

Curriculum Vitae

Date Prepared: September, 2015
Name: Gary Edward Borodic, MD
Office Address: 1440 Main Street, Suite 201, Waltham, MA 02451
1261 Furnace Brook Parkway, Suite 15, Quincy, MA 02169
Work Phone: 617-770-0011
Work Email: [Borodic@aol.com](mailto:borodic@aol.com)
Work FAX: 617-770-0030
Place of Birth: Providence, Rhode Island

Education

| | | | |
|-------------------|--------------------------------|-------------------------|----------------------------|
| 9/1970- 5/1974 | BA with highest distinction | Chemistry/Bio-Chemistry | University of Rhode Island |
| 9/1974- 5/1978 | MD | Medicine | University of Vermont |

Postdoctoral Training

| | | | |
|-------------------|------------------------------|-------------------|---|
| 7/1978- 6/1979 | Intern | Internal Medicine | Rhode Island Hospital and Brown University |
| 7/1979- 6/1980 | Junior Assistant Resident | Ophthalmology | Rhode Island Hospital and Brown University |
| 7/1980- 6/1981 | Assistant Resident | Neurology | Yale New Haven Hospital |
| 7/1980- 6/1981 | Post Doctorate Fellow | Neuroscience | Yale University |
| 7/1981- 6/1983 | Resident | Ophthalmology | Massachusetts Eye and Ear Infirmary, Harvard Medical School |
| 7/1983- 6/1984 | Chief Resident | Ophthalmology | Massachusetts Eye and Ear Infirmary, Harvard Medical School |

Faculty Academic Appointments

| | | | |
|------------------|---------------------------------|---------------|------------------------|
| 1984-1988 | Clinical Assistant | Ophthalmology | Harvard Medical School |
| 1988-1993 | Clinical Instructor | Ophthalmology | Harvard Medical School |
| 1988-1990 | Assistant Clinical Professor | Ophthalmology | Boston University |
| 1993- present | Assistant Clinical Professor | Ophthalmology | Harvard Medical School |

Appointments at Hospitals/Affiliated Institutions

| | | | |
|-------------------|--------------------|---------------|-------------------------------------|
| 4/1984-1987 | Clinical Assistant | Ophthalmology | Massachusetts Eye and Ear Infirmary |
| 1987-1994 | Assistant Surgeon | Ophthalmology | Massachusetts Eye and Ear Infirmary |
| 1994-2000 | Associate Surgeon | Ophthalmology | Massachusetts Eye and Ear Infirmary |
| 2000-Present | Surgeon | Ophthalmology | Massachusetts Eye and Ear Infirmary |
| 1996-Present | | Ophthalmology | South Shore Hospital |
| 3/21/1985-Present | Courtesy | Ophthalmology | Milton Hospital |

Other Professional Positions

| | | |
|-----------|--|---|
| 1987 | Visiting Professor of Ophthalmology, Neurology | University of Vermont |
| 1988 | Program Director | Benign Essential Blepharospasm Research Foundation |
| 1989 | Visiting Professor | Dartmouth Medical College |
| 1992-1995 | Industrial Safety Monitor | Food and Drug Administration Filings |
| 1995 | Round Table on Facial Movement Disorders | National Institute of Health |
| 1999 | Beaumont Lecturer in History of Medicine Series | University of Vermont College of Medicine |
| 1999-2006 | University of Vermont Medical College | Advisory Committee to Medical School Dean |
| 2002 | Chair Pain Division | International Scientific and Therapeutic Symposium on Neurotoxins |
| 2004-2010 | Consultant for Botulinum toxin Development for pure neurotoxin | Johnson and Johnson, Mentor Corporation |

Major Administrative Leadership Positions

Local

| | | |
|--------------|--|-------------------------------------|
| 1983-1984 | Assistant Director of Residency Training and Clinical Fellow | Harvard Medical School |
| 1984-1987 | General Eye Service | Massachusetts Eye and Ear Infirmary |
| 1984-1991 | Attending, Oculoplastics and Orbital Clinical Surgical | Massachusetts Eye and Ear Infirmary |
| 1984-Present | Attending, Oculoplastic Trauma Service Surgical | Massachusetts Eye and Ear Infirmary |
| 1986-1987 | Conference Lecturer and Organizer, Oculoplastic Surgery | Harvard Medical School |

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|-----------------|---|--|
| 1986-1987 | Greater Boston Residents Course and Lecturer, Orbital Anatomy Course | Harvard Medical School |
| 1988 | Director, Clinical Applications of Botulinum Toxin | Harvard Medical School |
| 1989-1998 | Oculoplastic Consultant, Facial Nerve Clinic | Massachusetts Eye and Ear Infirmary Massachusetts Eye and Ear Infirmary |
| 1993-2003 | Organizer and Attending Ophthalmologist Benign Essential Blepharospasm Research Foundation, Facial Nerve Clinic | |
| 2006, 2009-2010 | Teaching conferences in Oculoplastic Surgery for Ophthalmology Residents | Massachusetts Eye and Ear Infirmary |

Regional

| | | |
|-----------|---|---|
| 1986-1995 | Attending Surgeon, Oculoplastics Clinic | Boston University Hospital |
| 1987-1995 | Director, Oculoplastics Service | Boston University School of Medicine, University Hospital |

National and International

| | | |
|-----------|----------------------------|---|
| 1988 | Director | Benign Essential Blepharospasm Research Foundation Meeting National |
| 1993-1999 | Associate Medical Director | National Spasmodic Torticollis Association |
| 1999 | Regional Meeting Director | Benign Essential Blepharospasm Research Foundation Meeting |
| 2004 | Regional Meeting Director | Benign Essential Blepharospasm Research Foundation Meeting |
| 2008 | Regional Meeting Director | Benign Essential Blepharospasm Research Foundation |

Committee Service

Local

| | | |
|-----------|--|-------------------------------------|
| 1985-1988 | By Laws Committee | Massachusetts Eye and Ear Infirmary |
| 1998-2001 | Ad hoc committee on Wydase Use and intra-ocular surgical complication rate | Massachusetts Eye and Ear Infirmary |
| 2002-2008 | Pharmacy Committee | Massachusetts Eye and Ear Infirmary |

Regional

| | | |
|-----------|---------------------------|---------------------------------------|
| 1999-2006 | Dean's Advisory Committee | University of Vermont Medical College |
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National

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|-----------|---|--|
| 2004-2007 | Initial Chair of Committee to establish clinical study plan and sites for newer botulinum toxin preparation | Sponsored by Mentor, Inc and now Johnson and Johnson |
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Professional Societies

| | | |
|-------------------|--|---|
| 1973- Present | Phi Kappa Phi, Phi Beta Kappa | Member |
| 1974-1994 | American Medical Association | Member |
| 1977- Present | Alpha Omega Alpha | Member |
| 1983-1998 | American Academy of Ophthalmology | Fellow |
| 1984-1996 | Massachusetts Medical Society | Member |
| 1984-1993 | Association for Research in Vision and Ophthalmology | Member |
| 1987-1989 1988 | American Board of Ophthalmology Benign Essential Blepharospasm Research Foundation, Cambridge | Test question preparation National Program Chairman, Harvard Course on applications of botulinum toxin for facial movement disease |
| 1992- Present | American Society of Ophthalmic Plastic and Reconstructive Surgeons | Fellow |
| 1994-1998 | National Spasmodic Torticollis | Associate Medical Advisor, Scientific Committee |
| 2001-2002 | International Symposiums on Botulinum Toxin | Hanover Germany |

Editorial Activities

Ophthalmology
Neurology
Movement Disorders
Archives of Dermatology
Drug Safety
Ophthalmic Plastics and Reconstructive Surgery
The Medical Letter on Drugs & Therapeutics
Expert Opinion on Investigational Drugs
Expert Opinion on Pharmacotherapy
Journal of Pain
Ophthalmic Surgery, Lasers and Imaging
American Journal of Ophthalmology
Survey of Ophthalmology
Plastic and Reconstructive Surgery
Toxicon

Honors and Prizes

| | | | |
|------|--------------------------|---------------------------------------|----------------------------|
| 1974 | Highest Distinction | University of Rhode Island | Chemistry and Humanities |
| 1974 | Phi Kappa Phi | University of Rhode Island | |
| 1977 | Alpha Omega Alpha | University of Vermont | |
| 1999 | Beaumont Annual Lecturer | University of Vermont Medical College | Beaumont Honorary Lecturer |
| 2010 | Achievement Award | American Academy of | Distinguished Service in |

Report of Funded and Unfunded Projects

Funding Information

Past

Many projects were funded by limited grants from industry and private sources.

Report of Local Teaching and Training

| | | |
|-----------|--|------------------------|
| 1984-1988 | Harvard Medical Students Course in Ophthalmology | Harvard Medical School |
| 1998 | Medical Student Preceptor Teaching | Harvard Medical School |
| 2008 | Medical Student Preceptor Teaching | Harvard Medical School |

Formal Teaching of Residents, Clinical Fellows and Research Fellows (post-docs)

| | | |
|--------------|--|---|
| 1989 | Borodic GE. Surgical Anatomy of the Eyelids, Annual Course on Oculoplastic Surgery | Harvard Medical School |
| 1990 | Borodic GE. Surgical Anatomy of the Nasolacrimal System, Orbital Course | Massachusetts Eye and Ear Infirmary |
| March 1990 | Borodic GE. The Concept of Using Botulinum Toxin to Achieve Facial Dynamic Symmetry in Unilateral Facial Nerve Paralysis (Initiating the Human Studies Protocol: Botulinum A Toxin to Achieve Facial Dynamic Symmetry at Massachusetts Eye and Ear Infirmary | Facial Nerve Meeting, Massachusetts Eye and Ear Infirmary |
| August 1991 | Borodic GE. Botulinum Toxin for the Treatment of Oculopalpebral. Report of three cases. | Grand Rounds, Massachusetts Eye and Ear Infirmary |
| January 1992 | Borodic GE, Ferrante R. Denervation field and Complications Associated with Large Dose Botulinum Toxin Injections | Grand Rounds, Massachusetts Eye and Ear Infirmary |
| 1995-2002 | Borodic GE. ENT Residency Course, BOTOX Applications Annual Lecturer | Massachusetts Eye and Ear Infirmary |
| 1999 | Borodic GE. Current Concepts in Botulinum Toxin Therapy | Grand Rounds, Massachusetts Eye and Ear Infirmary |

Clinical Supervisory and Training Responsibilities

| | |
|-----------|--|
| 1983-1986 | Massachusetts Eye and Ear Infirmary General Eye Service |
| 1983-1988 | Massachusetts Eye and Ear Infirmary |

1987-1988 Trauma Service
 Massachusetts Eye and Ear Infirmary
 Co-Acting Director Plastics Service
 1988-1995 Director of Boston University Oculoplastic
 Clinic
 1993-2002 Ophthalmology Consultant to facial nerve
 Clinic

Formally Supervised Trainees:

1995 Vicki Kevadar, MD (Fellow) Ophthalmic Plastic and Reconstructive Surgery

Formal Teaching of Peers (e.g., CME and other continuing education courses)

| | | |
|--------------|---|-------------------------------|
| May 1990 | Borodic GE. Overview and Surgical Variations of the Hughs Flap, Massachusetts Eye and Ear Infirmary Alumni Meeting | Single Presentation Boston |
| May 1990 | Borodic GE. Mini Atlas of Eyelid Tumors Massachusetts Eye and Ear Infirmary Alumni Meeting | Single Presentation Boston |
| 1991 | Borodic GE. Use of Gold Weight Implants for the Management of Paralytic Lagophthalmos Massachusetts Eye and Ear Infirmary Alumni Meeting | Single Presentation Boston |
| January 1994 | Borodic GE. Otolaryngology and Botulinum Toxin, ENT Grand Rounds, Massachusetts Eye and Ear Infirmary | Single Presentation Boston |
| April 2000 | Borodic GE, Acquadro MA. Botulinum Toxin, Efficacy for Pain Application and Mechanisms, Pain Conference, Massachusetts General Hospital | Single Presentation Boston |
| 2000 | Borodic GE. Application of Botulinum Toxin for Migraine Headache, Discovery and Development Status, Grand Rounds Ophthalmology, Massachusetts Eye and Ear Infirmary | Single Presentation Boston |
| 2002 | Acquadro MA, Borodic GE. Botulinum Toxin for Human Pain, Head and Neck Experience and Mechanisms, Pain Conference, Massachusetts General Hospital | Single Presentation Boston |
| 2006 | Botulinum Toxin Pharmacology and Plastic Application, Massachusetts Eye and Ear Infirmary Oculoplastic | Lecture (2 hours) |
| January 2010 | Borodic GE. Diagnosis and Management of Eyelid Lesions, with Emphasis on Lid | Single Presentation Boston |

Reconstruction, Massachusetts Eye and Ear
 Infirmery Residents Program
 January 2011 Borodic GE. Diagnosis and Management of Eyelid Lesions, with Emphasis on Lid Reconstruction
 Single Presentation Boston
 Massachusetts Eye and Ear Infirmery Residents Program

Local Invited Presentations

March 1985 Borodic GE, Townsend DJ. Ophthalmologic Evaluation of Meige Syndrome and Clinical Applications of Botulinum Toxin
 Boston Neurological Society
 January 1987 Hochberg FH, Borodic GE, Growdon J, Henneman. Treatment of Focal Forearm Dystonias with Oculinum, A Report of the First Thirteen Cases
 Department of Neurology & Human Studies Committee
 Massachusetts General Hospital, Neurology Grand Rounds
 September 1989 Borodic GE. Botulinum Toxin: Therapeutic Applications in Ophthalmic and Neurologic Diseases
 Grand Rounds – Neurosurgery
 Massachusetts General Hospital
 Brigham and Women’s Hospital
 August 1989 Borodic GE. Ophthalmic and Neurologic Applications of Botulinum A Toxin
 Neurologic/Neurosurgical Grand Rounds
 Brigham and Women’s Hospital
 March 1990 Borodic GE. Application of Botulinum Toxin for Larger Muscle Dystonias/ Grand Rounds
 Braintree Hospital
 New England Sinai Hospital
 October 1990 Borodic GE. Topographic Diffusion of Botulinum Toxin and Regional Complications/Clinical Applications of Botulinum Toxin/ Neurology Grand Rounds
 Spaulding Rehabilitation Hospital
 October 1990 Borodic GE. Reconstruction of the Upper and Lower Eyelid/ Combined Grand Rounds, Ophthalmology
 Boston University/Tufts University
 1991 Borodic GE. Review of Reconstructive Techniques for Upper and Lower Eyelids
 Greater Boston Review Course on Oculoplastic and Reconstructive Surgery
 January 1995 Borodic GE. Botulinum Toxin for the Treatment of Human Muscle Disease
 Ether Dome-Oral Surgery Grand Rounds, Massachusetts General Hospital
 2011 Dorchester Medical Society
 2013 Massachusetts Eye and Ear Alumni Meeting
 2014 Regional Facial Dystonia Meeting, Update on Facial Movement Disease
 2014 Vermont Medical College Blepharospasm and its Treatment
 2016 Update on Botulinum Toxin Vermont Medical College

2018 Borodic GE Grand Rounds at Longwood Ophthalmology New Approach to a Common Blinding

Disease, December 21, 2018

- 2020 Dorchester Medical Society -- Intra ocular Effects of Botulinum Toxin Feb 2020
- 2020 International Zoom Conference on Botulinum Toxin: Macular Effects of Botulinum Toxin
August New Bedford Mass Invited Guest
- 2021 International Zoom Conference on Botulinum Toxin: Macular Effects of Botulinum Toxin
August New Bedford Mass Invited Guest

Report of Regional, National and International Invited Teaching and Presentations
Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings and
Invited Presentations and Courses

Regional

- June 1980 Borodic GE, Geltzer A, Kinder, R. Scatter Retinal Photocoagulation and Hyperglycemic
State
New England Ophthalmology Society
- 1983 Borodic GE, Chess J, Bienfang DC. Temporal Arteritis and the Vertebral Artery
Syndrome
New England Ophthalmology Society
- 1984 Borodic GE, Sadun A, Bienfang DC. The Optic Nerve and Sarcoidosis
New England Ophthalmology Society
- October
1984 Borodic GE. Clinical Use of Botulinum Toxin Neurology/ Grand Rounds
New England Deaconess Hospital
- 1984 Borodic GE, Townsend DJ, Papale J. The Optic Nerve and Leukemia
New England Ophthalmology Society
- June 1985 Borodic GE, Townsend DJ. Treatment of Neurologic Blepharospasm with Botulinum
Toxin
New England Ophthalmology Society
Audio Digest Ophthalmology (vol. 23, no. 17, September 1985)
- May 1987 Borodic GE, Beyer CK. Autogenous Dermis Fat Graft for the Treatment of Synthetic
Implant Extrusion in an Eviscerated Socket
New England Ophthalmology Society
- 1987-1991 Borodic GE. Lecturer, Medical College Courses
Boston University
- 1988 Borodic GE. Lecturer, Medical College Courses
University of Vermont

Dartmouth University Medical College

January 1989 Borodic GE. Use of Botulinum Toxin for Hemifacial Spasm/Neurosurgery Grand Rounds
Massachusetts General Hospital

May 1989 Borodic GE. Research and Clinical Applications of Botulinum A Toxin in Ophthalmology and Medicine
Vermont Ophthalmology Society Meeting, Manchester, Vermont

May 1989 Borodic GE. Reversible Blindness after Surgical Drainage of Orbital Abscess
New England Ophthalmological Society

August 1990 Borodic GE. Applications of Botulinum A Toxin for the Treatment of Segmental Dystonia
Neurology Grand Rounds
Dartmouth Medical College

1991 Borodic GE. Evaluation and Management of Involuntary Neurologic Blepharospasm
Greater Boston Review Course on Oculoplastic and Reconstructive Surgery

October 1992 Borodic GE. Diagnosis and Evaluation of Orbital Blowout Fractures/ Grand Rounds
Boston University/Tufts University

May 1992 Borodic GE. Blepharospasm, An Update
New England Ophthalmology Society

May 1992 Borodic GE. Current Concepts in Botulinum Toxin Therapy/New England Oculoplastic Course
Tufts University

1994 Borodic GE. Lecturer, Medical College Courses
Tufts University
Boston University

1994 Borodic GE. In Vitro Demonstration of Phaco-Chop Maneuver
Tufts University Course on Phacoemulsification Surgery

June 1994 Borodic GE. Live Surgery Demonstration of Levator Resection Techniques/ Oculoplastics Series
Tufts University

December 1994 Borodic GE. Botulinum toxin and Strabismus
Boston University

May 1995 Borodic GE. Surgical Anatomy of the Anterior Orbit/ Annual Course on Eyelid Surgery
Tufts University

August 1998 Borodic GE. Botulinum Toxin as an Anti-inflammatory, Neurobiologic Effects
University of Vermont

1998 Borodic GE. Lecturer, Medical College Courses
University of Vermont

1998 Borodic GE, Acquadro MA. Symposia on Neurobiology of Botulinum Toxin, Physiology
University of Vermont

1998 Borodic GE. Surgical Methods for Creating Tarsorrhaphy
New England Ophthalmology Society

1998 Borodic GE. Update on BOTOX
New England Ophthalmic Plastics Society

1998 Borodic GE. Molecular Mechanisms of Botulinum Toxin
New England Oculoplastic Meeting

January 1999 Borodic GE. Botulinum Toxin/ Grand Rounds
Tufts New England Medical Center

1999 Borodic GE. Beaumont History of Medicine Lecturer, History of Botulinum Toxin

Development for the Treatment of Human Diseases
University of Vermont

March 1999 Borodic GE. Botulinum Toxin in Ophthalmology
Invited Lecturer, Tufts University

March 1999 Borodic GE. Use of Mitomycin C in Sebaceous Eyelid Cancer
New England Oculoplastic Meeting, Stowe, Vermont

May 1999 Borodic GE. Outcome instrument for the Morbidity Measurements in Hemifacial Spastic
Disease
New England Ophthalmology Society

Spring 1999 Borodic GE. Surgical Tarsorrhaphy, Review of Techniques and Applications
New England Ophthalmology Society

December 1999 Borodic GE. Botulinum Toxin for Human Essential Headache Disorders
New England Otolaryngology Society

May 2000 Borodic GE. Botulinum Toxin for Essential Headache Disorders
New England Otolaryngology Society

June 2000 Borodic GE. Botulinum Toxin for Essential Headache Disorders
New England Ophthalmology Society

October 2000 Borodic GE. Neurobiology of Botulinum Toxin
Special Conference with Department of Neurobiology, Physiology
University of Vermont, College of Medicine

May 2001 Borodic GE. Botulinum Toxin for Chronic Facial Pain Disorders and Mechanism of
Action
New England Ophthalmology Society

2007 Borodic GE. Update on Botulinum Toxin Pharmacology
New England Ophthalmology Society, Boston, Massachusetts

September 2010 Borodic GE. Pharmacology Update on Botulinum Toxin
Cape Cod Review Course in Ophthalmology

September 2010 Borodic GE. Management of Blepharospasm
Cape Cod Review Course in Ophthalmology

2010 Regional Meeting of the Benign Essential Blepharospasm Research Foundation

October 2011 Borodic GE. Botulinum Toxin for Management of Headache
Cape Cod Review Course in Ophthalmology

2011 Regional Meeting of the Benign Essential Blepharospasm Research Foundation

August 2012 Borodic GE. History of Botulinum Toxin as a Medical
Agent – Past, Present, and Future
Sixth Annual Dartmouth Botulinum Symposium and Workshop

2014 Regional Meeting of the Benign Essential Blepharospasm Research Foundation

National

1983 Borodic GE, Beyer CK, Mullin J, Foster S. Conjunctival Amyloidosis, an Unusual Case of
Ptosis
Oculoplastic Research Symposium, American Academy of Ophthalmology, Chicago,
Illinois

1984 Borodic GE, Sadun A, Bienfang DC. Pulsating Exophthalmos After a Closed Head Injury
Frank Walsh Society

1984 Sadun A, Borodic GE. Optic Neuropathy Secondary to Ophthalmic Artery Aneurysm

Frank Walsh Society

April 1984 Borodic GE, Bienfang D. Anterior Optic Nerve Circulation Changes Observed in Temporal Arteritis
Neurology Clinical Conference, Roberto Heros, Maryland

May 1985 Borodic GE, Conte J, Aswad M, Hilles S, Robinson D, Melvin C, Caron LA, Foster CS. Aqueous Humor Leukotriene Concentrations in Animal Models of Inflammation
Association for Research in Vision and Ophthalmology

1986 Borodic GE, Townsend DJ. Dose Response Relationships of Oculinum in the Treatment of Neurologic Blepharospasm
Association for Research in Vision and Ophthalmology

1987 Borodic GE. Lecturer, Medical College Courses
University of Utah

1988 Borodic GE, Cozzolino DJ, Ferrante R. Histologic Changes in Human Orbicularis Oculi Muscle Treated with Botulinum Toxin
American Academy of Ophthalmology, Las Vegas, Nevada

1988 Townsend DJ, Borodic GE. Toxin Injection Technique
Meige Disease Meeting, Cambridge, Massachusetts

1989 Borodic GE. Lecturer, Medical College Courses
Ohio State

August 1989 Borodic GE, Ferrante R, Cozzolino D. Geometric Field of Action of Botulinum Toxin Using Acetylcholinesterase Stain
Blepharospasm Foundation, Ohio State University

1989 Borodic GE, Young R, Cozzolino D, Weigner A. Innervation Zone Analysis of Orbicularis Oculi Muscle and its Significance to Botulinum A Toxin Therapy
American Academy of Ophthalmology, New Orleans, Louisiana

1990 Borodic GE. Lecturer, Medical College Courses
Duke University

1990 Borodic GE, Ferrante R. Effects of Repeated Injections of Botulinum A Toxin on the Histology of Human Orbicularis Oculi Muscle
American Academy of Ophthalmology, Atlanta, Georgia

1990 Borodic GE, Mill L, Joseph M. Blepharospasm, Spasmodic Torticollis. Clinical Application of Botulinum A Toxin for Adult Onset Spasmodic Torticollis
American Academy of Ophthalmology, Atlanta, Georgia

September 1990 Borodic GE, Fay L, Joseph M, Ferrante R, Mills L, Cozzolino D. Regional Toxin Spread, Botulinum Toxin Diffusion Kinetics and Complications in the Applications of Botulinum A Toxin
Essential Blepharospasm, Meige Disease, Facial Dystonia Foundation, Duke University
Durham, North Carolina

1990 Borodic GE, Fay L, Joseph M, Ferrante R, Mills L, Cozzolino D. Sub-classification of Adult Onset Spasmodic Torticollis and Standardization in the Botulinum Toxin Injection Strategy
Essential Blepharospasm, Meige Disease, Facial Dystonia Foundation, Duke University
Durham, North Carolina

September 1990 Borodic GE. Botulinum A Toxin in Clinical Medicine: Dysphagia, Ophthalmic Complications and Regional Toxin Spread
U.S. Food and Drug Administration

1991 Medicinal Applications of Botulinum A Toxin
US Army Chemical Meeting, Boston, Massachusetts

Spring 1991 Borodic GE, Jankovic J. Clinical Applications of Botulinum A Toxin in Neuro Medicine and Ophthalmology
American Academy of Neurology

Spring 1991 Borodic GE. Demonstrated Method of Injection of Botulinum Toxin into Cervical Muscles for the Treatment of Spasmodic Torticollis
American Academy of Neurology

June 1991 Borodic GE. Botulinum Toxin for Treatment of Facial Dyskinesias, Scientific Review of Techniques
American Academy of Ophthalmology, Regional Meeting, Cambridge, Massachusetts

1991-1992 Borodic GE. Botulinum Toxin and Adult Onset Spasmodic Torticollis
New England Meeting of the National Spasmodic Torticollis Association

1992 Borodic GE. Lecturer, Medical College Courses
Baylor University

August 1992 Borodic GE, Sillman J, Waters K. Digitalization and Computer Analysis of Human Facial Movements
Baylor Medical College

August 1992 Borodic GE, Pearce B, Ferrante R. New Concepts in Botulinum Toxin Pharmacology
Baylor Medical College

1993 Borodic GE. Lecturer, Medical College Courses
University of Wisconsin

November 1993 Borodic GE, Pearce LB, Ferrante R. Anti-botulinum Toxin Antibodies After Repetitive Injection of Botulinum Toxin for the Treatment of Essential Blepharospasm
American Association of Ophthalmic Plastic and Reconstructive Surgeons
24th Annual Scientific Symposium, Chicago, Illinois

November 1993 Borodic GE, Pearce LB. Regional Denervation, Implication for Standardization of Botulinum Activity Important for Medicinal Use
Inter-agency Meeting on Botulinum Toxin
University of Wisconsin, Madison, Wisconsin

1994 Borodic GE. Lecturer, Medical College Courses
University of Minnesota
Columbia University

1994 +Borodic GE. Differential Dysphagia Rates for Spasmodic Torticollis Based on Botulinum Toxin Formulation.
University of Minnesota

November 1994 Borodic GE. Current Approaches to the Use of Botulinum Toxin for Spasmodic Torticollis
Annual Scientific Symposium, National Spasmodic Torticollis Association,
Orlando, Florida

December 1994 Borodic GE. Dynamic Lines in the Periorbital Region, and Botulinum Toxin Applications in Ophthalmology
Columbia University Course on Facial Plastic and Reconstructive Surgery

1995 Borodic GE. Lecturer, Medical College Courses
National Institutes of Health-Neuroscience Division
Round Table on Movement Disorders

February 1995 +Borodic GE, Johnson E, Goodnough M. Standardization and Formulation Issues in the Preparation of Botulinum Therapeutic Toxin
National Institute of Health

December + Borodic GE, Goode M. Immunoresistance in Craniocervical Dystonia Patients Treated

1995 with Repetitive Botulinum Toxin Injections.
Interagency Botulism Meeting, Center of Disease Control, Atlanta, Georgia

1996 + Borodic GE, Quigg C. Photophobia and Essential Blepharospasm
American Society of Ophthalmic Plastic and Reconstructive Surgeons

1996 + Borodic GE. Pharmacology of Botulinum Toxin
Interagency Botulism Meeting, US Army, Fort Dietrick

1998 Borodic GE. Botulinum Toxin Can Precipitate Myasthenia Crisis
American Society of Ophthalmic Plastic and Reconstructive Surgeons

October 1999 Borodic GE. Outcome Instrument for the Morbidity Measurements in Hemifacial Spastic Disease- Validation Methods
American Society of Plastic and Reconstructive Surgeons

October 1999 Borodic GE. Mitomycin C as Adjuvant Chemotherapy for Post Operative Treatment of Sebaceous Cell Carcinoma
American Society of Plastic and Reconstructive Surgeons

September 2001 +Borodic GE. Outcome Measurements and Efficacy Criterion
FDA Advisory Panel Meeting Bethesda, Maryland

2004 Borodic GE Botulinum Toxin for Hypersecretion Blepharitis
American Society of Ophthalmic plastic and Reconstructive Surgery, New Orleans

2004 Borodic GE Antibodies to botulinum toxin after repeated use in cosmetic applications
American Society of Ophthalmic plastic and Reconstructive Surgery, New Orleans

October 2004 Borodic GE. Botulinum Toxin Course
American Academy of Ophthalmology, New Orleans, Louisiana

October 2005 Borodic GE. Botulinum Toxin Course
American Academy of Ophthalmology, Chicago, Illinois

2005 Borodic GE. Botulinum Toxin Course
American Society of Ophthalmic Plastic Reconstructive Surgery, Chicago, Illinois

2005 Kahn J, Bushwach K, Leese P, Borodic GE, Johnson E, Goodnough M, Milizio C, Weilert D. A First Look at the "Next Generation" High Purity Neurotoxins Safety and Efficacy Results in the First Patients
American Society of Ophthalmic Plastic Reconstructive Surgery , Chicago, Illinois

2005 Bushwach K, Kahn J, Leese P, Borodic GE, Johnson E, Goodnough M, Milizio C, Weilert D. High Purity Neurotoxins Safety and Efficacy Results in the First Patients
American Society of Plastic Reconstructive Surgery, San Diego, California

2006 Borodic GE. Botulinum Toxin Course Contributor
American Academy of Ophthalmology, Las Vegas, Nevada

November 2007 Borodic GE. Botulinum Toxin Course
American Academy of Ophthalmology, New Orleans, Louisiana

November 2008 Borodic GE. Botulinum Toxin Course
American Academy of Ophthalmology, Atlanta, Georgia

October 2009 Borodic GE. Botulinum Toxin Course
American Academy of Ophthalmology, San Francisco, California

2009 Borodic GE, Hinkle D, Cai Y. Drug induced Graves Disease from CTLA-4 Suppression
American Society of Ophthalmic Plastic and Reconstructive Surgery, San Francisco, California

2009 Borodic GE. Orbicularis Oculi Myo-Osseous Fixation: A New Treatment for Benign Essential Blepharospasm and Blepharospasm Associated with Diffuse Facial Dystonia (Meige Syndrome)
American Society of Ophthalmic Plastic and Reconstructive Surgery, San Francisco,

- California
- 2009 Borodic GE. Enhancement of Gold Weight Ballasting Effect with Placation of Lateral Retinalculum- Lateral Canthal Tendon via Single Self Drilling Titanium Screw
American Society of Ophthalmic Plastic and Reconstructive Surgery, San Francisco, California
- October 2010 Borodic GE. Botulinum Toxin Course (co-director)
American Academy of Ophthalmology Chicago, Illinois
- 2010 Borodic GE. Video Presentation of Cases of Blepharospasm and Meige Syndrome Treated with Myo-osseous Fixation- Browpin, One to Two Year Follow-up
American Society of Ophthalmic Plastic and Reconstructive Surgery, Chicago, Illinois
- 2010 Borodic GE. Comparative Compositional Pharmacology of Botulinum Toxin Preparations
American Society of Ophthalmic Plastic and Reconstructive Surgery, Chicago, Illinois
- October 2011 Borodic GE. Canalicular Stenosis Treated with Self Expanding 3-0 Supramyd Loop
American Society of Ophthalmic Plastic and Reconstructive Surgery, Orlando, Florida
- 2011 Borodic GE. Orbicularis Oculi Myo-Osseous Fixation (MOF-Facepin, BrowPin) for Blepharospasm not Responsive to Botulinum Toxin, 3 Year Experience
American Society of Ophthalmic Plastic and Reconstructive Surgery, Orlando, Florida
- 2011 Borodic GE. Use of Brow Pin (FacePin) for the Treatment of Involuntional and Paralytic Brow Ptosis and Midface Descent
American Society of Ophthalmic Plastic and Reconstructive Surgery, Orlando, Florida
- 2011 Borodic GE. Use of Hyaluronidate Filler for the Treatment of Lower Facial Deformity Associated with Hemifacial Spasm
American Society of Ophthalmic Plastic and Reconstructive Surgery, Orlando, Florida
- 2012 Borodic GE. Cosmetic Botulinum Toxin and Facial Fillers: An Introductory Course
American Academy of Ophthalmology Chicago, Illinois
- 2013 Borodic GE. Extended Report on Brow Pin for Treatment of BTX Resistant Essential Blepharospasm
American Academy of Ophthalmology, New Orleans, Louisiana
- 2014 Borodic GE. Cosmetic Botulinum Toxin and Facial Fillers: An Intermediate Course
American Academy of Ophthalmology Chicago, Illinois
- 2015 Borodic GE. Cosmetic Botulinum Toxin and Facial Fillers: An Intermediate Course
American Academy of Ophthalmology Los Vegas, Nevada
- 2016 Borodic GE. Cosmetic Botulinum Toxin and Facial Fillers: An Intermediate Course
American Academy of Ophthalmology Chicago, Illinois
- 2016 Borodic GE Management of Blepharospasm, inclusive of Surgical Overview
Facial Movement Disorders and Related Conditions
University of Vermont College of Medicine, Neurology, Ophthalmology
- 2016 Borodic GE Overview of Pharmacology of Botulinum Toxin with Emphasis on the Future
REVANCE Inc. (NASDQ) San Francisco, CA
- 2016 Borodic GE Review of New Indication for Botulinum Toxin with Emphasis on CNS disorders,
Mood and Affect, CNS Glutamate Effects and Future Enhanced Delivery Techniques
REVANCE Inc. (NASDQ) San Francisco, CA
- 2016 BorodicGE Allergy, Topical Formulations of botulinum Toxin and External Ocular Disease
REVANCE Inc. (NASDQ) San Francisco, CA
- 2016 Borodic GE Milestone in the Devlopment of Botulinum Toxin Therapeutic Technology
King and Spaulding Conference, NYC
- 2017 Borodic GE. Cosmetic Botulinum Toxin and Facial Fillers: An Intermediate Course

- American Academy of Ophthalmology New Orleans Louisiana
- 2018 Borodic GE Comprehensive Review of Orbital Block Techniques and Pharmacology with emphasis on Patient Safety, Anesthesia Grand Rounds June 2018 Massachusetts Eye and Ear Infirmary
2018. Borodic GE. Cosmetic Botulinum Toxin and Facial Fillers: An Intermediate Course American Academy of Ophthalmology Chicago, Illinois
- 2019 Borodic GE Botulinum Toxin Administration techniques for Facial Application, American Academy of Ophthalmology San Francisco 2019
- 2019 Borodic GE Dasgupta Memorial Lecture International Botulinum Toxin Conference University of Massachusetts Does Botulinum Toxin penetrate the Central Nervous System Clinical and Scientific Evidence (New Bedford , Massachusetts August 2019)
- 2019 Borodic GE Keynote Presentation of the International Botulinum Toxin Conference University of Massachusetts. Pharmacologic Effects of Botulinum Toxin on the Human Retina (New Bedford, Massachusetts August 2019
- 2019 Borodic GE. Cosmetic Botulinum Toxin and Facial Fillers: An Intermediate Course American Academy of Ophthalmology San Francisco, Oct 2019
- 2020 Borodic GE Macular degeneration and a discovery made in Quincy/ Massachusetts Dorchester Medical Society Invited Lecture February 13,2020

Commented [G1]:

International

- June 1982 Borodic GE, Gragoudas E, Brockhurst R. Choroidal Neovascularization Complicating Congenital Optic Nerve Pits International Neuro-Ophthalmology Symposium, Hamilton, Bermuda
- 1984 + Borodic GE, Bienfang DC. The Topographic Neuropathology of Opsoclonus International Congress of Neuro-Ophthalmology, Antwerp, Belgium
- 1985 Borodic GE. Lecturer at Neuro-Ophthalmic Society International Neuro-Ophthalmic Symposium
- September 1987 +Borodic GE. Evidence of Drug Resistance with Repeated Injections of Oculinum in Essential Blepharospasm 5th International Meeting of the Benign Essential Blepharospasm Research Foundation
- 1988 + Borodic GE, Townsend DJ, Cozzolino DJ. Dose Relationships of Botulinum Toxin for Blepharospasm 6th International Conference on Facial Dyskinesia, Cambridge, Massachusetts
- 1988 + Borodic GE, Weigner A, Young R. Innervation Zone Analysis and Botulinum Toxin Therapy (Blepharospasm) 6th International Conference on Facial Dyskinesia, Cambridge, Massachusetts
- May 1992 + Borodic GE, Ferrante R, Pearce B. Review of Histologic Changes in Muscle After Clinical Botulinum Toxin Injections and Importance of Diffusion International Symposium on Botulinum Toxin, Madison, Wisconsin
- November 1999 +Borodic GE, Acquadro MA. Retrospective Analysis of 97 Botulinum Toxin Patients with Blepharospasm, and Essential Headache Disorders International Botulinum Toxin Conference, Orlando, Florida
- November 1999 +Tarsy D, Borodic GE. Botulinum Toxin Injection in Patients with Myasthenia Gravis International Botulinum Toxin Conference, Orlando, Florida
- 2002 +Borodic GE, Acquadro MA. Botulinum Toxin for Chronic Facial Pain 140 Patient Experience

- 2005 International Botulinum Conference, Hanover, Germany
+Borodic GE, Goolsy H, Ferrante R. Histologic Analysis of Pure Botulinum Type A Neurotoxin on Motor Denervation After Point Injection
- 2008 International Botulinum Toxin Conference, Denver, Colorado
+Pellet S, Tepp W, Borodic GE, Johnson EA. Neuronal Cell Based Assay for Detection of Botulinum Toxin Antibodies
International Botulinum Toxin Conference, Lake Majori, Dino, Italy

Report of Clinical Activities and Innovations

Current Licensure and Certification

- 1979 Diplomat, National Board of Examiners
1979-Present Rhode Island Board of Registration
1981-Present Massachusetts Board of Registration
1985 Board Certification: Ophthalmology

Practice Activities (Current)

- | | | | |
|------------------|-----------------------------|---|----------------------------|
| 1985- present | Ophthalmology | Associated Eye Physicians & Surgeons, Inc., Quincy | Three days week |
| 1985- present | Outpatient surgeries | Massachusetts Eye and Ear Infirmary, Boston | One to four days per month |
| 2005- present | Ophthalmology/Oculoplastics | Associated Eye Physicians & Surgeons, Inc., Cambridge | Two days week |

Clinical Scientific Accomplishments and Innovations:

1. Botulinum Toxin Pharmacology:
 - a. Principle investigator for phase 2 and phase 3 trials on botulinum toxin for facial spastic diseases. (Oculinum-TM, now Botox)
 - b. Discovered and Published the first use of botulinum toxin pharmaceuticals for the treatment of a primary pain syndrome (tension and myofascial headache, post operative pain 1991-1995)(see Press release on Oct 13, 2010 on FDA approval for Chronic migraine).
 - c. Developed Original Diffusion nomograms and technic of administering botulinum toxin for human spasticity disorders
 - d. Developed Criterion for high likely responders to Botulinum Injection for Migraine based on clinical history
 - e. Discovered and developed post sinus headache application for botulinum toxin
 - f. Discovered the application of botulinum toxin by injection or topical applications for the treatment of human inflammation, including atopic allergy, eczema, neurogenic inflammation, arthritis, blepharoconjunctivitis, ocular surface disease, and generic applications.
 - g. Discovered Primary Mood and Affect Responses., Use of botulinum Toxin for Human depression, Depression as selection criterion for Migraine, and Chronic headache

disorders. Discovered effect of peri-ocular botulinum toxin for primary and secondary sleep disorders based on blepharospasm patient interactions and interaction with patient with essential headaches

- h. Recognized the importance of Rho protein family effects of botulinum toxin and applications to human disease states
- i. Recognized the increasing problem of immunity after continuous use of botulinum toxin, and the corresponding compositional defect in BOTOX responsible for this complication. With publication and use of patents, the problem received industrial attention to this issue resulting in formulation changes of existing neurotoxin (BOTOX and DYSPORT). The future directional activities towards purer botulinum based products ensued with industry investing new compositions and formulation relative to drug safety.
- j. Initial discovery finding extra-ocular muscle necrosis using lidocaine anesthetic formulations in the absence of hyaluronidase for peri-bulbar injections
- k. Introduced and popularized the notion of photophobia as an important component to Meige Disease-Blepharospasm
- l. Conceived and designed a novel surgical procedure for the treatment of benign essential blepharospasm using neurophysiologic and oculoplastic principles, conducting initial clinical study, publishing and teaching the procedure to other surgeons.
- m. Described a novel neuronal cell based assay to assess botulinum toxin immunologic resistance.
- n. Developed , based on clinical experience, literature meta-analysis and laboratory experiments, a method to enhance potency (and duration) of botulinum formulations using adjuvant proteins effecting increased axon terminal uptake of botulinum toxin
- o. Designed multiple clinical studies to assess efficacy of botulinum toxin in disfiguring and blinding facial spastic disease, dystonia and facial esthetics.
- p. Teaching surgical technique to residents and fellows when possible.
- q. Developed surgical understanding , novel procedure, and approaches to the management of blepharospasm syndromes
- r. Successful surgical practice covering anterior eye segment and oculoplastic for over thirty years.
- s. Discovery of intra-ocular disease applications of botulinum toxin

Report of Technological and Other Scientific Innovations

US Patents

US Patent 5,053,005 filed Apr 1989
Chemomodulation of the Curvature of the Juvenile Spine

US Patent 5,183,462 filed Aug 1990
Controlled Administration of Chemodernervating Pharmaceuticals

US Patent 5,298,019 filed Jan 1993
Chemomodulation of the Curvature of the Juvenile Spine

US Patent 5,401,243 filed Apr 1993
Controlled Administration of Chemodernervating Pharmaceuticals

US Patent 5,696,077 filed Oct 1994
Pharmaceutical Composition Containing Botulinum B Toxin Complex

US Patent 7,537,773 filed Aug 1998
Chemodernervating Pharmaceutical as Anti-Inflammatory Agent

US Patent 6,429,189 filed Dec 1999
Cytotoxin (non-neurotoxin) for the Treatment of Human Headache Disorders and Inflammatory Diseases

US Patent 7,459,164 filed May 2002
Composition for Therapeutic and Cosmetic Botulinum Toxin

US Patent 7,491,403 filed Dec 2002
Pharmaceutical Botulinum Toxin Compositions

US Patent 7,335,367 filed March 2003
Treatment of Chronic Chalazion and Hordeolum with Botulinum Toxin

US Patent 7,670,608 filed March 2003
Selection of Patients with Increased Responsiveness to Botulinum Toxin

US Patent 7,270,826 filed Jan 2004
Methods of Using Botulinum Toxin for the Treatment of Hypervolemic Lip Deformity (lip ectropion)

US Patent 8,192,979 filed Feb 2005
Compositions, Methods and Devices for Preparing Less Painful Botulinum Toxin Formulations

US Patent 7,691,394 filed April 2005
High-Potency Botulinum Toxin Formulations

US Patent 8,580,745 filed Feb 2007
Composition for Therapeutic and Cosmetic Botulinum Toxin

US Patent 7,943,152 filed Jan 2008
Treatment of Chronic Chalazion and Hordeolum with Botulinum Toxin

US Patent 8,241,640 filed March 2008

Pharmaceutical Botulinum Toxin Compositions

US Patent 8,580,745 Composition for therapeutic and cosmetic botulinum toxin November 12, 2013

US Patent 8,679,486 filed April 2010
High-Potency Botulinum Toxin Formulations (March 25, 2014)

US Patent 8,691,769 filed March 2004
Treatment of Sinusitis Related Chronic Facial Pain and Headache with Botulinum Toxin Injections

US Patent 8,926,991 filed June 2006
Botulinum Toxin and the Treatment of Primary Disorders of Mood and Affect (June 6,2015)

US Patent 9,066,851 Extended Length botulinum toxin formulation for human and mammalian use (June 30, 2015)

US Patent 9,393,291 Use of Botulinum Toxin for the treatment of cerebrovascular disease, renovascular disease, and retinovascular disease 9,393,291 (July 19,2016)

US 9375476 Patent Anti –inflammatory topical botulinum toxin composition (June 28,2016)

US 9,901,627 Formulation of botulinum toxin for ocular surface disease. February 27,2018

US Patent 10,441,641 Botulinum Toxin for primary disorders of mood and affect, with application to human depression associated with sleep disorders (Oct 15, 2019)- Major Depression Covered

US Patent 10,857,215 Use of botulinum toxin for the treatment of cerebrovascular disease, renovascular and retinovascular circulatory beds
December 8, 2020

US Patent 11,123,412 Method of treating macular degeneration using botulinum toxin-based pharmaceuticals **September 21, 2021**

US Patent 11,123,411 Method of treating macular degeneration using botulinum toxin-based pharmaceuticals **September 21, 2021**

US Patent 11,096,993 Method of treating macular degeneration using botulinum toxin-based pharmaceuticals **August 24, 2021**

Foreign Patents

China Pat 100525831C filed Dec 2003
Improved Pharmaceutical Botulinum Toxin Compositions

Colombia filed Dec 2003

Improved Pharmaceutical Botulinum Toxin Compositions

European Patent Convention Pat 1594523
Improved pharmaceutical botulinum toxin compositions

India Pat 206509 filed Dec 2003
Improved Pharmaceutical Botulinum Toxin Compositions

Indonesia Pat IDP0024294 filed 2003
Improved Pharmaceutical Botulinum Toxin Compositions

Mexico Pat 268879 filed Dec 2003
Improved Pharmaceutical Botulinum Toxin Compositions

New Zealand Pat 540425 filed Dec 2003
Improved Pharmaceutical Botulinum Toxin Compositions

Singapore Pat 112594 filed Dec 2003
Improved Pharmaceutical Botulinum Toxin Compositions

South Africa Pat 2005/04982 filed Dec 2003
Improved Pharmaceutical Botulinum Toxin Compositions

South Africa Pat 2005/04982 filed Dec 2003
Treatment of Chronic Chalazion and Hordeolum with Botulinum Toxin Injections

Mexico Pat 276893 filed Mar 2004
Treatment of Chronic Chalazion and Hordeolum with Botulinum Toxin Injections

Australia Pat 2004216904 filed Mar 2004
Treatment of Sinusitis Related Chronic Pain and Headache with Botulinum Toxin Injections

China Pat 20048000591 filed Mar 2004
Treatment of Sinusitis Related Chronic Pain and Headache with Botulinum Toxin Injections

New Zealand Pat 541779 filed Mar 2004
Treatment of Sinusitis Related Chronic Pain and Headache with Botulinum Toxin Injections

Singapore Pat 114943 filed Mar 2004
Treatment of Sinusitis Related Chronic Pain and Headache with Botulinum Toxin Injections

Singapore Pat 114943 filed Mar 2004
Treatment of Sinusitis Related Chronic Pain and Headache with Botulinum Toxin Injections

European Patent Convention Pat 1706141 filed Jan 2005
Use of Botulinum for the Treatment of Hypervolemic Lip Deformity

France Pat 1706141 filed Jan 2005
Use of Botulinum for the Treatment of Hypervolemic Lip Deformity

Germany Pat 1706141 filed Jan 2005
Use of Botulinum for the Treatment of Hypervolemic Lip Deformity

Italy Pat 1706141 filed Jan 2005
Use of Botulinum for the Treatment of Hypervolemic Lip Deformity

Spain Pat 1706141 filed Jan 2005
Use of Botulinum for the Treatment of Hypervolemic Lip Deformity

EU Pat Number pending Jan 2014
Use of Botulinum Toxin for Sinus Headache

EU Pat Number pending Jan 2013
Botulinum Toxin for Select Disorder of Mood and Affect

US Applications

App. 2002/0192239 filed Jan 2002
Use of Botulinum Toxin for the Treatment of Chronic Facial Pain

App. 2002/0187164 filed Aug 2002
Cytotoxin (non-neurotoxin) for the Treatment of Human Headache Disorders and Inflammatory Diseases

App. 2004/0037853 filed May 2003
Composition for Therapeutic and Cosmetic Botulinum Toxin

App. 2004/0151741 filed Dec 2003
Pharmaceutical Botulinum Toxin Compositions

App. 2004/0175390 filed Mar 2004
Selection of Patients with Increased Responsiveness to Botulinum Toxin

App. 2004/0175400 filed Mar 2004
Treatment of Chronic Chalazion and Hordeolum with Botulinum Toxin

App. 2004/0247606 filed Mar 2004
Treatment of Sinusitis Related Chronic Facial Pain and Headache with Botulinum Toxin Injections

App. 2005/0208075 filed Jan 2005
Methods of Using Botulinum Toxin for the Treatment of Hypervolemic Lip

Deformity (lip ectropion)

App. 2006/0147471 filed Feb 2005
Compositions, Methods and Devices for Preparing Less Painful Botulinum Toxin Formulations

App. 2006/0147471 filed Feb 2005
High-Potency Botulinum Toxin Formulations

App. 2007/0009555 filed Jan 2006
Botulinum Toxin and the Treatment of Primary Disorders of Mood and Affect

App. 11/447,984 filed Jun 2006
Botulinum Toxin and the Treatment of Depressive, Anxiety and Sleep Disorders

App. 12/083,058 filed Oct 2006
Botulinum Toxin Based Pharmaceutical Composition

App. 2008/0118533 filed Jan 2008
Treatment of Chronic Chalazion and Hordeolum with Botulinum Toxin

App. 2009/0148476 filed Dec 2008
Chemo- denervating Pharmaceutical as Anti-Inflammatory Agent

App. 2009/0324647 filed Aug 2009
Albumin-Free Botulinum Toxin Based Pharmaceutical Compositions Containing a Hyaluronidase and Methods of Use

App 20160051645 Use of Botulinum Toxin for the Treatment of Cerebrovascular Disease, Renovascular Disease and Retinovascular Disease (published Feb 25 , 2016)

App 20160095908 Treatment of Mood and Affect Disorder using Neurotransmitter CNS imaging studies (April 7, 2016)

App1 20140105883 Use of Botulinum Toxin for the Treatment of Cerebrovascular Disease, Renovascular Disease and Retinovascular Disease (published February 25, 2016)

App 20160051645 Use of Botulinum Toxin for the Treatment of Cerebrovascular Disease, Renovascular Disease and Retinovascular Disease (published April 17, 2014)

App 2016005164 (published Feb 2 ,2016)
Botulinum Toxin and the Treatment of Depressive, Anxiety

App 2016004557 Botulinum Toxin for Circadian Rhythm Disorders (published February 18,2016)

App 20160051643 Botulinum Toxin for Depression (February 25,2016)

App 2015029768 Botulinum selecting Mood and Affect Disorders for Treatment of Migraine and Tension headache (published October 22, 2015)

App 20160015794 Topical Ocular preparation of Botulinum Toxin for Use in Ocular Surface Disease (published Jan 21, 2016)

Appl 20150297688 Botulinum Toxin for Human Depression (published Oct 22, 2015).

Appl 20150297684 Extended Length Botulinum Toxin for human Use October 22, 2015

Appl 20150258183 Botulinum Toxin for Primary Disorders of Mood and Affect (September 17,2015)

Appl 20150132283 Botulinum Toxin and Treatment of Primary Disorders of Mood and Affect published May 14, 2015)

Appl 20150086533 Botulinum Toxin for the Treatment of Anxiety (March 26,2015)

Appl 20140315820 High Potency Botulinum Formulations (October 23, 2014)

Appl 20150086532 Botulinum for Primary Disorders of Mood and Affect (March 26, 2015)

Appl 20110319944 Submuscular Facial Muscle Fixation for the Treatment of Migraines (December 29,2011)

Appl 20120164657 Method of Detecting human antibodies that neutralize botulinum toxin action botulinum toxin action (June 28, 2012)

App 20110293663 Pharmaceutical Botulinum Compositions (December 1,2011)

App 20100279945 Potency and Botulinum Toxin Nov 4, 2010

App Use of Botulinum Toxin for the Treatment of Chronic Facial Pain Nov 4, 2010)

App 2009 0324647 Albumin Free Botulinum Toxin Based Compositions containing Hyaluronidase (December 31,2009)

Appl 20090148476 Chemodenervating pharmaceutical as an anti-inflammatory

agent (June 11, 2009

Appl 2017031 9667) Botulinum Toxin for Primary Disorders of Mood and Affect (September 7,2017) (Borodic)

Appl 20170252415 Botulinum Toxin for Primary Disorders of Mood and Affect (November 9, 2017) (Borodic)

Appl 20170165331 Botulinum Toxin for Primary Disorders of Mood and Affect (June 15,20 17) (Borodic)

Appl 20170165330 Botulinum Toxin for Primary Disorders of Mood and Affect (June 15,20 17) (Borodic)

Appl 20170143807) Botulinum Toxin for Primary Disorders of Mood and Affect (May 25,20 17) (Borodic)

Appl 20170143807) Botulinum Toxin for Primary Disorders of Mood and Affect Using neurotransmitter imaging (April 7,20 16) (Borodic)

Appl 20170246268 Borodic GE Acquadro M Longevity Enhancement associated with Repetitive Botulinum Toxin (Centurion Effect) (August 31,2017)

Appl **2018030391**Borodic GE Novel Method of treating Macular Degeneration Using Botulinum Toxin Based Pharmaceuticals (October 25,2018)

Appl **2018296651** Borodic GE Novel Method of treating Macular Degeneration Using Botulinum Toxin Based Pharmaceuticals (October 18, 2018)

Appl **20180161407** Borodic GE Novel Method of treating Macular Degeneration Using Botulinum Toxin Based Pharmaceuticals (October 18, 2018)

Appl 20180344806 Borodic GE Novel Method of Treating Macular Degeneration Using Botulinum Toxin-Based Pharmaceuticals (Published December 6 ,2018).

Appl Topical Ocular Preparation of Botulinum Toxin for Use in Ocular Surface Disease **20190262438 August 29, 2019**

Appl **20210252116** Botulinum Toxin and the Treatment of Primary Disorders of Mood and Affect **August 19, 2021**

Appl 20200046813Novel Method of Treating Macular Degeneration Using Botulinum Toxin-Based Pharmaceuticals

Appl **20200078450**Botulinum Toxin and the Treatment of Primary Disorders of

Mood and Affect **March 12, 2020**

Appl 20200222512 Topical Ocular Preparation of Botulinum Toxin for Use in Ocular Surface Disease **July 16, 2020**

Appl **20200368331** Novel Method of Treating Macular Degeneration Using Botulinum Toxin-Based Pharmaceuticals **November 26, 2020**

Appl **20210283228** BOTULINUM TOXIN AND THE TREATMENT OF PRIMARY DISORDERS OF MOOD AND AFFECT **September 16, 2021**

Appl 20210308236 BOTULINUM TOXIN AND THE TREATMENT OF Aapl **2020022251** PRIMARY DISORDERS OF MOOD AND AFFECT **October 7, 2021**

Foreign Applications

Most Recent: WO: 2016040932 A1 March 2016 Centurion Effect induced by Repetitive Botulinum Toxin

France App. 03814518.1 filed Dec 2003
Improved Pharmaceutical Botulinum Toxin Compositions

Germany App. 60326887.0 filed Dec 2003
Improved Pharmaceutical Botulinum Toxin Compositions

Japan App. 2004-564369 filed Dec 2003
Improved Pharmaceutical Botulinum Toxin Compositions

Netherlands App. 03814518.1 filed Dec 2003
Improved Pharmaceutical Botulinum Toxin Compositions

United Kingdom App. 03814518.1 filed Dec 2003
Improved Pharmaceutical Botulinum Toxin Compositions

Japan App. 2006-506300 filed Mar 2004
Treatment of Chronic Chalazion and Hordeolum with Botulinum Toxin Injections

Japan App. 2006-506302 filed Mar 2004
Treatment of Sinusitis Related Chronic Pain and Headache with Botulinum Toxin Injections

European Patent Convention App. 4718358.7 filed Mar 2004 Method of Selecting Patients Suffering from Pain for Treatment with Botulinum Toxin

European Patent Convention App. 4718358.7 filed Mar 2004 Method of Selecting Patients Suffering from Pain for Treatment with Botulinum Toxin

European Patent Convention App. 06772449.2 filed Jun 2006 Botulinum Toxin and the Treatment of Depressive, Anxiety and Sleep Disorders (patent deals with trans-cranial effects of subcutaneous botulin toxin)

WO: 2016040932 A1 March 2016 Centurion Effect induced by Repetitive Botulinum Toxin US Number Pending Gary Borodic MD and Martin Acquadro , MD , DMD

WO PCT – 2018/107005) Novel Method of Treating Macular Degeneration and Associated disorders by Gary Borodic, MD published June 14,2018 (PCT US2017/065271) –see corresponding US applications

Report of Education of Patients and Service to the Community

Activities

1988, 1990, Patient Support Group Meeting for Dystonias of the Face
1994, 1998,
2001, 2003,
2006, 2008

Educational Material for Patients and the Lay Community

| | | | |
|------|-------------------------------------|------------------|--|
| 1986 | Dan Rather CBS Evening News (8 min) | Interview | The Tragedy on the Loss of Botulinum Toxin Because of Product Liability Insurance Issues |
| 1987 | MacNeil-Lehrer news Hour | Interview | Product Liability Insurance Problems and the Treatment of |

| | | | |
|------|--|------------------------------------|--|
| 1999 | Benign Essential Blepharospasm Letters | Author | Blepharospasm (20 min) Managing Blepharospasm Over the Years |
| 2008 | Allure Magazine | Contributor, worked with author | Botulinum Toxin Possible Spread and Effects on the Human Brain |

2015 (October) Regional Meeting Blepharospasm Society North Shore Rehabilitation

2017 (October) Regional Meeting Blepharospasm Society Newton Wellesley Hospital

2018* (March) Regional Meeting Connecticut Blepharospasm Society Farmington, Conn

Report of Scholarship

[Peer reviewed publications in print or other media](#)

- Ashikkaga T, Borodic GE, Sims EAH:
Multiple Daily Insulin Injections and the Treatment of Diabetic Retinopathy
Diabetes 1978 vol. 27:592 (Abstract: JAMA Oct. 6, 1978)
(Abstract: International Medicine News, Oct. 1978)
- Borodic GE, Gletzer A, Kinder R:
Scatter Retinal Photocoagulation and the Hyperglycemic State
(Abstract: Ophthalmology Times, Nov. 1980)
- Calderone JP, Chess J, Borodic GE, Albert DM:
Intraocular Pathology in Trisomy 18 (Edwards Syndrome)
British Journal of Ophthalmology vol. 67, no. 3:162 1983
- Borodic GE, Sadun A, Bienfang DC:
Pulsating Exophthalmos after a Closed Head Injury
Publication: Case Records of MGH, New England Journal of Medicine,
Vol. 311, no. 8:520-528, 1983
- Borodic GE, Gragoudas E, Brockhurst R:
Choroidal Neovascularization Complicating Congenital Optic Nerve Pits
Archives of Ophthalmology vol. 102:229-231, 1984
- Borodic GE, Beyer C, Millin J, Foster S:
Immunoglobulin Deposition in Primary Conjunctival Amyloidosis

- American Journal of Ophthalmology vol. 98:617-622, 1984
- Walsh TJ: Book review by Borodic GE:
Neuro-Ophthalmology; Clinical Signs and Symptoms
Lea & Febiger, 1985. Arch. of Ophthal.
- Char DH: Book Review by Borodic GE:
Thyroid Eye Disease. Williams & Wilkins, 1985 Arch. of Ophthal.
- Jankovic J Book review by Borodic GE:
Facial Dyskinesias, Raven Press, 1988 Arch of Ophthalmol
- Borodic GE, Townsend DJ:
Oculinum (Botulinum Toxin) for the Treatment of Facial Spastic Disease
Oculoplastic Orbital & Reconstructive Surg. Hornblase, Williams, Wilkins, Baltimore 1988
- Borodic GE, Townsend DJ:
Dose-Response Relationships in 241 Patients with Blepharospasm
Cambridge, Mass. 1988 Meige Disease Foundation Meeting
Ears, Nose & Throat Journal, 1988 vol. 67 (12):914
- Borodic GE, Weigner A, Young R:
Motor Point Analysis and Botulinum Toxin Administration
Cambridge, Mass. 1988 Meige Disease Foundation Meeting
Ears, Nose & Throat Journal, 1988 vol 67:915
- Borodic GE, Townsend DJ:
Method of Injecting Botulinum Toxin for the Treatment of Blepharospasm
1988 Meige Disease Foundation Meeting. Ears, Nose & Throat Journal, 1988 vol 67:915
- Borodic GE, Cozzolino D:
Blepharospasm and its Treatment with Emphasis on the Use of Botulinum A Toxin
Invited by Robert Goldwyn, Editor in Chief, Plastic & Reconstructive Surgery
vol. 83, no. 3:546-553, 1989
- Borodic GE, Townsend DJ, Beyer C:
Management of Implant Extrusion in an Eviscerated Socket with Autogenous Dermis Fat Graft
Ophthalmic Plastic & Reconstructive Surgery vol. 5 (2):144-149, 1989
- Borodic GE, Miller D, Bienfang D:
Opsoclonus Report of Three Autopsies and Literature Reviews
Neuro-ophthalmology Into the Nineties, Smith JL, Katz RS,
Dutton Press, Hialeah, FL, 1989
- Borodic GE, Joseph M, Fay L, Cozzolino D, Ferrante R:
Botulinum A Toxin for the Treatment of Spasmodic Torticollis, Dysphagia and Regional Toxin
Spread
Head & Neck, 12:392-398, 1990
- Borodic GE:
Involuntary Eyelid Closure and Orbicularis Paralysis
Current Opinions in Ophthalmology Vol. 1:30, 1990
- Borodic GE, Mills L, Joseph M:
Botulinum A Toxin for Adult Onset Spasmodic Torticollis
Ophthalmic Plastic and Reconstructive Surgery 87:2, 285-289, 1991
- Borodic GE, Cozzolino D, Weigner A, Ferrante R, Young R:
Orbicularis Oculi Innervation Zone and Implications for Botulinum A Toxin Therapy
Ophthalmic Plastics and Reconstructive Surgery, Volume 7, No 1, 54-60, 1991
- Borodic GE, Pearce LB, Johnson E, Schantz E:
Clinical and Scientific Aspects of Therapeutic Botulinum Toxin Administrations. Ophthalmology

- Clinics of N America, September, Vol. 4, No. 3, 1991 (Invited)
- McKenna MJ, Cheney M, Borodic GE:
Management of Facial Paralysis after Intracranial Surgery
Contemporary Neurosurgery, 13(22), 1-8, 1991
- Borodic GE:
Botulinum A Toxin for (Expressionistic) Ptosis Overcorrection after Frontalis Sling
Ophthalmic Plastic and Reconstructive Surgery 8(2):137-42, 1992
- Borodic GE, Pearce LB, Smith K, Joseph M:
Botulinum Toxin for Spasmodic Torticollis, Multiple vs. Single Point Injections per Muscle
Head and Neck 14:33-37, 1992
- Borodic GE, Cheney M, McKenna M:
Contralateral Injection of Botulinum Toxin to Achieve Facial Dynamic Symmetry for the
Treatment of Hemifacial Spasm
Ophthalmic Plastic and Reconstructive Surgery, 90(6),972-7,1992
- Borodic GE, Ferrante R:
Histologic Effects of Repeated Botulinum Toxin over Many Years in Human Orbicularis Oculi
Muscle
Journal of Clinical Neuro-Ophthalmology 12(2):121-127, 1992
- Borodic GE, Pearce LB:
United States Pharmacopial Drug Information for the Health Care Professional
January, 1992
- Borodic GE, Ferrante R, Wiegner AW, Young RR:
Treatment of Spasticity with Botulinum Toxin
Ann Neurol 31(1):113,1992
- Borodic GE, Smith K, Pearce LB, Ferrante R:
Botulinum B Toxin as an Alternative to Botulinum A Toxin, a Histologic Study
Ophthalmic Plastic and Reconstructive Surgery, 9(3):182-90, 1993
- Borodic GE, Metson R, Townsend D, McKenna M, Pearce LB:
Botulinum Toxin for Aberrant Facial Nerve Regeneration. Dose Response Relationships.
Ophthalmic Plastic and Reconstructive Surgery, (91)6, 1042-5, 1993
- Borodic GE, Ferrante R, Pearce B:
Review of Histologic Changes in Muscle after Clinical Botulinum Toxin Injections and Importance
of Diffusion
International Symposium on Botulinum Toxin, Madison Wisconsin in Botulinum and tetanus
Neurotoxins edited by BR Dasgupta, Plenum Press, New York, New York 1993
- Borodic GE:
Hemifacial Spasm, Evaluation and Therapy
Textbook of Botulinum Toxin Therapy Eds J Jankovic, M
Hallet, Marcel Dekker, New York, Hong Kong, Chapter 24, page 331-353,1994
- Borodic GE, Aldersen K, Pearce, Ferrante R:
Histology and Pharmacology of Botulinum Toxin Injections
Textbook of Botulinum Toxin Therapy Eds J Jankovic, M
Hallet, Marcel Dekker, New York, Hong Kong, Chapter 10, page 119-158, 1994
- Borodic GE, Pearce LB, Johnson E:
Botulinum Toxin Antibodies after Repetitive Eyelid Injections
Ophthalmologyh, 101:1158-9, 1994
- First E, Pearce LB, Borodic GE:
Dose Standardization with Botulinum Toxin for Human Use

- Lancet, 343(8904):1035, 1994
- Pearce LB, Borodic GE, First E, MacCallum R:
Measurement of Botulinum Toxin Activity: Evaluation of the Lethality Assay
Toxicology and Applied Pharmacology 128, 69-77, 1994
- Borodic GE, Ferrante R, Pearce LB, Smith K:
Histologic Assessment of Dose Related Diffusion and Muscle Fiber Response after Therapeutic Botulinum Toxin Injections
Movement Disorders 9(1):31-9, 1994
- Acquadro MA, Borodic GE:
Treatment of Myofascial Pain with Botulinum Toxin
Anesthesiology 80(3):705-706, 1994
- Borodic GE:
Cystic Lesions of the Orbit
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Canthoplasty (Chapters 2)

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Management of Graves and Thyroid Eye Disease (Chapter 3)

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Surgical Reconstruction of the Human Eyelids (Chapter 4)

Borodic GE

Ptosis Surgery (Chapter 5)

Borodic GE

Medical and Surgical Management of Blepharospasm (Chapter 8)

Narrative Report (Academic Accomplishments Contributing to Medical and Surgical Practice)

My career in ophthalmology has been a hybrid, encompassing interests in basic ophthalmic surgical practice, oculoplastic surgery, pharmacology of botulinum toxin relative to ophthalmology as well as other specialties. Particular focus continues to be benign essential blepharospasm and related disorders. Although an orphan disease, this condition can be blinding and therefore devastating to quality of life. My interest in this disease did not only originate from ophthalmology and eye plastic surgical experience, but also prior training received in the field of neurology. For this condition, my work has contributed to acceptance of botulinum toxin for this indication (1980's), refinement in the administration techniques, enhanced understanding of treatment method and materials (1990's), enhancements on understanding pharmacology and new clinical approaches to both ophthalmic conditions and other medical/neurologic indications.

In research and development, I have interested industry to commit tremendous resources in the study and development of botulinum pharmaceuticals while still maintaining an active practice in eye plastics and ophthalmology. Most recently, I have assisted Johnson and Johnson's Mentor Corporation to initiate a novel botulinum formulation for national studies using altered type A botulinum toxin with a novel formulation of excipients. This program has been expanded to treatment in over 3000 patients nationally and intended to provide another supplier of materials to reduce cost based on competition and perhaps even provide a more contained pharmacologically active agent allowing for safer high dose administration. Most recently, I have helped Revance Inc. work on its target development projects and indications with the same intension.

In clinical research area, I co-published the first article on the BTX treatment of human headache disorders and primary pain disorders, an observation (1993- J Anesthesiology) that was further corroborated in the mid 1990's. This indication was expanded to an FDA approval of human chronic

migraine headache disorders for migraine prophylaxis in October 2010. Migraine and associated myofascial headache disorders are the second most common reason a human being will use a medication. I will continue to try to work in the scientific medical and civic issues relative to these discoveries. I received the first headache patent issued internationally (Japan Patent 4381477, June 1993, US Pat 8,691,769, US Pat 7,670,608) and have worked in this area in my practice and development interest for many years.

In the period between 1990-1997, published work of led to understanding defects in BOTOX formulation that threatened the efficacy of this agent for potentially millions of patients. Toxoid in the vials was an issue leading to secondary resistance in numerous high dose applications (dystonia spasticity, pain management) , a fact missed by US FDA regulators and denied by commercial industry at that time. By use of academic literature and national conference, this problem eventually received appropriate attention. In 1998, the two major pharmaceutical companies changed their formulations which subsequently almost eliminated the secondary immunity rate.

In 1998 and subsequent years, my work focused on use of botulinum toxin as an anti-inflammatory agent. The US Patent office has awarded a series of patents dealing with the utilization of the toxin for various regional inflammatory conditions (see US Pat 7,537,773 (June 1998), US Pat 9,375,476). In 2016 using the principles and indications, Revance (NASDQ) imitated the first multi centered placebo controlled trial for the treatment of a regional inflammatory condition (plantar fasciitis). This high profile prototype study can introduce and expand the utility of botulinum toxin across multiple disease categories in the future.

My work has also dealt with issues regarding potency of botulinum preparation. In 2016 and 2017, the use of adjuvant protein capable of enhancing neuronal cell protein uptake was initially described as a method of improving formulation performance (see Borodic US Pat 8679486, US Pat 9066851). Multi centered clinical studies have demonstrated this approach to formulation can increase potency and duration of action over existing formulations by factor of about 50% in both low dose application (facial cosmetics) and high dose applications (craniofacial dystonias, torticollis). Linking formulation with clinical improvement in the highly valuable botulinum technology has the potential to improve treatment for millions of patients afflicted with spasticity from cerebral palsy, stroke and blepharospasm. I have continued interest materials pharmacology is driving the current industry.

An interesting clinical observation made in my clinical practice treating benign essential blepharospasm has been a subject of national and international interest. I made an original observation on effects of periocular botulinum on depression, sleep and other disorders of mood and affect (see US Pat 8,926,991 with continuations and continuations in part, see US Fed News Service Jan 6, 2015). This observation led me to conduct basic lab experiments showing the effects of eyelid injections on central nervous system caused major changes in glutamate, GABA central nervous system transmission in the rostral brainstem in animal studies. Further the integration of these observations were used to further analyze and select patients with migraine and related headache syndromes. US Patent office awarded US Pat 8,926,991) On January 6, 2017, TIME MAGAZINES cover story highlighted this indication which is still in clinical studies. Further, Academic movement disorders organizations have initiated changes in validation and endpoint development including mood and affect concepts taught in the aforementioned publications (see TWSTRS 2 scales).

Most recently, I am working on the previously unappreciated biologic effects of botulinum toxin on epithelial cell division, relative to wound healing and epithelial biologic barrier functions.

Over the last several years, I conceived, based on surgical anatomy and neurophysiology, a novel minimally invasive surgical procedure for refractory treatment of blepharospasm and related disorders. This procedure has now been presented at two national academy meetings and has started to be reproduced internationally by other surgeons. Two papers have been published to date.

Civic activities that can be cited relate to helping the original botulinum toxin effort obtain product liability insurance after the national study had been halted for one year between 1985-1986. This activity required interviews with Dan Rather and an appearance on the McNeil-Leher News Hour. I have participated in advocacy for the Benign Essential Blepharospasm Foundation, National Spasmodic Torticollis Foundation, and National Trigeminal Neuralgia Foundation.

I have always enjoyed teaching at Massachusetts Eye and Ear Infirmary and occasionally in other Boston Hospitals and continue to welcome interested residents or medical students in my office or operating room. In the past, I have authored a book primarily written to assist ophthalmology residents and fellows on plastic techniques on the eyelid. In the past, I have functioned as acting co-director of the Massachusetts Eye and Ear Infirmary plastic service, director of Boston University's plastic service, Co-ophthalmic director of Massachusetts Eye and Ear Infirmary Facial Nerve Clinic, temporary director of eye trauma service, and attending on the general eye service. Recently (October 2010), I received the achievement award from the American Academy of Ophthalmology for sustained efforts to this organization's teaching programs over the years. However, I still believe that the best opportunity for medical student, resident and fellow teaching is on hospital and clinic based training. When asked, I am happy to try to contribute in an appropriate fashion. A recent office medical student thanked me with the following gift which :



Although many years have now passed, I hope to continue contributing to ophthalmic and related medical practice and be helpful as a physician and surgeon.

In the past year, the recognition of my observation on central nervous system effect of botulinum toxin on mitigating mood and affect disorders has been acknowledged by the US Patent and Trademark office. The application of injectable botulinum toxin for the treatment of human depression was published as US Pat. 10,441,641 (October 15,2019) which teaches the utility of application for human depression and sleep disturbances. Further, my patent on use of botulinum toxin for the treatment of anxiety (associated

with insomnia) has also received notice of allowance with publication anticipated in 2020.

The above discovery seems unusual for an ophthalmologist. However, the discovery came from careful observations made from patient responses and interviews with benign essential blepharospasm, various essential headache disorders including migraine, and Meige syndrome as well as complex benefits achieved by aesthetic applications. Each of these ophthalmic conditions I have treated for over 30 years involving hundreds of afflicted individuals. Each of these conditions are associated with important psychogenic overlays and emotional co morbidity, but in different respects.

In infect, the mechanism by which botulinum toxin works in headache and facial pain, has well as many involuntary movements of eyelids, facial muscles involves mitigating depression and anxiety among other important mechanisms.

Further, the inconsistencies in early blinded trials for migraine showed bizarre inverted dose response curves poorly explained by open label observations. Retrospectively, defective induction stratifications in the clinical study samples between control and treatment seemed to explain the aberration in study results. Emotional factors and sleep disturbance were not factored into the stratification formula in study design. Clinical observations uncovered this important previously unrecognized effect. Further, work published here showed anti-glutamate neuro-transmission activity in thalamus from subcutaneous botulinum injections, supporting the effect of a neuro-transmitter linked to human depression.

In subsequent studies, the significance of botulinum toxin as a anti-depressant, anti-anxiety agent has been further supported (phase 2 double blinded placebo controlled studies under US FDA IND). Phase 3 studies are being planned by major pharma companies.

The hope from the above is that a long acting agent such as botulinum toxin can be used for major depression with no dosing administration participation required by the patient. Therefore, no chance of patient induced overdose and/or suicide. This complication is feared by most psychiatrist and clinicians when administering an anti-depressant medication.

Current Research and Development Project on Intra-Ocular Botulinum Effects:

Based on original observation of a coincident effect in a hemifacial spasm patient with early macular leakage associated with AMD, botulinum toxin appeared to have a coincident effect to reduced leakage in the peri-foveal area in a patient 3 weeks after a para-orbital injection given as routine for this form of blepharospasm. Botulinum toxin has a unique property of axoplasmic transport with transcytosis in nervous system. Para-orbital anatomy with autonomic/sensory nerve projection into the posterior macular is a plausible conduit of BTX delivery from injection pterygopalatine fossa. Projection fibers into the macular through the anterior portion of the inferior orbital fissure provide a pathway for intra ocular delivery avoiding extra ocular muscle paralysis. Botulinum type A neurotoxin has been noted to have anti-inflammatory effects with alteration in secretion mast cells and leukocyte degranulation. Actin stimulation with sprouting has been consistently observed in nerve terminals. Further other intercellular adhesion molecule genetic upregulation based on cell culture study (dorsal root ganglion cells) using large gene chips assessing down regulation/upregulation of known gene components corresponding fragments of such adhesion molecules. Botulinum further has a known effect on increasing blood flow in plastic surgical flaps and scleroderma associated fingertip ischemia. Treatment of flow voids in choriocapillaris and retinal circulation are possible from administration.

In several cases where the conventional anti VEGF did not work on sub-foveal edema (choroidal polyposis), BTX seemed to convert a non-responder to Avastin-TM and Eylea-TM to a responder when given in benign location commonly used to treat skin wrinkles.

BTX target molecule SNAP-25 is richly expressed in the inner segment outer segment photoreceptor interface and ganglion cell layer, so possible effects on the retina may be exploitable for treatment of leaking maculopathies and transportable by an innocuous unique intracellular axoplasmic delivery conduit allowing bypass of neuro muscular paralyzing effects of the neurotoxin on extra-ocular muscle cone.

Base on the above, I have undertaken a project to work with Harvard junior faculty on a retinopathy of prematurity animal model to evaluate potential protective effects on oxygen deprivation on mice pups with Dr Ye Sun at Children's Hospital. Currently intravitreal injections are being analyzed with immunofluorescent antibodies for effects on photoreceptor SNAP-25, photo disc stacking, SNAP -25 cleavage products, VEGF isoforms and genetic expression, and VEGF expression in vitreous using ELISA. Further gross pathology is being evaluated relative to neovascularization. This project seeks to expand the known pharmacology of botulinum toxin and can serve as model for study of a very unique drug delivery method for the toxin. I have worked many years in this technology both in studies, clinics, basic research and inventive observation and application and hope to help the careers of younger professions to focus on this valuable technology.

Publications: US Patent Application 20180344806 Borodic GE Novel Method of Treating Macular Degeneration Using Botulinum Toxin-Based Pharmaceuticals (Published December 6 ,2018).
US Patent Application 201803303917 Borodic GE Novel Method of Treating Macular Degeneration Using Botulinum Toxin-Based Pharmaceuticals (Published October 25 ,2018
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