with NF1, NF2, and schwannomatosis. Prior to 2005, there were no clinical trials for NF being performed at MGH. Since that time, Dr. Plotkin has developed a robust clinical trials program that has studied multiple drugs for a variety of NF-related tumors. Dr. Plotkin’s other research interests include determining the number and size of internal tumors for patients with NF using whole body MRI scanning and determining the genetic basis of schwannomatosis.

Fawn Leigh, MD

Dr. Leigh is a pediatric neurologist and Instructor in Neurology at Harvard Medical School. At The Family Center for NF, she cares for children and adults with all forms of NF. Her current research is directed at searching for modifiers of tumor development that may explain clinical variability of NF1. Identification of trait-specific modifier genes may lead to potential therapeutic targets, as well as clues to a better understanding of the underlying mechanisms in tumor development.
**CLINICIANS AT THE FAMILY CENTER FOR NF**

**Fabio Nunes, MD**

Dr. Nunes is a Clinical Genetics Fellow and Instructor in Neurology at Harvard Medical School. His main research interest is drug discovery for meningiomas. Meningiomas occur in about half of all neurofibromatosis 2 patients and cause significant morbidity and mortality. In addition to NF2, meningiomas can also occur as sporadic tumors, or as part of the rare syndrome of familial multiple meningioma. By studying the molecular biology of all three clinical settings in which meningiomas occur, Dr. Nunes is hoping to better understand the mechanisms of meningioma formation and progression, and to use this knowledge to develop new treatments for these tumors. To date, there are very few treatment options available for tumors which are not amenable to surgical resection, or that recur after surgery or radiation. By using his previous experience working with Dr. Mia MacCollin in the Neurofibromatosis Laboratory at MGH, and his clinical training in Internal Medicine and Genetics, Dr. Nunes is focusing his efforts on translational research for NF2 and associated diseases.

**Margaret Klehm, NP**

Margaret Klehm is the Nurse Practitioner in the Family Center for Neurofibromatosis. She is interested in the neurological and genetic aspects of neurofibromatosis. Her clinical work focuses on the management of the multisystem symptoms associated with NF. This includes optimizing the quality of life of individuals with neurofibromatosis by facilitating connections and helping them develop resilience and utilize healthy coping strategies. Outside of the clinic, her interests include educating and raising awareness about neurofibromatosis in school systems, in other healthcare systems, and in the general public.
EDUCATION

**Neuro-Oncology Clinical Fellows**

Stephen Clark, MD, PhD  (2010-present)  Erik Uhlmann, MD (2009-2010)
Mikael Rinne, MD, PhD   (2010-present)  Jethro Hu, MD (2008-2009)
Shota Tanaka, MD       (2010-present)  Maciej Mrugala, MD, PhD (2003-2006)
Christine Lu–Emerson, MD (2009-present)
Ryan Merrell, MD       (2009-2010)

**Research Fellows**

Anna Terry, MD (Neurosurgery)
Fabio Nunes, MD (Genetics)
Miriam Smirh, PhD (Molecular Biology)

**Clinical Research Coordinators**

Vanessa Merker (2010-present)
Daphne Wang (2008–present)
Sonia Esparza (2008-2010)
Caroline O’Donnell (2006-2008)
RESEARCH HIGHLIGHTS

**NF1**
- Showed that PET scanning could help identify malignant peripheral nerve sheath tumors in neurofibromatosis 1 patients (Bredella et al., Value of PET in the assessment of patients with neurofibromatosis type 1. AJR Am J Roentgenol. 2007 Oct;189(4):928-35).

- Developed a computerized volumetry technique to calculate whole body tumor volume in patients with NF1, NF2, and schwannomatosis (Cai et al., Tumor Burden in Patients with Neurofibromatosis Types 1 and 2 and Schwannomatosis: Determination on Whole-Body MR Images. Radiology 2008; 250(3): 665-673).

**NF2**

- Showed that Merlin, the NF2 protein, negatively regulates mTORC1 activity, and that activation of mTORC1 activity leads to meningioma and schwannoma growth (James et al., NF2/merlin is a novel negative regulator of mTOR complex 1, and activation of mTORC1 is associated with meningioma and schwannoma growth. Mol Cell Biol. 2009 Aug;29(15):4250-61).

- First to show that a medical therapy—bevacizumab—has activity against vestibular schwannoma and that hearing loss related to vestibular schwannoma may be reversible (Plotkin et al., Hearing improvement after bevacizumab in patients with neurofibromatosis type 2. N Engl J Med. 2010 Jul 23;361(4):358-67).

**Schwannomatosis**

CURRENT AREAS OF RESEARCH

Medical Treatments for Progressive Vestibular Schwannomas in NF2

Bevacizumab

Our initial studies of vestibular schwannomas (VS) resected at MGH indicated that these tumors are highly vascular and express VEGF in 100% of tumor cells. For this reason, we hypothesized that bevacizumab, an anti-VEGF antibody, might be effective in treatment of VS. We offered bevacizumab on a compassionate-use basis to patients who fulfilled the clinical diagnostic criteria for neurofibromatosis type 2, had evidence of progressive VS, and were considered poor candidates for surgery and radiation therapy or declined these treatments. In the first ten patients treated with bevacizumab, the median annual growth rate of the target VS before treatment was 62%. After treatment, 9 of 10 patients experienced some tumor shrinkage as measured by volumetric analysis, with six of the 10 patients experiencing tumor shrinkage of 20% or more. For 7 patients eligible for hearing response, 4 had hearing improvement, 2 had stable hearing, and 1 had hearing decline. Given the encouraging results in these 10 patients, other NF2 patients with imminent hearing loss are receiving treatment with bevacizumab. Our team continues to monitor the clinical response to bevacizumab and to collect data about the side effects of treatment. At this time, it is not known how long patients will respond to treatment and whether bevacizumab can be tolerated for long periods of time.
CURRENT AREAS OF RESEARCH

Medical Treatments for Progressive Vestibular Schwannomas in NF2

PTC299

Emerging data indicates that vestibular schwannomas associated with NF2 are highly vascular tumors and rely upon over-expression of VEGF to maintain tumor growth. For this reason, anti-VEGF therapy may offer promise in ameliorating the clinical manifestations of this disease. MGH is partnering with PTC Therapeutics to run a clinical trial of PTC299. PTC299 is an orally available inhibitor of VEGF production that acts by binding to the 5'UTR of the VEGF transcript. Preclinical characterization of PTC299 reveals that it effectively inhibits VEGF synthesis in multiple tumor types. In animal models, oral PTC299 significantly reduces VEGF concentrations in tumors and in plasma, reduces tumor microvascular density, induces tumor growth delay in a variety of human xenograft models, and has activity that compares favorably to existing methods of VEGF inhibition (eg, bevacizumab or sunitinib). Further evaluation of PTC299 as a treatment for NF2 has sound scientific rationale founded on knowledge of its actions to potently inhibit VEGF production, angiogenesis, and tumor growth in multiple nonclinical tumor models and knowledge that the drug efficiently crosses the blood-brain barrier. We are conducting a phase 2 clinical trial in NF2 patients with progressive vestibular schwannomas that is designed to assess the effects of oral PTC299 on tumor volume and word recognition.
CURRENT AREAS OF RESEARCH

Meningiomas and NF2

Meningiomas are a major cause of morbidity and mortality in NF2. Over half of all NF2 patients will develop one or more meningiomas during their lifetime. Despite the high frequency of tumors occurring in NF2 patients, as well as in the general population, there are currently no medical treatments for unresectable tumors. To address this clinical problem, we are currently studying the natural history and molecular biology of meningiomas in NF2 patients, sporadic patients, as well as the rare syndrome of familial multiple meningiomas (two or more meningiomas without any other clinical features of NF2). Some of the ongoing research taking place at the MGH Neurofibromatosis clinic includes: clinical trials for patients with meningiomas, genotype-phenotype correlations for analysis of underlying genetic events involved in meningioma formation and progression, and development of new clinical markers of meningioma progression and responsiveness to therapy. As part of this research effort, we are focused on testing existing medication for the treatment of meningiomas, as well as working on developing new therapeutic options for patients with meningiomas by better understanding the molecular biology of tumors and the cellular pathways involved in tumor formation. We are actively recruiting patients with multiple meningioma syndrome, as well as NF2 patients who might be undergoing clinically indicated surgery for their meningiomas.
CURRENT AREAS OF RESEARCH

Finding new Treatments for Cutaneous Neurofibromas in NF1

Imiquimod and Ranibizumab

The hallmark finding in neurofibromatosis 1 is cutaneous neurofibromas (i.e., skin tumors). Cutaneous neurofibromas are encapsulated tumors that develop along nerves in the dermis or epidermis. The probability of developing cutaneous tumors is greater than 80% by age 20 and approaches 100% over life for people with NF1. Physical pain or bleeding may occur in some tumors when they are irritated, or when rubbed by clothing in areas such as the neckline or waistline. However, cosmetic disfigurement is the main source of morbidity related to cutaneous tumors and often leads to significant psychological distress.

Imiquimod, a Toll-like receptor 7/8 agonist, has already been approved by the Food and Drug Administration for treatment of various skin lesions, including actinic keratosis and superficial basal cell carcinoma. Toxicity associated with imiquimod treatment is modest and reversible with dose reduction or discontinuation of study drug. Ranibizumab, a high affinity Fab, has been shown to neutralize all forms of VEGF-A. Immunohistochemical analysis of archival tissue at MGH showed strong VEGF immunopositivity in the tumor, endothelial, and mast cells of neurofibromas. Ranibizumab has higher tissue penetration then bevacizumab and has not shown a significant increase in the number of systemic adverse events associated with other anti-VEGF agents.

Given these positive indications, we are performing pilot studies of intratumor ranibizumab and topical imiquimod to treat cutaneous neurofibromas in patients with neurofibromatosis 1. If these pilot studies reveals activity against cutaneous neurofibromas, it will open a new avenue of investigation into treatments for these tumors.
Imaging patients with NF1, NF2, and schwannomatosis presents unique challenges due to multifocal involvement of nerve sheath tumors. *Regional, or traditional, MRIs* can identify tumors in a limited area but cannot be used to estimate whole body tumor burden. In contrast, *whole body MRI* is a new technique by which the entire body can be imaged in a relatively short period of time (~ 45 minutes) without the use of ionizing radiation or intravenous contrast. When combined with computerized volumetry, this technique can assess the distribution and number of nerve sheath tumors in patients with NF. Whole body MRI can be performed over time to provide tumor-specific and global assessment of tumor progression, to identify both symptomatic and asymptomatic nerve sheath tumors, and to correlate whole body tumor burden with clinical characteristics. The long-term goals of this research are (1) to better understand which patients are at risk for malignant peripheral nerve sheath tumor by stratifying patients into low-, medium-, and high-risk based on whole body tumor burden and (2) to empower patients and clinicians by providing information about whole body tumor burden when making clinical decisions.
Quality of Life Among Patients with Neurofibromatosis (NF)

Quality of life is a major issue for patients with neurofibromatosis. NF1, NF2, and schwannomatosis are multisystem disorders that can affect the skin, nerves, brain, spine, bones, and eyes. Many of the manifestations can adversely affect quality of life. Patients with NF1 may have multiple skin tumors which cause significant distress; patients with NF2 may have facial weakness, hearing loss, and vestibular dysfunction (e.g., imbalance and dizziness); and patients with schwannomatosis may have debilitating pain. In addition, many female NF patients are concerned about the possibility that hormonal treatments (e.g. contraceptives) may stimulate the growth of their tumors. At the present time, the rates of anxiety, depression, and other quality of life indicators are not well known for these conditions. This research attempts to measure established metrics of psychological function, including mood/anxiety symptoms, self-esteem, stress, body image, social intimacy, and social anxiety in patients with all forms of neurofibromatosis. The long-term goal is to develop strategies to address this concerns and to support patients with NF.
OUR MULTIDISCIPLINARY MODEL OF NF CARE

THE FAMILY CENTER FOR NEUROFIBROMATOSIS

- Genetics
- Psychiatry
- Pathology
- Imaging
- Medical Oncology
- Dermatology
- Surgery
- Radiation Oncology
- Fertility
- Laryngeal Surgery and Voice Rehabilitation
- Audiology
- Neurosurgery
- Facial Plastics
- Endocrinology
- Orthopedics
- Social Work
- Plastics
- Neuro-Ophthalmology
- Symptom Management
- Otolaryngology
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<th>Massachusetts General Hospital Team</th>
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<td><strong>Dermatology</strong></td>
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<td>Sandy Tsao, MD</td>
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<td><strong>Fertility</strong></td>
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<td>Irene Souter, MD, PhD</td>
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<td><strong>Imaging</strong></td>
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<td>Miriam Bredella, MD</td>
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<td>Wenli Cai, PhD</td>
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<td>Paul Caruso, MD</td>
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<td>Gordon J. Harris, PhD</td>
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<td>Dominique Jennings, PhD</td>
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<td>Greg Sorensen, MD</td>
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<td><strong>Orthopedics</strong></td>
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<td>Francis Hornicek, Jr. MD, PhD</td>
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<td>Brain Grottkauf, MD</td>
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<td>Jesse Jupiter, MD</td>
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<td>Kevin Raskin, MD</td>
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<td>Dempsey Springfield, MD</td>
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<td><strong>Psychiatry</strong></td>
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<td>Kelly Smith, PhD</td>
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<td>Elyse Park, PhD</td>
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18
Radiation Oncology
Jay Loeffler, MD
Yen-Lin E. Chen, MD
Thomas DeLaney, MD
Kevin Oh, MD
Helen Shih, MD

Surgery
Richard Hodin, MD
John Mullen, MD

Social Work
Nancy Bloomstein, LICSW

Symptom Management
Vicki Jackson, MD
Pat O’Malley, MD
James Rathmell, MD
Christine Sang, MD

Multidisciplinary Clinics

Stephen E. and Catherine Pappas Center for Neuro-Oncology
http://brain.mgh.harvard.edu/

Cranial Base Center
http://neurosurgery.mgh.harvard.edu/CranialBaseCenter/

Brain D Silber Spine Tumor Clinic
http://spinetumorcenter.mgh.harvard.edu/

Connective Sarcoma and Connective Tissue Oncology
http://www.mgh.harvard.edu/cancer/services/centers/sarcoma.aspx
Fred Barker, MD
Dr. Barker is a neurosurgeon in the Pappas Center for Neuro-Oncology. His clinical practice is centered on surgery for vestibular schwannomas, meningiomas, and other brain tumors. His research interests include drug treatment of benign brain tumors and health care disparities.

Paul Boepple, MD
Dr. Boepple is a member of both the Pediatric and Reproductive Endocrine Units at Massachusetts General Hospital. He cares for NF patients with hormone issues, such as precocious puberty. His main research focuses on the molecular basis of disorders of pubertal development.

Larry Borges, MD
Dr. Borges is the director of the Neurosurgical Spine Center at MGH. His clinical and research interests include spine surgery, spinal cord tumors, spine tumors, and chiari malformations.

Miriam Bredella, MD
Dr. Bredella is a radiologist in the musculoskeletal imaging and intervention division. She leads a team with expertise in identifying nerve sheath tumors. Her clinical interests include MRI imaging and Positron Emission Tomography (PET) of musculoskeletal neoplasm and spectroscopy of the musculoskeletal system.
Nancy Bloomstein, LICSW
Ms. Bloomstein is a social worker with expertise in caring for patients with NF. She is available to patients and families for emotional support and resource assistance.

William Butler, MD
Dr. Butler is a pediatric neurosurgeon, with experience in caring for children with NF. His clinical and research interests include computer-assisted image-guided neurosurgery and stereotactic surgery.

Wenli Cai, PhD
Dr. Cai is an imaging scientist in the 3D Imaging Lab. His primary research interest is developing novel imaging techniques for computer-aided volumetry (CAV) and computer-aided diagnosis (CAD). Dr. Cai provides volumetric quantification and visualization analysis of tumors for the NF clinic.

Paul Caruso, MD
Dr. Caruso is the director of pediatric neuroimaging at the MGH Hospital for Children. He is also a practicing neuroradiologist at the Massachusetts Eye and Ear Infirmary. His clinical interests included head and neck as well as ophthalmologic imaging.
Yen-Lin E. Chen, MD

Dr. Chen is an attending radiation oncologist who also practices at the Francis H. Burr Proton Therapy Center. Her major research efforts have been in translational research and clinical trials in sarcomas (including those affecting NF patients). This includes the application of advanced radiation oncology technologies using charged particle radiation with protons and combined modality approaches employing radiation and angiogenesis inhibitors.

Jean-Valery Coumans, MD

Dr. Coumans is in the Neurosurgical group at MGH. His clinical interests include resection of spinal schwannomas, spinal neurofibromas, and spinal meningiomas.

William Curry, MD

Dr. Curry is a neurosurgeon in the Pappas Center for Neuro Oncology. His clinical interests include neurofibromatosis, spine and spinal cord tumors, and benign and malignant tumors of the brain.
Thomas DeLaney, MD

Dr. DeLaney is the medical director of the Francis H. Burr Proton Therapy Center and an active member of the Sarcoma Team that cares for patients with NF. His major research efforts have been in the development and testing of innovative cancer treatment approaches through clinical trials. This includes the application of advanced radiation oncology technologies using charged particle radiation with protons and brachytherapy (i.e. placement of radiation sources in close proximity to the tumor to deliver high doses of radiation to the tumor while sparing nearby normal tissue).

David Ebb, MD

Dr. Ebb serves in the Pediatric Hematology-Oncology group at MGH. His clinical interests include pediatric brain tumors and hemoglobinopathies. Dr. Ebb provides compassionate care for pediatric NF patients with brain tumors.

Brian Grottkau, MD

Dr. Grottkau is the head of Pediatric Orthopedics. His clinical interests include pediatric orthopedics, pediatric sport injuries, pediatric fractures, adult spine surgery, and scoliosis.

David Harmon, MD

Dr. Harmon is in the Division of Hematology/Oncology and is the medical oncologist involved in the Sarcoma clinic. His clinical interests include lymphoma, myeloma, aplastic anemia, neutropenia, and sarcoma (including those that arise in the setting of NF1).
Gordon Harris, PhD

Dr. Harris is director of the 3D Imaging Service, and the Radiology Computer Aided Diagnostics Laboratory at MGH, as well as the Tumor Imaging Metrics Core of the Dana-Farber/Harvard Cancer Center. Dr. Harris and his team have developed methods for semi-automated volumetric segmentation analysis of plexiform neurofibromas and vestibular schwannomas, and have developed a Web-based system for longitudinal tracking of these lesions to assess change in lesion volumes over time. This system has been made available to clinicians at MGH, as well as 12 other hospitals around the U.S. and internationally, and over 100 NF patients’ scans are loaded into this system.

Robert E. Hillman, PhD

Dr. Hillman, a speech-language pathologist, is Co-Director and Research Director of the Center for Laryngeal Surgery and Voice Rehabilitation at Massachusetts General Hospital, Associate Professor of Surgery and Health Sciences and Technology at Harvard Medical School, and Associate Provost for Research at the MGH Institute of Health Professions. His team of speech-language pathologists at the MGH Voice Center is well-versed in the rehabilitation of patients with voice disorders that are caused by neurological conditions.

Richard Hodin, MD

Dr. Hodin is the Chief of Endocrine Surgery as well as the Surgical Director at the MGH Crohns and Colitis Center. His clinical interests include gastrointestinal and endocrine surgery, with particular focus on the surgical treatment of both benign and malignant adrenal tumor. He cares for NF1 patients with pheochromocytomas.
Francis Hornicek, Jr. MD, PhD

Dr. Hornicek is the Chief of MGH Orthopedic Oncology Service, Director of the MGH Stephen L. Harris Chordoma Center, co-leader of the Dana-Farber/Harvard Cancer Center Sarcoma Group, and the Director of the Center for Sarcoma and Connective Tissue Oncology at the MGH. His clinical interests include benign & malignant bone and soft tissue tumors (including benign and malignant nerve tumors), metastatic bone disease, bone infections, and metabolic bone disease. He has specialized experience dealing with patients with malignant peripheral nerve sheath tumors in the multidisciplinary care setting at the sarcoma center in MGH.

Vicki Jackson, MD

Dr. Jackson is a general internist and the Associate Director of the Palliative Care Service at MGH. Her research and education interests include improving physicians’ care of patients with chronic illness.

Dominique Jennings, PhD

Dr. Jennings is an imaging specialist at the Athinoula A. Martinos Center for Biomedical Imaging. Her research includes developing novel imaging techniques to study tumor biology, including NF-related tumors.
Jesse Jupiter, MD

Dr. Jupiter is in the Orthopedic Hand Surgery service at MGH. During his twenty-nine years on the academic faculty he has had the opportunity to head the Trauma Service, Foot and Ankle Program and the Hand Service. His clinical interests include elbow and wrist problems, fracture non-union and malunion, and hand surgery.

Chien-Wei Liao, MD, PhD

Dr. Liao is a plastic surgeon with special expertise in facial and breast surgery. He cares for NF patients with superficial and deep tissue tumors. Dr. Liao is dedicated to bringing the latest techniques in cosmetics and reconstructive surgery to his patients.

Ruth Lim, MD

Dr. Lim is a radiologist in the Division of Pediatric Radiology and the Division of Nuclear Medicine/Molecular Imaging-PET/CT at MGH. Her clinical interests include PET/CT and other hybrid modalities, oncologic imaging, and genitourinary imaging.

Angela Lin, MD

Dr. Lin is a member of the Genetics Unit at the Massachusetts General Hospital for Children. She has a longstanding interest in NF1 and other syndromes of the Ras/MAPK pathway. Dr. Lin assesses NF patients with complex genetic issues and needs. With prior training in pediatric cardiology, most of her clinical research has focused on the heart.
Jay Loeffler, MD

Dr. Loeffler is the Chief of Radiation Oncology at MGH. He pioneered the use of stereotactic radiosurgery for brain tumors. Dr. Loeffler’s clinical interests include treatment of benign and malignant brain tumors, proton therapy, radiosurgery, and intracranial vascular malformations, as well as clinical and translational research in neuro-oncology in adults.

David Louis, MD

Dr. Louis is the Chief of Pathology at MGH. His research team has made important contributions to the field of neurofibromatosis. Currently, his lab investigates the molecular genetic basis of human brain tumors. Dr. Louis also provides expert diagnostic pathology review of patient biopsy materials.

Robert Martuza, MD

Dr. Martuza is the Chief of Neurosurgery at MGH and Director of the MGH Brain Tumor Center. He founded the Neurofibromatosis Clinic at MGH in 1982. His clinical interests include meningiomas and schwannomas in various locations including vestibular schwannomas.

John Mullen, MD

Dr. Mullen is a surgical oncologist. His clinical and translational research is designed to optimize the treatment and outcomes of patients with soft tissue sarcomas, desmoid tumors, and cancers of the stomach.
Kevin Oh, MD

Dr. Oh is a radiation oncologist whose clinical interests include radiation therapy for benign and malignant tumors of the brain and spine. He cares for NF patients with malignant and benign brain tumors.

Pat O'Malley, MD

Dr. O'Malley is the medical director of the pediatric palliative care team. Her goal is to enhance joy, comfort, safety, autonomy, and meaning in the lives of children with lifespan limiting conditions. She also works as an attending in the pediatric emergency department. She has a clinical interest in teaching self-hypnosis techniques to children and young adults so that they are better equipped to manage pain, anxiety, and other troublesome symptoms.

Elyse Park, PhD

Dr. Park, a clinical psychologist, is the Director of Behavioral Health Research at the Benson-Henry Institute for Mind Body Medicine and Director of Behavioral Science for the MGH Cancer Center's Center for Psychiatric & Behavioral Science Research. Her clinical and research interests include designing and testing behavioral interventions for medical populations, with a primary focus on oncology and obstetric settings. She also has expertise in developing and analyzing qualitative research to inform behavioral intervention and survey development.
James Rathmell, MD

Dr. Rathmell is Chief of the Division of Pain management at MGH. Much of his research has focused on the treatment of pain related to disorders of the spine.

Kevin Raskin, MD

Dr. Raskin is an orthopedic oncologist with expertise in caring for patients with NF. His clinical interests include benign & malignant bone and soft tissue tumors, bone infections, metabolic bone disease, and metastatic bone disease.

Andrew Rosenberg, MD

Dr. Rosenberg serves in the pathology department at MGH. His research interests include clinical and pathological correlations of neoplastic diseases of the musculoskeletal system as well as the application and diagnostic utility of immunohistochemistry and flow cytometry in bone and soft tissue tumors.

Christine Sang, MD

Dr. Sang is an anesthesiologist and pain specialist at the Brigham and Women's Hospital. Her clinical and research focus is in chronic pain, including neuropathic pain following damage to the peripheral nerve and spinal cord, and headache.
Helen Shih, MD

Dr. Shih is the Associate Medical Director of the Francis H. Burr Proton Therapy Center. Her clinical interests include benign and malignant CNS/brain tumors, ocular tumors, proton therapy, stereotactic radiosurgery, and stereotactic radiotherapy.

Kelly Smith, PhD

Dr. Smith is currently a postdoctoral fellow in Behavioral Medicine and the Cancer Center at MGH. Dr. Smith’s research and clinical interests focus on quality of life issues among patients with chronic medical conditions. As part of the NF Clinic, Dr. Smith is involved with research examining quality of life and body image among persons with NF.

Greg Sorensen, MD

Dr. Sorensen is a member of the Neuro-radiology department and founder of the Athinoula A. Martinos Center for Biomedical Imaging. His clinical interests include application of advanced neuro-imaging techniques to neurologic illness, with a special interest in stroke, brain tumors, and migraine.

Irene Souter, MD, PhD

Dr. Souter is the Director of the Preimplantation Genetic Diagnostis (PGD) Program at MGH fertility center. She is double boarded in Obstetrics and Gynecology and Reproductive Endocrinology. Dr. Souter helps families with NF who are interested in prenatal diagnosis or PGD, which is a groundbreaking technology that helps detect and prevent genetic diseases like NF in embryos.
Dempsey Springfield, MD

Dr. Springfield’s is an orthopedic surgeon. His clinical interests include benign & malignant bone and soft tissue tumors, bone infections, metabolic bone disease, and metastatic bone disease.

Anat Stemmer-Rachamimov, MD

Dr. Stemmer-Rachamimov is a staff neuro-pathologist whose primary interest is neurofibromatosis. She works in the neuropathology department in MGH and in the Cogan Lab at Massachusetts Eye and Ear Infirmary. Her lab and research focus on identifying the underlying molecular changes in the lesions and malformations associated with hereditary brain tumor syndromes (neurofibromatosis 1, neurofibromatosis 2, schwannomatosis and tuberous sclerosis), and the identification of activated pathways or events that lead to tumor progression.

Sandy Tsao, MD

Dr. Tsao is a member of the Dermatology Laser Center at Massachusetts General Hospital. She cares for NF patients with cutaneous neurofibromas and other skin disorders. Her clinical interests include cosmetic dermatology and laser treatments of vascular malformations. She is also involved in research on laser-assisted nanosuturing.
Jonathan Winograd, MD

Dr. Winograd is in the department of Plastic and Reconstructive Surgery at MGH. As part of the Peripheral Nerve Surgery Program, Dr. Winograd helps evaluate and treat the nerve sheath tumors of NF patients. He is also board certified in hand surgery, which is also one of his many clinical interests.

Steven Zeitels, MD

Dr. Zeitels is the Director of the Center for Laryngeal Surgery and Voice Rehabilitation the Massachusetts General Hospital (MGH). He is internationally recognized for designing a number of techniques and procedures that enhance the voice and swallowing function of patients who suffer from NF.
MASSACHUSETTES EYE AND EAR INFIRMARY TEAM

**Audiology**
Chris Halpin, PhD, CCC-A
Barbara Herrmann, PhD, CCC-A

**Facial Plastics**
Tessa Hadlock, MD

**Otolaryngology**
Daniel Lee, MD
Derrick Lin, MD
Michael McKenna, MD
Phillip Song, MD

**Neuro-Ophthalmology**
Dean Cestari, MD
Simmons Lessell, MD
Joseph Rizzo, MD

**Multidisciplinary Clinics**
Facial Nerve Center
http://www.facialnervecenter.org/
The Helene and Grant Wilson Auditory Brainstem Implant Program
http://www.harvardabi.org
**Dean Cestari, MD**

Dr. Cestari is double-boarded in Ophthalmology and Neurology. His clinical interests include adult strabismus and diseases of the optic nerve and pseudotumor cerebri. Dr. Cestari is also an expert in the evaluation of the optical and surgical management of adults with acquired strabismus, which in the context of NF is seen most often in patients with diplopia consequent to cranial nerve palsies.

**Tessa Hadlock, MD**

Dr. Hadlock is a surgeon in the Facial Nerve Center at Massachusetts Eye and Ear Infirmary. Her clinical and research interests include facial nerve disorders, aesthetic surgery, and facial reconstruction. Dr. Hadlock’s expertise in facial reanimation surgery improves facial function and movement for NF2 patients with facial paralysis caused by tumor pressure.

**Chris Halpin, PhD, CCC-A**

Dr. Halpin’s research and clinical interests focus on optimizing hearing aid output to damaged cochleae. His current work is directed toward diagnosis of cochlear regions using word recognition, psychophysics, genetic investigations and analysis of audiologic results. Dr. Halpin has been an investigator in clinical trials of medications and techniques designed to improve hearing function in both neurofibromatosis type 2 and sudden idiopathic sensory loss.
Barbara Herrmann, PhD, CCC-A

Dr. Herrmann’s research concentrates on the electrophysiology of human auditory and vestibular systems primarily in clinical populations with the purpose of gaining a more thorough understanding of the mechanisms underlying system disorders and consequently optimizing these measures for diagnosis and treatment monitoring.

Daniel Lee, MD

Dr. Lee is a Neurotologic surgeon and director of The Helene and Grant Wilson Auditory Brainstem Implant (ABI) program at Massachusetts Eye and Ear Infirmary. The program is the first of its kind in New England. NF candidates for a Cochlear Implant or Auditory Brainstem Implant are referred to Dr. Lee. Dr. Lee also performs vestibular schwannoma surgery in NF patients with neurosurgeons from MGH.

Simmons Lessell, MD

Dr. Lessell, the Paul Austin Chandler Professor of Ophthalmology at Harvard Medical School, cares for both adults and children with disorders of vision and ocular motility. Dr. Lessell’s clinical and research interests are broad, but he has a longstanding interest in the ocular and neuro-ophtalmic manifestations of heritable disorders of the nervous system, prominent among them NF. He has worked closely with the NF clinic at MGH and has been the primary consulting neuro-ophthalmologist for more than 20 years. Dr. Lessell has collaborated with MGH faculty members in several studies on NF1 and NF2 and related disorders including gliomas and meningiomas of the optic nerve and optic chiasm. He also co-authored the most complete histological study of the eye in NF2 to date.
Derrick Lin, MD

Dr. Lin is in the division of Head and Neck Surgery and co-director of the Cranial Base Center at Massachusetts Eye and Ear Infirmary. His clinical interests include head and neck oncology. Patients with tumors of the head and neck often consult with Dr. Lin to determine surgical and management options.

Michael McKenna, MD

Dr. McKenna is the lead ENT surgeon at MEEI. He recently helped develop The Helene and Grant Wilson Auditory Brainstem Implant (ABI) program. NF patients with vestibular schwannomas see Dr. Mckenna to discuss tumor management plans and the timing of surgery.

Phillip Song, MD

Dr. Song is a member of the laryngology team at MEEI with a special interest in neurolaryngology. His clinical interests are in neurological disorders which impact speech and swallowing function. NF patients who have difficulties swallowing or experience dysphonia may be referred to Dr. Song.

Joseph Rizzo, III, MD

Dr. Rizzo is double-boarded in Ophthalmology and Neurology. His wide interests include optic nerve disease, pseudotumor cerebri, giant cell arteritis, and unexplained visual problems. He directs a large laboratory research effort that is seeking to develop a functioning electronic-biological interface in the visual system. If successful, this research could make devices analogous to the cochlear implant available to the visually handicapped.
PUBLICATIONS TO DATE

**2010 publications**


2009 publications


PUBLICATIONS TO DATE

2009 publications


2008 publications


PUBLICATIONS TO DATE


PUBLICATIONS TO DATE


PUBLICATIONS TO DATE

2001 – 2000 publications


