THE AMERICAN ACADEMY OF NEUROLOGICAL SURGERY

85TH ANNUAL MEETING

THE CLOISTER, SEA ISLAND, GEORGIA

OCTOBER 4 – 7, 2023

Congress of Neurological Surgeons

Jointly Provided by the CNS

FUTURE MEETINGS

October 16-19, 2024
The Ritz-Carlton
Half Moon Bay, CA

October 22-25, 2025
The Hotel Grande Bretagne
Athens, Greece

Mark your calendars now!

General Information

Hotel Information

THE CLOISTER AT SEA ISLAND
100 Cloister Drive, Sea Island, GA 31561
855-572-4975

Registration Location:	**www.americanacademyns.org**
Registration:	
On-site Registration is currently open.	
Complete form on website. Email inquiries directly to shelbey@voilameetings.com	

A Special Thanks to the following exhibitors supporting the

THE AMERICAN ACADEMY OF NEUROLOGICAL SURGERY
85TH ANNUAL SCIENTIFIC MEETING

Please take time to visit with them during the Break

- Clearpoint Neuro
- BrainLab, Inc.
- DePuy Synthes
- Insightec
- Integra LifeSciences
- Leica Microsystems, Inc.
- Medtronic
- Stryker Neurosurgical
- Synaptive
- Zap Surgical

WEDNESDAY, OCTOBER 4

1:00 – 6:30 pm	**Registration**	Cloister Foyer II
3:30 – 5:00 pm	**Executive Committee Meeting**	Sea Island Summit Board Room
6:00 – 6:30 pm	**New Members Reception**	Black Banks Terrace
6:30 – 8:30 pm	**Opening Reception**	Black Banks Terrace

THURSDAY, OCTOBER 5

6:00 am – 4:00 pm	**Registration**	Cloister Foyer II
6:30 – 7:30 am	**Members Breakfast & Business Meeting** (Voting Membership Only)	Mizner Ballroom
8:00 – 10:00 am	**Guest & Spouse/Partner Breakfast**	Spanish Lounge
7:30 – 7:35 am	**Welcoming Remarks**	Cloister Ballroom
7:35 – 7:45 am	**Round Robin Roundup!**	Cloister Ballroom
7:45 – 8:50 am	**Peer Reviewed Abstract Session I:** Cerebrovascular Basic Science	Cloister Ballroom
8:50 – 9:55 am	**Peer Reviewed Abstract Session II:** Epilepsy/Functional/Pain Basic Science	Cloister Ballroom
9:55 – 10:10 am	Break	Cloister Foyer
10:10 – 10:40 am	**Special Debate Session I:** The Artificial Intelligence revolution in Medicine and Neurosurgery - Blessing or Curse?	Cloister Ballroom
10:40 – 11:45 am	**Peer Reviewed Abstract Session III:** Cerebrovascular Clinical Science	Cloister Ballroom
11:45 am – 12:40 pm	**Peer Reviewed Abstract Session IV:** Tumor Clinical Science	Cloister Ballroom
2:00 – 3:30 pm	**Academy Innovator Program**	Mizner Ballroom
6:30 – 9:30 pm	**Dinner**	Rainbow Island

FRIDAY, OCTOBER 6

6:00 am – 4:00 pm	**Registration**	Cloister Foyer II
6:30 – 7:30 am	**Members Breakfast & Business Meeting** (Voting Membership Only)	Mizner Ballroom
8:00 – 10:00 am	**Guest & Spouse/Partner Breakfast**	Spanish Lounge
7:30 – 7:35 am	**Welcoming Remarks**	Cloister Ballroom
7:35 – 9:00 am	**Peer Reviewed Abstract Session V:** Spine/ Peripheral Nerves	Cloister Ballroom
9:00 – 9:55 am	**Peer Reviewed Abstract Session VI:** General Interest	Cloister Ballroom
9:55 – 10:10 am	Break	Cloister Ballroom Foyer
10:10 – 10:40 am	**Special Debate Session 2:** Social Media in Medicine and Neurosurgery - Blessing or Curse?	Cloister Ballroom
10:40 – 11:55 am	**Peer Reviewed Abstract Session VII:** Tumor Basic Science	Cloister Ballroom
11:55 am – 12:40 pm	**Presidential Address**	Cloister Ballroom
2:00 – 5:00 pm	**Academy Emerging Investigators' Program**	Mizner Ballroom
6:00 – 6:30 pm	**Cocktail Reception**	Ocean Room
6:30 – 9:30 pm	**Gala Dinner** (Black Tie Optional)	Ocean Room

SATURDAY, OCTOBER 7

7:00 – 12 pm	**Registration**	Cloister Foyer II
7:00 – 9:30 am	**Members & Guests Breakfast**	Mizner Ballroom
7:30 – 8:30 am	**Special Abstract Session VIII:** The Oldfield Session	Cloister Ballroom
8:30 – 9:14 am	**Academy Award Presentation and Lecture**	Cloister Ballroom
9:14 – 9:50 am	**Peer Reviewed Abstract Session IX:** Pediatrics	Cloister Ballroom
9:50 – 10:05 am	Break	Cloister Ballroom Foyer
10:05 – 11:40 am	**Peer Reviewed Abstract Session X:** Tumor Clinical Science	Cloister Ballroom
11:40 am – 12:43 pm	**Peer Reviewed Abstract Session XI:** Epilepsy/Functional/Pain Clinical Science	Cloister Ballroom
12:43 – 12:45 pm	**Closing Remarks & Meeting Adjourn**	Cloister Ballroom

THE AMERICAN ACADEMY OF NEUROLOGICAL SURGERY

2022 – 2023 OFFICERS

PRESIDENT
Fred G. Barker II, MD

PRESIDENT – ELECT
Shenandoah Robinson, MD

VICE PRESIDENT
Bob S Carter, MD, PhD

SECRETARY
E. Sander Connolly Jr., MD (2023)

TREASURER
Russell Lonser, MD (2025)

HISTORIAN
Michael Schulder, MD (2025)

PAST PRESIDENT
James M. Markert, MD, MPH

EXECUTIVE COMMITTEE

Fred G. Barker II, MD

Shenandoah Robinson, MD

James M. Markert, MD, MPH

Bob S Carter, MD, PhD

E. Sander Connolly Jr., MD

Russell Lonser, MD

Michael Schulder, MD

Sepideh Amin-Hanjani, MD (2024)

2022 – 2023 Committees

Academy Award Committee
Kendall Lee, MD, PhD – Chair (2023)
Michael Vogelbaum, MD, PhD (2024)
Praveen Mummaneni, MD (2025)

Auditing Committee
Gelareh Zadeh, MD, PhD – Chair (2023)
Gerald Grant, MD (2024)
Praveen Mummaneni, MD (2025)

Bylaws Committee
Linda Liau, MD, PhD – Chair
Fred G. Barker II, MD
Shenandoah Robinson, MD
James M. Markert, MD, MPH

Future Sites Committee
Aviva Abosch, MD, PhD (2023)

Membership Advisory Committee
Douglas Kondziolka, MD – Chair
James M. Markert, MD, MPH (ex officio)
Fred G. Barker II, MD (ex officio)
E. Sander Connolly Jr., MD (ex officio)
Shenandoah Robinson, MD (ex officio)
Nicholas Theodore, MD (2023)
Linda Liau, MD, PhD (2024)

Subcommittee on Corresponding Membership
Douglas Kondziolka, MD – Chair (2023)
Jacques Morcos, MD (2024)
Christopher Loftus, MD (2025)

Nominating Committee

James M. Markert, MD, MPH – Chair (ex officio)
Fred G. Barker II, MD (ex officio)
Shenandoah Robinson, MD (ex officio)

Scientific Program Committee

Jacques Morcos, MD – Chair (2023)
Daniel Resnick, MD (2024)
Zoher Ghogawala, MD (2025)
Gerald Grant, MD (2026)

Communications & Round Robin Committee

Quarterly Newsletter

Mark N. Hadley, MD
Gerald Grant, MD

Local Arrangements

Cargill Alleyne Jr., MD – Chair (2023)

CNS Joint Sponsorship Education Representative

Gerald Grant, MD – Chair

WFNS Delegates

Jacques Morcos, MD – Senior Delegate
Nelson Oyesiku, MD, PhD – Second Delegate

Research Advisory Committee

Gregory Zipfel, MD – Chair (2023)
Amy Heimberger, MD, PhD (2023)
Howard A. Riina, MD (2024)
Mark Johnson, MD, PhD (2025)
Sameer Sheth, MD, PhD (2026)

PAST-PRESIDENTS

Dean H. Echols	1938 - 39
Spence Braden	1940
Joseph P. Evans	1941
Francis Murphey	1942
Frank H. Mayfield	1943
A. Earl Walker	1944
Barnes Woodhall	1946
William S. Keith	1947
Howard A. Brown	1948
John Raaf	1949
E. Harry Botterell	1950
Wallace B. Hamby	1951
Henry G. Schwartz	1952
J. Lawrence Pool	1953
Rupert B. Raney	1954
David L. Reeves	1955
Stuart N. Rowe	1956
Arthur R. Elvidge	1957
Jess D. Herrmann	1958
Edwin B. Boldrey	1959
George S. Baker	1960
C. Hunter Shelden	1961 - 62
Samuel R. Snodgrass	1963
Theodore Rasmussen	1964
Edmund J. Morrissey	1965
George Maltby	1966
Guy L. Odom	1967
James G. Galbraith	1968
Robert H. Pudenz	1969 - 70
William B. Scoville	1971
Robert L. McLaurin	1972
Lyle A. French	1973
Benjamin B. Whitcomb	1974
John R. Green	1975
William H. Feindel	1976
William H. Sweet	1977
Arthur A. Ward	1978
Robert B. King	1979
Eben Alexander, Jr.	1980
Joseph Ransohoff II	1981
Byron C. Pevehouse	1982
Sidney Goldring	1983
Russel H. Patterson, Jr	1984
Thomas Langfitt	1985
Phanor L. Perot, Jr	1986
Shelley N. Chou	1987
James T. Robertson	1988
Thoralf M. Sundt, Jr.	1989
Robert Ojemann	1990
Nicholas Zervas	1991
Henry Garretson	1992
George Tindall	1993
William A. Buchheit	1994
David L. Kelly, Jr	1995
John M. Tew, Jr	1996
Julian T. Hoff	1997
Edward Connolly	1998
J. Charles Rich	1999
George A. Ojemann	2000
Roberto C. Heros	2001
Donald O. Quest	2002
David G. Piepgras	2003
Volker K.H. Sonntag	2004
Martin B. Camins	2005
L. Nelson Hopkins	2006
Richard Morawetz	2007
Robert F. Spetzler	2008
Ralph G. Dacey, Jr.	2009
Steven Giannotta	2010
Robert A. Solomon	2011
James T. Rutka	2012
Griffith R. Harsh	2013
Fredric B. Meyer	2014
Mitchel S. Berger	2015
Mark N. Hadley	2016
William T. Couldwell	2017
Daniel L. Barrow	2018
E. Antonio Chiocca	2019
M. Sean Grady	2020
Douglas Kondziolka	2021
James M. Markert	2022

PAST VICE-PRESIDENTS

Francis Murphey	1941
William S. Keith	1942
John Raaf	1943
Rupert B. Raney	1944
Arthur R. Elvidge	1946
F. Keith Bradford	1949
David L Reeves	1950
Henry G. Schwartz	1951
J. Lawrence Pool	1952
Rupert B. Raney	1953
David L. Reeves	1954
Stuart N. Rowe	1955
Jess D. Hermann	1956
George S. Baker	1957
Samuel R. Snodgrass	1958
C. Hunter Shelden	1959
Edmund Morrissey	1960
Donald F. Coburn	1961 - 62
Eben Alexander, Jr.	1963
George L Maltby	1964
Robert Pudenz	1965
Francis A. Echlin	1966
Benjamin Whitcomb	1967
Homer S. Swanson	1968
Augustus McCravey	1969 - 70
Edward W. Davis	1971
John R. Green	1972
George J. Hayes	1973
Richard L. DeSaussure	1974
Ernest W. Mack	1975
Frank E. Nulsen	1976
Robert S. Knighton	1977
Robert G. Fisher	1978
H Thomas Ballantine, Jr.	1979
George Ehni	1980
Courtland H. Davis, Jr.	1981
John F. Mullan	1982
Hugo V. Rizzoli	1983
James W Correll	1984
E. Bruce Hendrick	1985
Griffith R Harsh, III	1986
Ellis B Keener	1987
Robert Grossman	1988
Jim Story	1989
John Jane, Sr.	1990
Stewart Dunsker	1991
Burton M Onofrio	1992
Martin H Weiss	1993
John M. Tew, Jr.	1994
John C. VanGilder	1995
Edward Connolly	1996
George Ojemann	1997
Charles H. Tator	1998
Donald O. Quest	1999
Howard M. Eisenberg	2000
Richard B. Morawetz	2001
Martin B. Camins	2002
Arthur L. Day	2003
William F. Chandler	2004
Steven L. Gianotta	2005
Robert F. Spetzler	2006
Griffith R. Harsh IV	2007
Daniel L. Barrow	2008
M. Sean Grady	2009
Warren Selman	2010
Jeffrey Bruce	2011
James Drake	2012
Corey Raffel	2013
Alan R. Cohen	2014
Michael T. Lawton	2015
James M. Markert, Jr.	2016
Robert Harbaugh	2017
Nelson M. Oyesiku	2018
Mark Johnson	2019
Matthew Howard III	2020
Michael W. McDermott	2021
Daniel Yoshor	2022

PAST SECRETARY-TREASURERS

Francis Murphey	1938 - 1940
A. Earl Walker	1941 - 1943
Theodore C. Erickson	1944 - 1947
Wallace B. Hamby	1948 - 1950
Theodore B. Rasmussen	1951 - 1953
Eben Alexander	1954 - 1957
Robert L. McLaurin	1958 - 1962
Edward W. Davis	1963 - 1965
Robert G. Fisher	1966 - 1968
Byron C. Pevehouse	1969 - 1972

PAST SECRETARIES

Byron C. Pevehouse	1973
Russel H. Patterson, Jr	1974 - 1976
Phanor L. Perot, Jr	1977 - 1980
John T. Garner	1981 - 1983
James T. Robertson	1984 - 1986
Nicholas T. Zervas	1987 - 1989
William A. Buchheit	1990 - 1992
Julian T. Hoff	1992 - 1995
Roberto C. Heros	1995 - 1998
David G. Piepgras	1999 - 2001
L. Nelson Hopkins	2002 - 2004
Ralph G. Dacey, Jr	2005 - 2007
James Rutka	2008 - 2010
Mitchel S. Berger	2011 - 2013
Daniel L. Barrow	2014 - 2017
James M. Markert	2018 - 2020

PAST TREASURERS

Russel H. Patterson, Jr.	1973
Phanor L. Perot, Jr	1974 - 1976
John T. Garner	1977 - 1980
James T. Robertson	1981 - 1983
Nicholas T. Zervas	1984 - 1986
William A. Buchheit	1987 - 1989
Julian T. Hoff	1990 - 1992
Roberto C. Heros	1992 - 1995
David G. Piepgras	1996 - 1998
L. Nelson Hopkins	1999 - 2001
Ralph G. Dacey, Jr.	2002 - 2004
James T. Rutka	2005 - 2007
Griffith Harsh	2008 - 2010
Daniel L. Barrow	2011 - 2013
E. Antonio Chiocca	2014 - 2017
Douglas Kondziolka	2018 - 2019
Shenandoah Robinson	2020 - 2022

OLDFIELD AWARD

Russell Lonser	2018
Amy Heimberger	2019
Fred G. Barker II	2021
Todd Hollon	2022
Kim Burchiel	2023

MEETINGS OF THE ACADEMY

Hotel Netherland Plaza, Cincinnati, Ohio	October 28 - 29, 1938
Roosevelt Hotel, New Orleans, Louisiana	October 27 - 29, 1939
Tudor Arms Hotel, Cleveland, Ohio	October 21 - 22, 1940
Mark Hopkins Hotel, San Francisco, California	November 11 - 15, 1941
Ambassador Hotel, Los Angeles, California	November 11 - 15, 1941
The Palmer House, Chicago, Illinois	October 16 - 17, 1942
Hart Hotel, Battle Creek, Michigan	September 17 - 18, 1943
Ashford General Hospital, White Sulphur Springs, West Virginia	September 7 - 9, 1944
The Homestead, Hot Springs, Virginia	September 9 - 11, 1946
Broadmoor Hotel, Colorado Springs, Colorado	October 9 - 11, 1947
Windsor Hotel, Montreal, Canada	September 20 - 22, 1948
Benson Hotel, Portland, Oregon	October 25 - 27, 1949
Mayo Clinic, Rochester, Minnesota	September 28 - 30, 1950
Shamrock Hotel, Houston, Texas	October 4 - 6, 1951
Waldorf-Astoria Hotel, New York City, New York	September 29 - October 1, 1952
Biltmore Hotel, Santa Barbara, California	October 12 - 14, 1953
Broadmoor Hotel, Colorado Springs, Colorado	October 21 - 23, 1954
The Homestead, Hot Springs, Virginia	October 27 - 29, 1955
Camelback Inn, Phoenix, Arizona	November 8 - 10, 1956
The Cloister, Sea Island, Georgia	November 11 - 13, 1957
The Royal York Hotel, Toronto, Canada	November 6 - 8, 1958
Del Monte Lodge, Pebble Beach, California	October 18 - 21, 1959
Copley Sheraton Plaza, Boston, Massachusetts	October 5 - 8, 1960
Royal Orleans, New Orleans, Louisiana	November 7 - 10, 1962
El Mirador, Palm Springs, California	October 23 - 26, 1963
The Key Biscayne, Miami, Florida	November 11 - 14, 1964
Terrace Hilton Hotel, Cincinnati, Ohio	October 14 - 16, 1965
Fairmont Hotel & Towers, San Francisco, California	October 17 - 19, 1966

The Key Biscayne, Miami, Florida	November 8 - 11, 1967
Broadmoor Hotel, Colorado Springs, Colorado	October 6 - 8, 1968
St. Regis Hotel, New York City, New York	September 21, 1969
Camino Real, Mexico City, Mexico	November 18 - 21, 1970
Sahara-Tahoe Hotel, Stateline, Nevada	September 26 - 30, 1971
New College, Oxford, England	September 4 - 7, 1972
Huntington-Sheraton Hotel, Pasadena, California	November 14 - 17, 1973
Southampton Princess Hotel, Bermuda	November 6 - 9, 1974
The Wigwam (Litchfield Park), Phoenix, Arizona	November 5 - 8, 1975
Mills Hyatt House, Charleston, South Carolina	November 10 - 13, 1976
Mauna Kea Beach Hotel, Kamuela, Hawaii	November 2 - 5, 1977
Hotel Bayerischer Hof, Munich, Germany	October 22 - 25, 1978
Hyatt Regency, Memphis, Tennessee	November 7 - 10, 1979
Waldorf-Astoria Hotel, New York City, New York	October 1 - 4, 1980
Sheraton Plaza, Palm Springs, California	November 1 - 4, 1981
Ritz-Carlton Hotel, Boston, Massachusetts	October 10 - 13, 1982
The Lodge at Pebble Beach, California	October 23 - 26, 1983
The Homestead, Hot Springs, Virginia	October 17 - 20, 1984
The Lincoln Hotel Post Oak, Houston, Texas	October 27 - 30, 1985
The Cloister, Sea Island, Georgia	November 5 - 8, 1986
Hyatt Regency, San Antonio, Texas	October 7 - 10, 1987
Omni Netherland Plaza, Cincinnati, Ohio	September 13 - 17, 1988
Loews Ventana Canyon, Tucson, Arizona	September 27 - October 1, 1989
Amelia Island Plantation, Amelia Island, Florida	October 2 - 7, 1990
Salishan Lodge, Gleneden Beach, Oregon	September 22 - 26, 1991
Ritz-Carlton Hotel, Naples, Florida	October 21 - 25, 1992
The Wigwam, Phoenix, Arizona	October 27 - 30, 1993
The Cloister, Sea Island, Georgia	November 3 - 6, 1994
Loews Ventana Canyon Resort, Tucson, Arizona	November 1 - 5, 1995
The Greenbrier, White Sulphur Springs, West Virginia	September 18 - 22, 1996
Rimrock Resort, Banff, Alberta, Canada	September 10 - 14, 1997
Four Seasons Biltmore, Santa Barbara, California	November 4 - 7, 1998
Ritz-Carlton, Amelia Island, Florida	November 10 - 13, 1999

The Broadmoor, Colorado Springs, Colorado	October 11 - 14, 2000
The Breakers, Palm Beach, Florida	November 14 - 17, 2001
The Phoenician, Scottsdale, Arizona	October 16 - 19, 2002
Colonial Williamsburg, Williamsburg, Virginia	October 29 - November 1, 2003
Four Seasons Berlin & Hotel Taschenbergpalais, Dresden, Germany	October 3 - 8, 2004
Ritz-Carlton, Half Moon Bay, California	September 21 - 24, 2005
Ritz-Carlton, Reynolds Plantation, Greensboro, Georgia	October 18 - 21, 2006
Ritz-Carlton, Lake Las Vegas, Nevada	October 31 - November 3, 2007
Barrow Neurological Institute Phoenix Enchantment Resort, Sedona, Arizona	September 10 - 13, 2008
The Breakers, Palm Beach, Florida	November 4 - 7, 2009
The Inn at Spanish Bay, Pebble Beach, California	November 3 - 6, 2010
The Fairmont Scottsdale Princess, Scottsdale, Arizona	October 19 - 22, 2011
The Chatham Bars Inn, Chatham, Massachusetts	October 17 - 20, 2012
The Resort at Pelican Hill, Newport Coast, California	September 25 - 28, 2013
WaterColor Inn & Resort, Santa Rosa Beach, Florida	September 17 - 20, 2014
Hotel Europäischer Hof, Heidelberg, Germany	October 7 - 10, 2015
Four Seasons Resort, Jackson Hole, Wyoming	September 14 - 17, 2016
Four Seasons Santa Barbara, Santa Barbara, California	September 13 - 16, 2017
The Breakers, Palm Beach, Florida	October 24 - 27, 2018
Rome Cavalieri Waldorf Astoria, Rome, Italy	September 18 - 21, 2019
Virtual	September 26, 2020
The Inn at Spanish Bay, Pebble Beach, California	September 22 - 25, 2021
The Broadmoor, Colorado Springs, Colorado	September 28 - October 1, 2022

MISSION STATEMENT

The purpose of the Academy meeting shall be to promote scientific and social interaction among its members, to foster neurological surgery as a specialty of medicine, to encourage and sponsor basic and clinical research activity in the neurological sciences, and to promote the knowledge and skill of those who devote themselves to neurological surgery in accordance with the high ideals of the medical profession.

This activity will include live presentations from faculty to include case presentations and discussion, as well as time for questions and answers.

THE AMERICAN ACADEMY OF NEUROLOGICAL SURGERY

Congress of Neurological Surgeons

LEARNING OBJECTIVES

- Describe the implications of artificial intelligence (AI) in the development of neurosurgical technology and publications
- Discuss new developments of surgical and anatomical knowledge that will impact the future of brain mapping and surgery for brain tumors
- Identify opportunities for enhancing diversity and scientific exploration through the proper leveraging of social media
- Define the impact of novel neuroscience performed by neurosurgeons which leverages the unique access to the central nervous system

ACCREDITATION STATEMENT

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Congress of Neurological Surgeons (CNS) and the American Academy of Neurological Surgery. The CNS is accredited by the ACCME to provide continuing medical education for physicians.

DESIGNATION STATEMENT

The CNS designates this live activity for a maximum of 20.25 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Link for CME reporting will be sent to you via email following the meeting.

DISCLOSURE STATEMENT

Before the program, anyone in control of the educational content of this activity will disclose the existence of any financial interest and/or the relationship they or their significant other have with the manufacturer(s) of any commercial product(s) to be discussed during their presentation. Disclosures are included in the final program.

The Congress of Neurological Surgeons controls the content and production of this CME activity and attempts to assure the presentation of balanced, objective information. In accordance with the Standards for Integrity and Independence in Accredited Continuing Education established by the Accreditation Council for Continuing Medical Education (ACCME), speakers are asked to disclose all relationships they have with ineligible companies* over the previous 24 months which may be related to the content of their lecture. Speakers who have disclosed a relationship with an ineligible company whose products may have relevance to their presentation will be listed for viewing prior to the event.

A list of financial disclosures relevant to the meeting will be posted prior to the meeting on the meeting's web page and app.

INTENDED AUDIENCE/BACKGROUND REQUIREMENT

The scientific program presented is intended for neurosurgeons either in training or in active practice.

CNS JOINT PROVIDERSHIP DISCLAIMER STATEMENT

The material presented at the 85th Annual Meeting of the American Academy of Neurological Surgery has been made available by the American Academy of Neurological Surgery and the Congress of Neurological Surgeons (CNS) for educational purposes only. The material is not intended to represent the only, nor necessarily the best, method or procedure appropriate for the medical situations discussed, but rather it is intended to present an approach, view, statement, or opinion of the faculty, which may be helpful to others who face similar situations.

Neither the content (whether written or oral) of any course, seminar or other presentation in the program, nor the use of a specific product in conjunction therewith, nor the exhibition of any materials by any parties coincident with the program, should be construed as indicating endorsement or approval of the views

presented, the products used, or the materials exhibited by the American Academy of Neurological Surgery and jointly provided by the CNS, or its Committees, Commissions, or Affiliates.

Neither the CNS nor the American Academy of Neurological Surgery makes any statements, representations or warranties (whether written or oral) regarding the Food and Drug Administration (FDA) status of any product used or referred to in conjunction with any course, seminar or other presentation being made available as part of the 85th Annual Meeting of the American Academy of Neurological Surgery. Faculty members shall have sole responsibility to inform attendees of the FDA status of each product that is used in conjunction with any course, seminar or presentation and whether such use of the product is in compliance with FDA regulations.

DISCLOSURE INFORMATION

The CNS and the American Academy of Neurological Surgery control the content and production of this CME activity and attempt to ensure the presentation of balanced, objective information. In accordance with the Standards for Commercial Support established by the ACCME, faculty, abstract reviewers, paper presenters/authors, co-authors, planning committee members, staff and any others involved in planning the educational content and the significant others of those mentioned must disclose any relationships they or their co-authors have with commercial interests which may be related to their content. The ACCME defines "relevant financial relationships" as financial relationships in any amount occurring within the past 12 months that create a conflict of interest.

CNS DISCLOSURE POLICY

The Congress of Neurological Surgeons controls the content and production of this CME activity and attempts to assure the presentation of balanced, objective information. In accordance with the Standards for Integrity and Independence in Accredited Continuing Education established by the Accreditation Council for Continuing Medical Education (ACCME), speakers are asked to disclose all relationships they have with ineligible companies* over the previous 24 months which may be related to the content of their lecture. Speakers who have disclosed a relationship with an ineligible company whose products may have a relevance to their presentation are listed below.

Any planner, reviewer, or faculty member not on the disclosure list has reported they have nothing to disclose.

All relevant financial relationships listed for these individuals have been mitigated.

***Ineligible companies** are those whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients. An ineligible company is not eligible for ACCME accreditation or participation in Joint Providership.

DISCLOSURE LISTING – SPEAKERS, PLANNERS AND EXECUTIVE COMMITTEE MEMBERS

Relationship refers to receipt of royalties, consultantship, funding by research grant, receiving honoraria for educational services elsewhere, or any other relationship to a commercial interest that provides sufficient reason for disclosure.

Individual's Name	Name(s) of Ineligible Company	Nature of Relationship(s)
Chetan Bettegowda	Depuy-Synthes, Privo Technologies, Bionaut Labs, Haystack Oncology	Consulting Fee
Fady Charbel	transonic, inc.	Consulting Fee
Christopher Cifarelli	Carl Zeiss Meditech AG	Speakers Bureau
Benjamin Elder	Injectsense	Stock Options
Benjamin Elder	Stryker	Contracted Research
Benjamin Elder	SI Bone	Contracted Research, Royalty, Consulting Fee, Depuy Synthes
Andrew Grande	NeuExcell, Medtronic	Consulting Fee
Constantinos (Costas) Hadjipanayis	Hemerion Therapeutics, Synaptive Medical, Stryker corporation	Consulting Fee

Roger Härtl	3D Bio (Advisor), RealSpine (Advisor)	Fees for Non-CME/CE Servives
	Zimmer Biomet	Royalty
	Brainlab, DePuy Synthes	Consulting Fee
Todd Hollon	Invenio Imaging, Inc.	Future Stock Options
Peter Kan	Imperative Care, Stryker International	Consulting Fee
Albert Kim	Stryker	Contracted Research
	Monteris Medical	Consulting Fee
Frederick Lang	DNAtrix	Receipt of IP/Patent
Bradley Lega	Nia Therapeutics	Future Stock Options
Adel Malek	CereVasc Inc.	Own Stock, Consulting Fee
Praveen Mummaneni	Pacira, AO Spine (Fellowship grant), PCORI, SLIP II, ISSG	Contracted Research
	Spinicity/ISD	Own Stock
	SI Bone, Brainlab, BK Medical, BK Medical, Nuvasive, Stryker, Globus, Depuy Synthes	Consulting Fee
Gary Steinberg	Peter Lazic, US	Receipt of IP/Patent
	Surgical Theater, SanBio, Zeiss	Consulting Fee
Michael Steinmetz	Globus, Zimmer/Biomet	Royalty
	Premia Spine, Cerapedics, Globus	Consulting Fee
Viviane Tabar	BlueRock Therapeutics	Consulting Fee, Contracted Research
Corey Walker	Globus	Fees for Non-CME/CE Services
Gabriel Zada	Integra, Stryker	Consulting Fee

Those who have reported that they do not have any relationships with commercial interests:

Vijay Agarwal
Manish Aghi
David Baskin
Gavin Britz
Ketan Bulsara
Kim Burchiel
Edward Chang
Clark C Chen
E. Antonio Chiocca
Dean Chou
Robert Dempsey
Rose Du
Peter Fecci
Isabelle Germano
Alexandra Golby
Kunal Gupta
Sepideh Amin-Hanjani
Daniel Hoh
Randy Jensen
Shawn Hervey-Jumper
Kristopher Kahle
Douglas Kondziolka
Vibhor Krishna
Michael Lawton
Eric Leuthardt
David Limbrick
Russell Lonser
Jorge González-Martínez
Kai Miller
Christopher Ogilvy
Ian Parney
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Srinivas Chivukula, MD, PhD	Dallas, TX	Guest of the Academy
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Christopher Cifarelli, MD PhD	Morgantown, WV	Ali Rezai
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Charuta Furey, MD	Phoenix, AZ	Michael Lawton
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Spyridon Karadimas, MD, PhD	Miami, FL	Guest of the Academy

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WEDNESDAY, OCTOBER 4, 2023

REGISTRATION AND RECEPTION

THURSDAY, OCTOBER 5, 2023

7:30 – 7:35 WELCOMING REMARKS

Jacques Morcos, MD

7:35 – 7:45 Round Robin Roundup! The Academy Round Robin Letters, 1939-2023

Mark Hadley, MD

7:45 – 8:50 Peer Reviewed Abstract Session I: Cerebrovascular Basic Science
Moderators: E. Sander Connolly, Jr and Robert Friedlander

7:45 – 7:54 Translation of Human Umbilical Cord Blood-Derived Stem Cells to the Clinic for Treating Stroke

Andrew Grande, MD

Introduction
Human umbilical cord blood (hUCB) is a rich source of stem cells that can be used to treat various disorders and diseases. We isolated a CD34- population of stem cells from hUCB (nhUCBSCs) that exhibited neuroprotective properties in animal models of ischemic brain injury.
Objectives
We conducted IND-enabling studies to translate nhUCBSCs to the clinic, including toxicity, tumorigenicity, and therapeutic efficacy studies to meet the milestones for a Phase I Clinical Trial.
Methods
Karyotyping was conducted at different passages to assess chromosomal translocation, and telomerase activity was evaluated in nhUCBSCs. After rats were injected with nhUCBSCs, cellular biodistribution was assessed. Adverse events (seizures, respiratory distress, decreased weight, and death) were monitored. Serum cytokines were monitored to assess systemic inflammation. Presence of tumors in organs was evaluated. To test therapeutic efficacy, animals received a middle cerebral artery occlusion (MCAO), were administered nhUCBSC 48h later, and then tested on a battery of behavioral tests.

Results
There were no signs of toxicity after the administration of nhUCBSCs, including no adverse events and no secretion of inflammatory cytokines. nhUCBSCs migrated to organ systems at early time periods, localizing in the bone marrow and spleen after 2h, then disappearing by 48h. There was no evidence of tumorgenicity or chromosomal translocation in nhUCBSCs. Treatment with nhUCBSCs 48h after MCAO significantly improved behavioral outcomes 28d after ischemia.
Conclusion
Treatment with nhUCBSCs prevented the infiltration of immune cells into the brain, attenuated inflammation, preserved brain tissue, and improved behavioral outcomes.

7:54 – 8:03 Protein-based CRISPR/dCas9 Delivery System for Treating Ischemic Stroke

Rose Du, MD, PhD

Introduction
A high percentage of acute stroke patients do not undergo thrombolysis or thrombectomy due to the highly time-sensitive requirements and the lack of access to a stroke center. A major obstacle is the ability to deliver therapeutics when the area affected has limited perfusion.
Objectives
We proposed a system for intranasal administration of gene therapy for the treatment of ischemic stroke to overcome the limitations of current delivery systems in the presence of arterial occlusion.
Methods
We performed intranasal delivery of nanoparticles containing the protein-based CRISPR/dCas9 system to the brain in a mouse model of ischemic stroke to target SIRT1. The CRISPR/dCas9 system was encapsulated with calcium phosphate (CaP) nanoparticles to prevent them from being degraded. They were then conjugated with β-hydroxybutyrates (bHb) to target monocarboxylic acid transporter 1 in nasal epithelial cells to facilitate their transfer into the brain.
Results
The intranasal administration of the dCas9/CaP/PEI-PEG-bHb nanoparticles effectively upregulated the target gene (SIRT1) and protected the brain from secondary effects from ischemia after permanent middle cerebral artery occlusion.
Conclusion
This study demonstrates that the proposed protein-based CRISPR-dCas9 system targeting neuroprotective genes in general, and SIRT1 in particular, can be a potential novel therapy for acute ischemic stroke.

8:03 – 8:12 Circulating Biomarkers for Prediction and Prevention of Stroke in Native American Population

Robert Dempsey, MD

Introduction
Native Americans (NA) have a higher incidence of cerebrovascular stroke risk factors as compared to all other racial groups in the United States. Identifying biological protein markers can help us both identify at risk patients and reduce the stroke burden.
Objectives
The objectives of this research in NA is to identify circulating protein biomarkers for prevention of stroke in the NA population.
Methods

All participants underwent clinical health history and assessment. We carried out targeted proteomic profiling to identify circulating blood biomarkers in 113 participants. Linear regression modeling was used to identify differentially expressed protein biomarkers associated with these traditional risk factors.

Results

We found that many traditional risk factors including obesity, high blood pressure, diabetes, coronary heart disease, and smoking were common in Native American (NA). The mean age of participants was 66.5 years and about 81.4% of participants had atherosclerotic plaque present. Out of 58 potential inflammatory proteins, 26 of them showed significantly higher levels in NAs compared to the Caucasian population. Among NA, aging was associated with significant alterations in 20 inflammatory proteins. Higher Cholesterol levels were associated with 7 inflammatory markers. We identified correlation of fibrinogen, HGF, Leptin, adiponectin, Angiopoietin like-3 in participants with higher BMI, hypertension, and A1C. Females showed increased Angiopoeitin-3 and leptin. No biomarkers were associated with non-HDL and plaque presence.

Conclusion

Higher levels of vascular-inflammatory proteins are associated with traditional risk factors in NA. These are both biomarkers as well as potential stroke treatment targets in NA.

8:12 – 8:21 Cavernous angiomas and brain-gut-axis as a paradigm for the dysfunctional neurovascular unit

Sean Polster, MD

Introduction

A permissive gut microbiome was identified in patients who develop CAs, favoring lipid polysaccharide-producing bacterial species. Micro-ribonucleic acids (miRNAs) and plasma levels of proteins reflecting angiogenesis and inflammation were also previously correlated with CA with symptomatic hemorrhage (CASH).

Objectives

Linking the microbiome and circulating metabolome in human CA and CASH.

Methods

The plasma metabolome (53 discovery, 109 validation cohort) of CA patients was assessed using liquid-chromatography mass spectrometry. Differential metabolites were identified using partial least squares-discriminant analysis ($p < 0.05$, FDR corrected). Interactions between these metabolites and the previously established CA transcriptome, microbiome, and differential proteins were queried for mechanistic relevance. Differential metabolites in CASH patients were then validated in an independent, propensity-matched cohort. A machine learning-implemented, Bayesian approach was used to integrate circulating proteins, micro-RNAs, and metabolites in a diagnostic model for CASH.

Results

Plasma metabolites, including cholic acid and hypoxanthine, distinguished CA patients, while arachidonic and linoleic acids distinguished CASH cases. Plasma metabolites are linked to the genes of permissive microbiome bacteria. The metabolites distinguishing CASH were validated in an independent propensity-matched cohort, and their integration, along with levels of circulating miRNAs, enhance the performance of plasma protein biomarkers (up to 85% sensitivity and 80% specificity).

Conclusion

The microbiome and metabolome reflect CAs and their hemorrhagic activity. As a model of multiomic integration, we propose a framework for the brain-gut axis as it applies to the pathophysiology of the neurovascular unit and outline a roadmap for application in other diseases, including aging and radiation necrosis.

8:21 – 8:30	Localized conditional induction of brain AVMs in a mouse model of hereditary hemorrhagic telangiectasia

Michael Lawton, MD

Introduction

Longitudinal mouse models of brain arteriovenous malformations (AVMs) are crucial for developing novel therapeutics and pathobiological mechanism discovery underlying brain AVM progression and rupture. The sustainability of existing mouse models is limited by ubiquitous Cre activation, which is associated with lethal hemorrhages resulting from AVM formation in visceral organs.

Objectives

To overcome this condition, we developed a novel experimental mouse model of hereditary hemorrhagic telangiectasia (HHT) with CreER-mediated specific, localized induction of brain AVMs.

Methods

Hydroxytamoxifen (4-OHT) was stereotactically delivered into the striatum, parietal cortex, or cerebellum of R26CreER;Alk12f/2f (Alk1-iKO) littermates. Mice were evaluated for vascular malformations with latex dye perfusion and 3D time-of-flight magnetic resonance angiography (MRA). Immunofluorescence and Prussian blue staining were performed for vascular lesion characterization.

Results

Our model produced two types of brain vascular malformations, including nidal AVMs (88%, 38/43) and arteriovenous fistulas (12%, 5/43), with an overall frequency of 73% (43/59). By performing stereotaxic injection of 4-OHT targeting different brain regions, Alk1-iKO mice developed vascular malformations in the striatum (73%, 22/30), in the parietal cortex (76%, 13/17), and in the cerebellum (67%, 8/12). Identical application of the stereotaxic injection protocol in R26CreER;Alk12f/2f;mT/mG reporter mice validated localized Cre activity near the injection site. The 4-week mortality was 3% (2/61). Seven mice were studied longitudinally for a mean (SD; range) duration of 7.2 (3; 2.3-9.53) months and demonstrated nidal stability on sequential MRA. The brain AVMs displayed microhemorrhages and diffuse immune cell invasion.

Conclusion

We present the first HHT mouse model of brain AVMs that produces localized AVMs in the brain. The mouse lesions closely resemble the human lesions for complex nidal angioarchitecture, arteriovenous shunts, microhemorrhages, and inflammation. The model's longitudinal robustness is a powerful discovery resource to advance our pathomechanistic understanding of brain AVMs and identify novel therapeutic targets.

8:30 – 8:39	Subarachnoid Haemorrhage Leads to Desialilation of Hippocampal Glycocalyx Followed by Complement System Activation

Gavin Britz, MD

Introduction

Subarachnoid haemorrhage (SAH) – the accumulation of blood in the subarachnoid space - is the most fatal stroke, with a 40% mortality rate and 95% of survivors suffer permanent disabilities. Hippocampal neuroinflammation following SAH has been recognized as a potential cause of post-SAH syndrome, and the complement system, in particular, has been identified as a major player. Levels of C1q, the activating protein of the classical pathway of the complement system, has been found to be significantly higher in hippocampus (HPC) following SAH. However, mechanisms of C1q activation, the first step in complement cascade activation, remain unknown.

Objectives

Our earlier data demonstrated that SAH triggers hippocampal neuroinflammation, which involves microglia activation and release of sialidase "trimming" terminal glycocalyx sialic acid (SA) and exposing potential binding sites for C1qOur earlier data demonstrated that SAH triggers hippocampal neuroinflammation,

which involves microglia activation and release of sialidase "trimming" terminal glycocalyx sialic acid (SA) and exposing potential binding sites for C1q.

Methods

To test this hypothesis in perforation of the Willis circle model of SAH we employed immunohistochemical staining using various lectins to detect changes in sialylation and sialidase inhibitor (SI) treatment to explore changes in the hippocampal layers in SAH and Sham mouse brains.

Results

Levels of C1q increased significantly in the hippocampal molecular layer (ML) and stratum lacunosum moleculare (SLM) ($P<0.002$ and $P<0.03$, resp. n=6) following SAH (areas of perforant pathway termination). Calculation of C1q/SA immunostaining ratio showed an increase ($P<0.005$, n=3) ratio in SAH versus Sham animals suggesting increased C1q binding due to cleavage of SA. Cleavage of terminal SA was confirmed by increased exposure of β-Galactose and N-acetyl-galactosamine ($P<0.04$, n=3, $P<0.005$, n=3, resp.) after SAH. Intra ventricular administration of SI reversed hippocampal synaptic loss ($P<0.0004$, n=6). Slice treatment with exogenous SI resulted in ($P<0.02$, n=4) higher levels of SA in Sham than in SAH animals.

Conclusion

Our findings suggest that desialylated glycans form a substrate for C1q binding and its subsequent activation respective activation of innate complement system

8:39 – 8:50 Discussion

8:50 – 9:55 Peer Reviewed Abstract Session II: Epilepsy/Functional/Pain Basic Science
Moderators: Ashwin Viswanathan and Ashwini Sharan

8:50 – 8:59 Modulation of cholinergic circuits during human episodic memory

Bradley Lega, MD

Introduction

Cholinergic circuits modulate oscillatory and synaptic activity in the hippocampus to support episodic memory formation. These circuits exhibit selective and early degeneration in Alzheimer's Disease, however the neurophsyiological processes linked with cholinergic input in humans remains entirely unknown.

Objective

Characterize neurophysiological changes in the human hippocampus elicited by cholinergic blockade via iEEG recordings.

Methods

We used an innovative experiment in which we administered scopolamine or placebo to human patients as they performed an episodic memory task during the acquisition of intracranial EEG. We measured oscillatory and aperiodic differences resulting from cholinergic blockade.

Results

For the first time in humans, we show that choilnergic blockade elicits differential attenuation of hippocampal slow (2~5 Hz) vs fast (5~9 Hz) theta oscillations. Depression of power preferentially occurred in the slow theta band, while disruption of inter trial phase coherence occurred across the spectrum and was correlated with the magnitude of memory disruption. We used gene expression analysis to link these oscillatory effects with CHRM3 receptors expressed in the human MTL, connecting our data with mechanistic models developed in rodents.

Conclusion

Cholinergic innervation of the human hippocampus supports generation and synchronization of theta oscillations and provides evidence to support a nascent two theta model in humans. These findings suggest specific mechanisms by which cholinergic degeneration impacts episodic memory formation as well as the therapeutic impact of cholinesterase inhibitors. They point towards new strategies for neuromodulation.

8:59 – 9:08 Anti-inflammatory effects of vagus nerve stimulation in pediatric patients with epilepsy

Nathan Selden, MD, PhD

Introduction

Neural control of the immune system is critical to maintaining immune homeostasis. Disruption of immune homeostasis plays a role in the cause of several diseases, including cancer, multiple sclerosis, rheumatoid arthritis, and Alzheimer's. We studied the role of vagus nerve stimulation (VNS) in pediatric patients with medically refractory epilepsy on gene expression in peripheral blood mononuclear cells (PBMCs).

Objectives

VNS is widely used as an alternative treatment for drug-resistant epilepsy. In order to define a potential role for immune hemostasis in the treatment of epilepsy, we studied the impact that VNS treatment has on PBMCs isolated from a cohort of pediatric patients with medically refractory epilepsy.

Methods

Four patients each in the study and reference groups were balanced for age, gender, seizure type and frequency, and number of anti-epileptic medications. A comparison of whole genome-wide changes in RNA sequencing in peripheral blood monocyte cells was made between epilepsy patients chronically treated (for 3 to 6 years) versus not treated with VNS.

Results

The analysis showed downregulation of genes related to stress, inflammatory response, and immunity, suggesting an anti-inflammatory effect of vagus nerve stimulation in epilepsy patients. VNS also resulted in the downregulation of the insulin catabolic process, which may reduce circulating blood glucose in VNS-treated patients.

Conclusion

These findings suggest that direct vagus nerve stimulation may be a useful therapeutic alternative for the treatment of chronic inflammatory conditions. These results also provide an additional potential molecular explanation for the beneficial role of ketogenic diet, which also reduces blood glucose, in treating medically refractory epilepsy.

9:08 – 9:17 Canonical Wnt activator Chir99021 prevents epileptogenesis in a mouse model of temporal lobe epilepsy

Kunal Gupta, MD, PhD

Introduction

The dentate gyrus of the hippocampus undergoes pathological remodeling during temporal lobe epilepsy. The pathways responsible are unknown and may represent novel targets to prevent epileptogenesis.

Objectives

In previous work we demonstrated that Canonical Wnt antagonism exacerbated pro-epileptogenic remodeling. We therefore hypothesize that Wnt agonism may be protective.

Methods

Focal temporal lobe epilepsy was induced by unilateral CA3-hippocampal kainate (KA) injection in 6-8wk-old C57BL/6J and POMC-eGFP transgenic mice. Animals received intraperitoneal vehicle or Wnt agonist Chir99021 (12.5mg/kg) daily. Mice were implanted with bilateral intrahippocampal recording wires and

electrocorticography recorded continuously for 21-days. POMC-GFP+ immature dentate granule cells were characterized by confocal microscopy 14-days after KA. Bilateral dorsal dentate gyri were collected after 3, 7 and 14-days for RNA sequencing. N=4-6/group.

Results

The canonical Wnt pathway was transcriptionally dysregulated in the epileptic dentate gyrus, in both the ipsilateral epileptogenic zone (EZ) and in the contralateral seizure network (SN), as early as 3-days after KA injection. Systemic Wnt agonist treatment significantly reduced electrographic seizure frequency and duration 14 and 21-days after KA ($p<0.01$), and restored dendrite arbor length and proximal dendrite orientation of immature dentate granule cells in epileptic animals, suggesting that Wnt activation may prevent pro-epileptogenic neuronal remodeling in the hippocampus. No effect was noted on granule cell dispersion extent or rate of neurogenesis in epileptic or control animals.

Conclusion

The pathogenesis of TLE is characterized by remodeling of the hippocampal dentate gyrus. The Wnt pathway may play a role in pathological remodeling of the dentate gyrus and represents a potential therapeutic target in epileptogenesis.

9:17 – 9:26 Strengthening Motor Output with Motor Thalamus Stimulation. Evidence for a novel neuromodulation modality for stroke

Jorge González-Martínez, MD, PhD

Introduction

Stroke patients often experience motor deficits in the limbs. Although physiotherapy is used to rehabilitate lost functions, most patients do not recover to a satisfactory level. Deep brain stimulation (DBS) can target intrinsic pathways that project to vital cortical areas. One structure of interest is the ventro-oralis posterior (VOP)/ventro-intermedium (VIM) nucleus of the motor thalamus. The VOP/VIM is a thalamic relay with outgoing excitatory connectivity to the motor cortex (M1), and, thus, could be a potential target for DBS to facilitate motor function after stroke.

Objectives

The objective is to test the hypothesis that VOP/VIM stimulation can increase the excitability of primary motor cortex (M1) and augment hand motor output and control.

Methods

In acute experiments in non-human primates (NHP), we implanted DBS electrodes into the VOP/VIM the internal capsule (IC) and intracortical microelectrode arrays over M1.We replicated this setup in human patients undergoing implantation of DBS electrodes targeting the VOP/VIM for ET with the addition of macroarrays placed over M1. Intraoperatively, we paired direct cortical stimulation (DCS) with VOP/VIM stimulation. In chronic human experiments, when patients returned for DBS programming, quantitative measures of upper limb force related tasks were analyzed in on and off DBS scenarios

Results

In the NHPs, we observed increased amplitude of evoked local field potentials (LFP) and single unit spike counts recorded in M1 with VOP/VIM stimulation. We found that IC stimulation with VOP/VIM stimulation increased the amplitude of motor evoked potentials (MEP) and kinematics of hand muscles. In the intraoperative human studies, with VOP/VIM stimulation, we observed similar amplification in M1 LFPs and MEPs recorded in the hand motor representation. Furthermore, during the force modulation tasks in the chronic experiments, we observed a reduction in the root-means-squared error when stimulation was on, in comparison with off stimulation.

Conclusion

There is evidence that direct electrical stimulation of the motor thalamus augment motor output in the upper limb segment, both in non-human and human primates. We hope to use these outcomes to implement DBS of motor thalamus as a potential therapeutic approach to treat post-stroke motor deficits.

9:26 – 9:35 A Motor Association Area in the Depths of the Central Sulcus

Kai Miller, MD, PhD

Introduction

Cells in the precentral gyrus (PCG) of the human brain send signals to the periphery to generate movement and are thought to be organized as a continuous yet overlapping map of the body. This has been electrophysiologically established through stimulation and recording of the brain surface1,2. We explored this organization in sulcal depths of the PCG using stereoelectroencephalography (sEEG).

Objectives

We sought to establish, electrophysiologically, that somatotopic representation of individual body parts extends from the cortical convexity into the sulcal depths of the PCG.

Methods

sEEG leads were implanted in 13 patients with drug resistant epilepsy to characterize seizures. Subjects performed a simple block-designed task of randomly interleaved foot, hand, or tongue movements with rest in between while electromyography (EMG) was recorded to identify movement. As broadband power is shown to be a general correlate of neural population firing rate3, variation in broadband power (65-115Hz) in each sEEG channel between EMG-defined movement and rest periods allowed for identification of movement-correlated cortex.

Results

Broadband changes show somatotopic extension of individual body parts from the cortical convexity into the sulcal depths following the canonical motor homunculus1. Surprisingly, in the depths of the central sulcus, at its mid-lateral aspect, the somatotopology of the homunculus was interrupted by a region active during each movement type, calling into question the uninterrupted motor homunculus described nearly a century ago1.

Conclusion

The motor homunculus is interrupted by an association area in the depths of the central sulcus at its mid-lateral aspect that is active during movement of distant body parts. DOI to our Manuscript: https://doi.org/10.1038/s41593-023-01346-z

9:35 – 9:44 Focused Ultrasound BBB Opening with Anti -Amyloid Antibody Accelerates Plaque Reduction in Alzheimers Disease

Ali Rezai, MD

Introduction

Anti-β-amyloid monoclonal antibodies are new class of FDA-approved treatments for Alzheimer's disease (AD) that reduce β-amyloid plaques and disease progression. However, this therapy requires long-term treatment of >18 months of monthly or bimonthly infusion, frequent and higher dosing, and associated side-effects such as amyloid related imaging abnormality (ARIA). The blood-brain barrier (BBB) is a significant challenge limiting antibody delivery to brain. Focused ultrasound (FUS) has been shown to non-invasively, safely, and reversibly open the BBB. We initiated a study combining aducanumab anti-β-amyloid antibody infusion with FUS-mediated BBB opening (BBBO) in AD.

Objectives

In this first in human proof-of-concept study, we evaluated the safety, feasibility, and effects of combining aducanumab anti-β-amyloid antibody with FUS-mediated BBB opening (BBBO) in AD.

Methods

Participants with AD underwent monthly Anti-β-amyloid monoclonal (aducanumab) infusion for six months followed by MRI-guided focused ultrasound (Insightec) BBBO in brain regions with high density of β-amyloid plaques. Participants were evaluated with serial neurological, cognitive, and imaging assessments as well as 18F-Florobetaben β-amyloid PET scans.

Results

Two males (ages 77 and 60 years) and one female (age 64) completed 6-cycles of monthly aducanumab infusions combined with FUS-BBBO. FUS-BBBO targeted the hippocampus, frontal, parietal, and temporal lobes with high β-amyloid plaque burden. All FUS procedures were tolerated well with immediate BBBO demonstrated by focal parenchymal gadolinium contrast enhancement followed by BBB closure within 24-48 hours. There were no serious neurological, cognitive, or imaging adverse events. PET scans revealed a rapidly progressive and significant ($p < 0.005$) decrease in β-amyloid levels in regions of FUS-BBBO as compared to non-FUS treated contralateral homologous regions. There was an accelerated reduction of 48%, 49%, and 52% respectively.

Conclusion

This first in human proof-of-concept study demonstrates that FUS-BBB opening can be safely combined with aducanumab infusions with accelerated and greater reduction in β-amyloid. This novel combined targeted therapeutic strategy has the potential to enhance delivery and impact of therapeutics in AD and other neurological disorders. Additional studies with larger number of patients are needed.

9:44 – 9:55 Discussion

9:55 – 10:10 Break

10:10 – 10:40 Special Debate Session I: The Artificial Intelligence revolution in Medicine and Neurosurgery - Blessing or Curse?
Moderators: Fred Barker and Praveen Mummaneni

10:10 – 10:11 Introduction

Fred Barker, MD and Praveen Mummaneni, MD

10:11 – 10:20 It's a blessing

Douglas Kondziolka, MD

10:20 – 10:29 It's a curse

Richard Byrne, MD

10:29 – 10:40 Discussion

10:40 – 11:45 Peer Reviewed Abstract Session III: Cerebrovascular Clinical Science
Moderators: Jacques Morcos and William Couldwell

10:40 – 10:49 Treatment of small intracranial aneurysms using the SMALLSS scoring system: A system for decision making and outcomes

Christopher Ogilvy, MD

Introduction
Treatment of intracranial aneurysms less than 7mm has evolved with the advances in both endovascular and microsurgery. Data has shown there are several patient and aneurysm specific risk factors that influence decision making for small aneurysms beyond aneurysm size.
Objectives
We aimed to create a scoring system to guide treatment decision making and to evaluate clinical outcomes in patients with small aneurysms who were treated with both endovascular and microsurgical procedures.
Methods
We performed a single center retrospective analysis of data collected prospectively for patients treated between the years 2014- 2021. Patients were offered surgical or endovascular treatment with the goal of lowest risk and highest efficacy by the treating neurovascular team. The system of evaluation of SMALLSS included Size, (4-7 mm - 1 point, < 3.9 mm - 0 points), Multiple aneurysms (yes - 1 point, no - 0 points), Autosomal dominant polycystic kidney disease (yes - 1 point, no - 0 points), Lineage- family history of aneurysm (yes - 1 point, no - 0 points), Lifetime risk (age <65 - 1 point, age >65 - 0 points), Smoking history (yes - 1 point, no - 0 points), Shape (irregular-1 point, smooth-0 points). Statistical analysis was then performed to calculate the percentage of aneurysms with each SMALLSS score and clinical outcomes of each group.
Results
A total of 1152 unruptured intracranial aneurysms were treated over the study interval, of which 771 aneurysms (66.9%) were under 7 mm (220, 28.5% <3.9 mm; 551, 71.5% 4-7 mm). Of these patients with small lesions, 45 (5.84%) had SMALLSS scores of 5, 155 (20.1%) had SMALLSS scores of 4, 269 (34.89%) score of 3, 224 (29.05%) score of 2 and 73 (9.47%) score of 1. Only 5 (0.65%) had a score of zero. During this same interval, an estimated 1126 patients with aneurysms <7mm were evaluated and not offered treatment, with the majority having SMALLSS scores of 2 and under (841, 74.7%). Serious neurologic complications occurred in 18 out of 771 aneurysms (2.33%) of which 4 were hemorrhagic and 14 were ischemic. These complications resulted in mRS outcomes of 0-2 in 15 patients and mRS 3-5 in 3 patients with 1 death related to remote hemorrhage after flow diversion.
Conclusion
The SMALLSS scoring system can be used to help guide treatment decision making with regard to aneurysm and patient specific factors while balancing the natural history of small intracranial aneurysms.

10:49 – 10:58 3 Year outcome results of the prospective international giant intracranial aneurysm registry

Peter Vajkoczy, MD

Introduction
Giant intracranial aneurysms (GIA) are a rare condition representing a small fraction of intracranial aneurysms. So far, little is known about the natural history and optimal treatment strategies. Therefore, current decision-making on when and how to treat is mainly based on expert opinions.

Objectives
To better understand the current treatment philosophies and study the outcomes of conservative, surgical, and endovascular therapies we have initiated the International Giant Aneurysm Registry 16 years ago. Here, we present the results of the 3-year follow up for unruptured GIAs
Methods
In this prospective part of an international observational registry study, we investigated the treatment outcomes for patients with an unruptured GIA who received conservative management (CM), surgical management (SM), or endovascular management (EM).
Results
Between 2008 and 2018, we have prospectively included 418 patients with Giant Aneuyrsms (>25mm diameter). 36 centers participated in the study world-wide. 296 patients presented with unruptured GIAs and are subject of this report. 79 (22.8%) of the patients were treated conservatively, 149 (43.1%) by endovascular, and 118 (34.1%) by surgical means, reflecting the current international treatment philosophies. The mean age was 59.1±14.7 years. Mean age was highest in the CM group (66.6±13.5 years), followed by the EM group with 59.8±12,6 years, and finally, the SM group with 53.3±15.8 years ($p<0.001$). In the CM group, the mortality rate after one year was 28% and increased to 42% after three years, resembling the malignant natural course of untreated GIAs. EM resulted in a mortality rate of 13% after one year and 19% after three years. SM resulted in a mortality rate of 2% after one year and 5% after three years ($p<0.001$ vs CM and EM). When analysed by locations, we subgrouped the aneurysms into 'ICA' and 'non-ICA' locations. 3Y Mortality rates for GIAs along the ICA were 25%, 10%, and 10% for CM, EM, and SM, respectively. In contrast, 3Y mortality rates for non-ICA GIAs were 52%, 42%, and 7% for CM, EM, and SM, respectively. After three years of follow-up, 25% of the patients in the EM group experienced retreatment of the index aneurysm, whereas, in the SM group, only 6 (5%) of the patients required retreatment ($p<0.001$).
Conclusion
The three-year follow-up results of the giant intracranial aneurysm registry emphasize the need to treat giant intracranial aneurysms because of their unfavorable natural history. Both endovascular and surgical treatment can positively affect their natural course. Surgical management appears to be superior to endovascular management in terms of mortality and re-treatment rates.

10:58 – 11:07 Long-term Patency in Extracranial-Intracranial Bypass Across Disease Etiology

Fady Charbel, MD

Introduction
Extracranial-intracranial (EC-IC) bypass has been well described in chronic vaso-occlusive cerebrovascular diseases, including both Moyamoya disease (MMD) and atherosclerotic disease (AD).
Objectives
This study aims to compare factors associated with bypass occlusion between these two diseases.
Methods
An institutional database of 357 patients with intracranial bypass procedures between 08/2001-05/2022 was retrospectively reviewed. Patients with MMD and AD were selected for study. Baseline characteristics, surgical technique, and flow-related measurements were compared in relation to the outcome of bypass occlusion.
Results
A total of 232 patients met inclusion criteria (AD n=108; MMD n=124). Average age and sex significantly differed between groups (AD 57.2 years, 56.5% male; MMD 36.6 years, 31.5% male, $p<0.001$). mRS at surgery and at follow-up were higher in the AD group, $p=0.004$ and <0.001, showing a slightly worse baseline functional status. Patients with AD also were more likely to require an interpositional graft, $p<0.001$. At 1-week follow-up, in patients with imaging available, higher rates of occlusion were seen in AD (13/33, 39.4%) compared to MMD (9/52, 17.3%), $p=0.023$. However, at last follow-up, rates of occlusion did not differ

between AD and MMD groups (25.2% vs. 25.4%, respectively); in patients with more than 1 year follow-up and more than 2 year follow-up, MMD tended to have higher rates of occlusion (31.2% vs. 26.1%, p=0.558, and 26.4% vs. 20.7%, p=0.564). Flow measurements did not differ between AD and MMD, but in subgroup analyses of patients with AD and with MMD, both bypass flow and cut flow index predicted occlusion in both groups.

Conclusion

Despite different etiologies for bypass, rates of occlusion at last follow-up did not vary between groups, although short-term follow-up would suggest earlier bypass failure in AD and extended follow-up trended toward higher occlusion rates in MMD. The bypass flow and cut flow index at the time of surgery predicted occlusion in both AD and in MMD. Importantly, the relatively significant occlusion rates in MMD may lend further support to a single vessel bypass, rather than more extensive surgery, thus saving the other branch for later rescue if needed.

11:07 – 11:16 Low Flow as a Stroke Risk Biomarker in Symptomatic Intracranial Atherosclerotic Stenosis

Sepideh Amin-Hanjani, MD

Introduction

Intracranial atherosclerotic stenosis (ICAS) is a major source of stroke world-wide, with high recurrence risk. Prior evaluation of posterior circulation ICAS from prospective studies has revealed regional hypoperfusion, assessed by large vessel flow measurements using quantitative MRA (QMRA), predicts subsequent vertebrobasilar stroke risk.

Objectives

We examined whether regional flow assessment similarly predicted stroke risk in anterior circulation ICAS in the prospective MYRIAD study.

Methods

MYRIAD enrolled patients with symptomatic 50-99% ICAS; primary outcome was ischemic stroke within one year. Flow was measured in the major intracranial arteries at baseline using QMRA. Patients were designated as low or normal flow based on an algorithm assessing distal flow and collateral capacity using age-normalized MCA and hemispheric (aggregate of ACA, MCA and PCA) flows.

Results

Of 73 subjects with anterior circulation ICAS, 7 (9.6%) patients had recurrent stroke. Z score thresholds for age-normalized flow ranging from -0.5 to -1.5 were examined, and identified the optimal threshold of -1 for the MCA and -0.75 for hemispheric flow. 24 (33%) of patients were categorized as low flow; recurrent stroke occurred in 21% of low flow vs 4% of normal flow patients (OR 6.2 (95% CI 1.1-34.7, p=0.04)). In the full MYRIAD cohort of 99 anterior and posterior circulation ICAS patients, low flow status had an age-adjusted OR of 3.8 (95% CI 1.02-14.2) for recurrent stroke.

Conclusion

Distal flow status assessed through QMRA regional flow measurement is predictive of recurrent stroke in both anterior and posterior circulation ICAS. Identification of high-risk patients has implications for future investigation of therapeutic interventions.

11:16 – 11:25 Factors predicting aggressive natural history in cranial dural arteriovenous fistulas: a CONDOR study

Gregory Zipfel, MD

Introduction

The natural history of cranial dural arteriovenous fistulas (dAVF's) has been previously studied only in single-center studies of limited size.

Objectives

Analyze retrospective data from 1076 patients in the CONDOR international consortium to determine the key risk factors associated with aggressive natural history of dAVF's.

Methods

Multiple imputation was performed to limit bias from missing values. The primary outcome was time to new or worsening hemorrhage or non-hemorrhagic neurologic deficits (NHND). A competing risk analysis was performed as patients were censored for treatment or loss to follow-up. Covariates significant at an alpha of 0.05 in univariate analysis were selected in a stepwise manner to build a multivariate Fine-Gray subdistribution hazard model in each imputed data set. Covariates present in the model of a majority of imputed data sets were used in the final model, which incorporated both hypothesized covariates and covariates from the exploratory phase of this study.

Results

On univariate analysis, the following covariates were associated with more aggressive natural history: cortical venous drainage (CVD), venous ectasia, aggressive presentation, NHND, and focal neurologic deficits. On the final model, the following covariates were associated with more aggressive natural history: CVD, focal neurologic deficits, drainage to the vein of Galen or straight sinus, and extradural arterial feeders not arising from the external carotid artery (ECA).

Conclusion

Our results show that in dAVF patients, CVD, focal neurologic deficits at presentation, drainage to the vein of Galen or straight sinus, and presence of non-ECA extradural arterial feeders were the strongest independent risk factors for shorter time to development of new or worsening hemorrhage or NHND.

11:25 – 11:34 Outcomes of 279 Brainstem Cavernous Malformation Resections, with and without use of CO2 Laser

Gary Steinberg, MD, PhD

Introduction

Resection of brainstem cavernous malformations is challenging and poses significant risks.

Objectives

To provide short and long-term outcomes of surgically treated brainstem cavernous malformations, and evaluate if there is a difference in outcomes using a CO2 laser.

Methods

The electronic and paper charts of all the patients who underwent resection of the brainstem cavernous malformations between 1990-2023 by a single surgeon was reviewed. Short and long-term follow up was assessed through chart review and telephone follow up as needed. A total of 279 brainstem cavernous malformation resections were reviewed, with regard to use of the CO2 laser, surgical approach, lesion characteristics, and patient outcomes.

Results

279 surgeries in 256 patients were recorded, with mean follow up of 56.2 mos. 127/279 surgeries were performed with use of a CO2 laser. 115/279 (41%) had immediate perioperative worsening of their neurologic status, but 224/276 (81%) demonstrated the same or improved mRS compared with preoperative status at their delayed postoperative follow-up. The use of the CO2 laser was significantly correlated with improvement in long term follow up mRS when compared to conventional microsurgery (Laser: Pre-Op mRS 1.92, Follow-up mRS 1.68; Conventional: Pre-Op mRS 1.95, Follow-up mRS 2.06, p= 0.02).

Conclusion

The use of the CO2 laser for resecting brainstem cavernous malformations was significantly correlated with better long-term improvement in mRS when compared to conventional surgery. It should be considered for resecting cavernous malformations in brainstem, as well as other eloquent areas.

11:34 – 11:45 Discussion

11:45 – 12:40 Peer Reviewed Abstract Session IV: Tumor Clinical Science
Moderators: Mitchel Berger and Linda Liau

11:45 – 11:54 Oncolytic clinical trial links immunoactivation to survival in glioblastoma

E. Antonio Chiocca, MD, PhD

Introduction
Treatment failures of immunotherapy are largely due to the highly suppressive tumor microenvironment characterizing aggressive forms of cancer, such as recurrent glioblastoma (rGBM).
Objectives
We sought to determine if oncolytic virus-based immunotherapy will change the immunosuppressive microenvironment of rGBM into one that is more immuno-active.
Methods
Here, we report the results of a "first-in-human" phase 1 trial in 41 subjects with rGBM, injected with CAN-3110, an oncolytic herpes virus (oHSV). Unlike other clinically approved oHSVs, CAN-3110 retains the viral neurovirulence ICP34.5 gene transcribed by a Nestin promoter, a protein over-expressed in GBM and other invasive tumors, but not in adult brain or healthy differentiated tissue. These modifications confer preferential replication of CAN-3110 in tumors.
Results
No dose-limiting toxicities were encountered. Surprisingly, positive HSV1 serology was significantly associated with both improved survival and clearance of CAN-3110 from injected tumors. Survival after treatment, particularly in HSV1 seropositive subjects, significantly associated with a-changes in tumor/PBMC T cell counts and clonal diversity, b- peripheral expansion/contraction of specific T cell clonotypes, and c- tumor transcriptomic signatures of immune activation.
Conclusion
In summary, CAN-3110 induced changes in tumor/peripheral immune metrics that were associated with post-treatment survival in this immunologically "cold" cancer. These data provide human validation that intralesional oHSV treatment enhances anticancer immune responses even in immunosuppressive tumor microenvironments, particularly in subjects with cognate serology to the injected virus. This provides a biologic rationale for use of this oncolytic modality in cancers that are otherwise unresponsive to immunotherapy (clinicaltrials.gov NCT03152318).

11:54 – 12:03 Predicting Survival in Glioblastoma Multiforme with Multimodal Neuroimaging

Eric Leuthardt, MD

Introduction

Glioblastoma multiforme (GBM) is the most common and deadly malignant glioma of the central nervous system, with an overall median survival of 14 months. The ability to predict survival before treatment in GBM patients could lead to improved disease management and patient care.

Objectives

The objective of this study was to develop a predictive model using multimodal neuroimaging data to accurately classify survival outcomes in patients with glioblastoma multiforme (GBM) without considering presentation symptoms, postsurgical outcomes, or genetic variants, aiming to enhance surgical decision making at the time of diagnosis.

Methods

GBM patients (N=133, mean age 60.8 years, median survival 14.1 months, 57.9% male) were retrospectively recruited from the neurosurgery brain tumor service at Washington University Medical Center. All patients completed structural neuroimaging and resting state functional MRI (RS-fMRI) before surgery. Demographics, measures of cortical thickness (CT), and resting state functional network connectivity (FC) were used to train a deep neural network to classify patients based on survival (<1y, 1-2y, >2y). Permutation feature importance identified the strongest predictors of survival based on the trained models.

Results

The models achieved a combined cross-validation and hold out accuracy of 90.6% in classifying survival (<1y, 1-2y, >2y). The strongest demographic predictors were age at diagnosis and gender. The strongest CT predictors included the superior temporal sulcus, parahippocampal gyrus, peri calcarine, pars triangularis, and middle temporal regions. The strongest FC features primarily involved dorsal and inferior somatomotor, visual, and cingulo-opercular networks.

Conclusion

The current work demonstrates the ability of machine learning to accurately classify survival in GBM patients based on multimodal neuroimaging at the very earliest time of imaging diagnmosis. These results were achieved without information regarding presentation symptoms, postsurgical outcomes, or genetic variants. Our results suggest GBMs have a global effect on both the structural and functional organization of the brain, which is predictive of survival.

12:03 – 12:12 Safety and interim survival data after sonodynamic therapy in pet French Bulldogs with sporadic high grade gliomas

Vijay Agarwal, MD

Introduction

High grade gliomas remain one of the most challenging entities to treat in the field of oncology, and improvement into overall survival remains elusive. One reason is that due to the highly invasive nature, complex in situ behavior, and significant heterogeneity of high grade gliomas, no animal model to date has been able to accurately test emerging therapeutics. However, naturally occurring gliomas in pet dogs accurately mimic tumors in the human counterpart, from a histopathological, radiological, and poor clinical survival standpoint. Survival in dogs with sporadic high grade gliomas is shorter than in humans. In addition, French Bulldogs with sporadic gliomas in particular have been found to have significantly shorter overall survival, allowing for quicker evaluation of potential treatments.

Objectives

Sonodynamic therapy (SDT) has shown promise in both pre-clinical and clinical settings for high grade gliomas. The non-invasive and easily repeatable nature make it well-suited to a clinical trial in pet dogs as no headframe, general anesthesia, or image guidance is needed for treatment. In this study, pet French Bulldogs with sporadic high grade gliomas were treated using low intensity diffuse ultrasound (LIDU) in combination with oral 5-ALA to assess both safety and interim survival.

Methods

The study is a Phase 1 canine safety trial of sonodynamic therapy, delivered via low intensity, diffuse ultrasound, in combination with oral 5-ALA for the treatment of sporadic high grade glioma in pet French Bulldogs. One treatment was conducted prior to safe maximal resection, followed by monthly treatments thereafter. Primary outcome was safety. Secondary outcomes included quantification of histopathological markers of efficacy (CC3, Iba1), PpIX accumulation in tumor cells via fluorescence spectroscopy, as well as overall survival.

Results

To date, 6 pet French Bulldogs have been enrolled with a total of 38 overall treatments completed. No complications or toxicities were noted at any point during the study. Regular MRI scans, including those obtained per trial requirement before the second SDT treatment commenced, did not show evidence of any damage or imaging abnormalities in normal brain structures. Histopathologic analysis confirmed significantly increased levels of CC3 and Iba1 in treated specimens, indicating treatment effect and potentiation of the immune system. Histopathologic results analyzed by a blinded, third-party academic institution confirmed the results. PpIX was noted to accumulate in the brain tumor histopathologic samples versus the normal brain samples. Durable imaging responses, as well as significantly increased survival, were noted in the trial participants. Median overall survival was found to be 192 days, with two participants still alive and tumor free on last MRI imaging (5/26/23, 5/31/23). This is in comparison to a median overall survival of 48 days found in breed matched controls at the same veterinary center. The current longest survival is 412 days with no evidence of tumor recurrence on MRI imaging (still enrolled and receiving treatments).

Conclusion

Although the results for this study are preliminary, they support the safety of 5-ALA-mediated SDT treatment in canines with sporadic high grade glioma. Interim analysis shows a significantly greater overall survival in French Bulldogs versus breed matched controls from the same academic veterinary center. A multi-center, First-In-Human clinical trial in recurrent high grade glioma utilizing the same technology is currently enrolling, and the data will be compared to further validate the use of canine trials for emerging therapeutics for high grade glioma.

12:12 – 12:21 Fast intraoperative detection of glioma infiltration using label-free optical microscopy and deep neural networks

Todd Hollon, MD

Introduction

Fast and accurate detection of tumor infiltration is a central challenge in the comprehensive management of diffuse glioma patients. Despite our best real-time tumor detection strategies, such as intraoperative MRI and fluorescence-guided surgery, dense and safely resectable tumor infiltration remains at the surgical margin in over 85% of diffuse glioma patients.

Objectives

Here, we present FastGlioma, an artificial intelligence (AI)-based intraoperative diagnostic system for fast (<10 seconds) detection of diffuse glioma infiltration at microscopic resolution without the need for tumor-specific markers.

Methods

FastGlioma is trained using large-scale self-supervised deep learning on stimulated Raman histology (SRH), a rapid, label-free, optical microscopy technique, and a GPT-style whole slide SRH tumor infiltration scoring method (i.e. SRH images in, tumor score out). We pushed the performance limits of FastGlioma by investigating the trade-off between imaging speed versus accuracy for microscopic tumor detection.

Results

In a large prospective external testing cohort of diffuse glioma patients (180 patients, 935 surgical margin specimens) who underwent intraoperative SRH imaging, we demonstrate that FastGlioma was able to detect

and quantify microscopic tumor infiltration with an average AUROC of 94.1 +/- 0.2%, performing on par with three expert neuropathologists on the same task. FastGlioma is over 10X faster than previous SRH-based methods and 100X faster than conventional H&E histology. Finally, we demonstrate that FastGlioma was > 20% more accurate at detecting dense tumor infiltration when compared to radiologic features or 5-ALA fluorescence (98.0% versus 77.8% accuracy) for both IDH-mutant gliomas and IDH-wildtype glioblastomas.
Conclusion
Our results demonstrate how optical imaging and deep neural networks can achieve fast and accurate intraoperative tumor detection, unlocking the role of AI in improving the surgical management of brain tumor patients.

12:21 – 12:30 Oncomagnetic Therapy-A Revolutionary Non-Invasive Mitochondrial Based Therapy to Replace Chemoradiation in GBM and DIPG

David Baskin, MD

Introduction
Oncomagnetic therapy is a revolutionary noninvasive technique for glioblastoma (GBM) and DIPG treatment. Exploiting a quantum phenomenon, using spinning oscillating magnetic fields (sOMF), cancer cell mitochondria are targeted.
Objectives
Assessment of selective toxicity and safety of sOMF in cancer and normal cells and the demonstration of its efficacy in end stage GBM and DIPG patients.
Methods
Human GBM, DIPG and normal human astrocytes cells were treated with sOMF for assessment of reactive oxygen species (ROS), mitochondrial membrane potential, DNA damage and cytotoxicity. Mice implanted tumors were treated with sOMF for assessing tumor volume, with MRI, and for overall survival. Oncomagnetic therapy has been used in six GBM and one DIPG patient under FDA approved compassionate use.
Results
In a range of cancer types, including GBM and DIPG, sOMF collapses mitochondria membrane potential and elevates ROS and DNA damage. Differential anti-cancer toxicity is apparent as human astroglia (SVGp12), neuronal, astrocytic and endothelial cells are spared from damage. Oncomagnetic therapy had no adverse effects on mice in safety studies. Oncomagnetic therapy in immunocompetent mice with intracranial mouse glioma xenografts showed marked reduction in tumor size and increased survival ($p < 0.05$, $n=10$). Oncomagnetic therapy in end-stage GBM patients reversed tumor progression and caused a >30% reduction in contrast-enhanced volume after 4-6 weeks. Oncomagnetic therapy in an end-stage DIPG patient completely eliminated all contrast enhancing tumor volume.
Conclusion
These results indicate that sOMF stimulation has high anticancer potency at the cellular level with an underlying mechanism of action that is substantially different from that proposed for Optune® TTF.

12:30 – 12:40 Discussion

2:00 – 3:30 Academy Innovator Program
Program Director: Kim Burchiel and Sam Browd

7:30 – 7:35 WELCOMING REMARKS

Jacques Morcos, MD

7:35 – 9:00 Peer Reviewed Abstract Session V: Spine/Peripheral Nerves
Moderators: Daniel Resnick, Zoher Ghogawala, and Mark Hadley

7:35 – 7:44 C4-C6 Laminoplasty with and without C3 Laminectomy, the fate of the C2-C3 level: A Cadaveric Biomechanical Study

Michael Steinmetz, MD

Introduction
Posterior cervical laminoplasty is a common decompressive procedure used in the treatment of cervical spondylotic myelopathy. Currently, options at C3 include either drilling the underside of the lamina or a complete laminectomy. Many providers feel that preservation of at least some of the C3 spinous process contributes to stability at the C2-C3 level.
Objectives
Determine the biomechanical stability of cervical laminoplasty with and without C3 laminectomy.
Methods
Four human cadaveric spines (C1-T2) were mounted to a six degree-of-freedom robot (simVITRO®) and underwent preconditioning. For testing, a 30 N head compressive force was maintained as a head load while ±1.5 Nm moments were applied to the native spine in FE, LB, AR, and in the coupled directions of flexion with axial rotation (FE±AR) and extension with axial rotation (E±AR). After testing, left sided open door laminoplasties were performed at C4, C5, and C6. After the second round of testing, a complete C3 laminectomy was performed and testing was repeated. Primary axes of rotation were compared at the C2-C3 level for each loading trajectory. Subsequent quaternion angles were calculated to quantify total changes in motion between specimens in the two surgical states and the native state.
Results
The C4-C6 laminoplasty construct showed a primary increase in the flexion motion at the C2-C3 level (Figure 1). The addition of a C3 laminectomy further increased instability in overall flexion and flexion with left axial rotation. Surprisingly, there appeared to be a reduction in motion with flexion and right axial motion. Laminoplasty alone demonstrated reduced motion at the C2-C3 level with extension. The addition of a C3 laminectomy demonstrated a trend towards baseline extension motion at the C2-C3 level, as supported through analysis of the Quaternion difference (Figure 2).
Conclusion
Augmenting the standard C4-C6 laminoplasty with a C3 laminectomy altered the biomechanics at C2-C3 level. The addition of a C3 laminectomy further increased instability overall primarily in flexion. Interestingly, the loss of extension and gain of flexion motion at C2-C3 can predispose patients to rest in increased kyphosis at this level. Further studies are necessary to validate these trends and explore the clinical correlation of these findings.

7:44 – 7:53 Machine learning predictive analytics of adverse outcomes after elective spinal fusion

Corey Walker, MD

Introduction
Machine Learning algorithms can be used to independently predict un-baised clinical outcome measures using large numbers of variables within large datasets. Improvements in predictive analytics can help identify vulnerable populations for adverse events after surgery and help isolate key characteristics that contribute most to undesired outcomes.
Objectives
In this study, we sought to utilize these state-of-the-art ML strategies to see how well we can predict hospital readmission, prolonged length of stay, unfavorable discharge disposition and opioid dependency using only pre-operative patient data.
Methods
A retrospective query of consecutive elective spinal fusion operations performed at a single institution between 2012 and 2021 was performed from the electronic medical record using CPT codes. Anterior cervical fusions were excluded from the analysis. Patient demographic information, laboratory data and medical history was collected for computational analysis. Re-admissions within 90 days were recorded, length of stay was measured with extended being above the 75% percentile (7 days in this cohort) and discharge disposition noted if patient was sent home or needed recovery in a rehabilitation or skilled nursing facility. Changes in opioid intake pre-operatively and at one year were recorded.
Results
5,808 patients receiving 6,190 fusion surgeries were included for analysis. Predictive analysis was most successfully used to predict the outcomes best for adverse discharge disposition with ROC_AUC of 0.762. Prediction of hospital re-admission, prolonged length of stay and opioid dependency was also completed with reasonable accuracy (AUC>0.60) depending on the specific ML algorith employed. Clustering analysis independently revealed a significant impact of comercial versus Medicare insurance. Feature importance modeling was performed with various auto-ML and regression analyses to determine the most-contributory variables to the model. Repeatedly, patient's marital status, age, BMI and pre-operative opioid intake had significant impact on the various models. Interestingly, patient's pre-operative hemoglobin values were consistently one of the variables with the greatest feature importance, and anatomic location of the surgery (cervical/thoracic/lumbar), had very little importance. Chronic pain-associated ICD10 codes had significant effects on the clustering analysis and were predictive of outcomes as well for specific models.
Conclusion
In this study, we utilized a large dataset of elective spinal fusion operations containing large amounts of granular patient data from the electronic medical record to perform advanced machine learning predictive modeling. Using these algorithms, we were successfully able to produce models that reliably predicted 90-day re-admission, prolonged hospital length of stay, non-home discharge and unfavorable opioid outcomes.

7:53 – 8:02 Surgical Simulation, 3D navigation and Augmented Reality as an Educational Tool in Minimally Invasive Spinal Surgery

Roger Hartl, MD

Introduction
We previously developed step-by step procedural metrics and educational material for minimally invasive spinal (MIS) procedures as part of an AOSpine funded initiative. Surgical simulation, navigation (NAV) and augmented reality (AR) can assist in surgical education.
Objective
This work assessed residents' learning curve and performance using surgical simulation with and without NAV and AR for 2 MIS procedures: Unilateral laminotomy for bilateral decompression (ULBD) for lumbar stenosis and transforaminal lumbar interbody fusion (TLIF) for spondylolisthesis.
Methods

Procedural metrics were developed for ULBD by a group of expert surgeons and a Delphi panel of 26 spine surgeons. This resulted in step-by-step procedural guidelines for ULBD and TLIF. A total of 24 residents then performed three ULBD and two TLIF procedures on a "Realist" spine simulator with and without NAV and AR. For procedures completed with AR, all relevant surgical landmarks were highlighted on an intraoperative CT. The learning curve was evaluated with attention to technical skills, skipped steps, errors, and timing. The NASA task load index was administered to assess mental demand of the procedure.

Results

For ULBD there was a decrease in procedural time by 31.7 minutes. Errors decreased by 73% and proficiency increased. Residents reported a 30% increase in perceived ability to complete the procedure ($p = 0.001$). In the TLIF group, residents reported that procedures performed without AR required higher mental demand ($p = 0.003$) and that it was more difficult for them to perform adequately without AR ($p = 0.019$).

Conclusion

These studies indicate that procedural metrics for MIS procedures in combination with a surgical simulator and NAV/AR can improve the skills and confidence of trainees. These tools should be explored further and could greatly enhance our ability to train surgeons safely and effectively.

8:02 – 8:11 Lumbar Spondylolisthesis Outcomes in the Elderly: Machine Learning Analysis of the Quality Outcomes Database

Dean Chou, MD

Introduction

The factors influencing surgical outcomes in the elderly remain incompletely defined.

Objectives

We use a machine learning approach to identify unique outcome clusters among elderly patients operated for lumbar spondylolisthesis.

Methods

Data was obtained from the prospective Quality Outcomes Database registry, including patients with grade 1 degenerative lumbar spondylolisthesis. We included patients age ≥ 65. Principal components analysis was used to generate a composite 24-month patient-reported outcome score. A k-means clustering approach was used to differentiate patients by composite operative outcome.

Results

233 patients were included with 24-month follow-up. Two distinct clusters were identified: cluster 1, optimal outcomes, and cluster 2, suboptimal outcomes. The optimal-outcomes cluster had 49.3% achieve MCID across both EQ5D and ODI as compared to 0% in the suboptimal-outcomes cluster ($p< 0.001$). Clusters did not differ significantly by age (cluster 1:71.3, cluster 2:73.0, $p=0.18$), though patients with suboptimal outcomes did report higher baseline ODI and VAS leg pain. Patients in the optimal-outcomes cluster (70.5%) were significantly more likely to have received a fusion procedure than were patients in the suboptimal cluster (51.7%)($p=0.01$). Performance of a fusion procedure was the only significant independent predictor of optimal outcomes (OR = 1.57; 95%CI 1.12-2.19; $p=0.01$).

Conclusion

For elderly patients undergoing surgery for degenerative lumbar spondylolisthesis, the addition of fusion was associated with superior outcomes, with patients receiving a fusion having nearly 1.5 times the odds of reaching an optimal outcome. There was no evidence that age was significantly different between clusters-failing to support an age cutoff for surgery.

8:11 – 8:20	**Preoperative prehabilitation reduces postoperative adverse events in frail multi-level thoracolumbar fusion**

Daniel Hoh, MD

Introduction

Preoperative frailty is correlated with increased adverse events after spine surgery, that may be resistant to perioperative ERAS protocols. Consequently, there is a need for therapies to optimize frailty before surgery to mitigate risk. Therefore, we developed a prehabilitation pathway for frail spine patients consisting of a structured physical therapy program (2-3 times/week for 6-12 weeks) plus nutrition optimization before surgery.

Objectives

In preparation for a prehab RCT, we performed a retrospective case-matched pilot study to assess prehab versus no prehab in frail thoracolumbar surgery.

Methods

The Univ. of Florida prehab pathway was implemented in 2017. Subjects were a consecutive cohort of frail degenerative thoracolumbar patients who underwent preop prehab. Controls (no prehab) were similar frail thoracolumbar patients (concurrent period), case-matched for age, Charlson Comorbidity Index (CCI), and Fried Frailty Score (FFS). Surgeries were decompression alone, 1-2 level fusion, and multi-level fusion (>2 levels). Outcomes were postop adverse events (AE), length of stay (LOS), discharge disposition (DD), and 30-day readmission rate (30-RR). Primary analysis compared total case-matched prehab versus controls. Secondary analysis was a sub-cohort of multi-level fusion patients.

Results

There was no difference in demographics, CCI, or FFS for the total case-matched cohorts (prehab, n=24; control, n=24). For the primary analysis, there was no prehab benefit for AE, LOS, DD, or 30-RR. However, secondary analysis of multi-level fusion (prehab, n=16; control, n=11) demonstrated a significant prehab benefit with decreased total AEs (p=0.029). Prehab had lower postop respiratory failure (p=0.026), urinary retention (p=0.018), and other AEs (hemodynamic instability, hemothorax, p=0.026). Prehab was not associated with improved LOS, DD, or 30-RR for multi-level fusion.

Conclusion

In a retrospective case-matched pilot study, prehab significantly reduced postop adverse events (respiratory failure, urinary retention) in frail patients undergoing multi-level degenerative thoracolumbar fusion. However, prehab may not have comparative benefit for routine decompression alone or 1-2 level fusion. Future analysis from our ongoing larger prehab RCT may delineate further relationships between sub-populations and unique outcomes.

8:20 – 8:29	**Change in Spinal Bone Mineral Density following Treatment with Romosozumab, Teriparatide, Denosumab, and Alendronate**

Benjamin Elder, MD, PhD

Introduction

Low spinal bone mineral density (BMD) as estimated by CT based opportunistic Hounsfield units (HU) has been shown to be a risk factor for mechanical complications following spine fusion surgery. While teriparatide has been shown to improve HU, the impact of other osteoporosis medications on spinal HU is unknown.

Objectives

The purpose of this study was to determine the effect of osteoporosis medications on spinal bone mineral density as estimated by opportunistic CT based HU, including romosozumab, teriparatide, alendronate, and denosumab.

Methods

A retrospective chart review identified spine and non-spine surgery patients treated with 3 to 12 months of romosozumab, 3 to 12 months of teriparatide, greater than 12 months of teriparatide, one year of denosumab, and one year of alendronate with a CT scan performed before and after treatment. Hounsfield units were measured in the L1, L2, L3, and L4 vertebral bodies with three measurements per level on axial CT images. One-way analysis of variance (ANOVA) compared the mean change in HU between the five treatment regiments.

Results

Three hundred and eighteen patients (70% women) were included with an average age of 69 and average BMI of 27. There was a significant difference in the mean HU improvement (p=<0.001) between romosozumab (n=32), 3 to 12 months of teriparatide (n=30), >12 months of teriparatide (n=44), denosumab (n=123), and alendronate (n=100). Treatment with an average of 10.5 months of romosozumab significantly increased mean HU by 26% from a baseline of 85 to 107 (p=0.012). Patients treated with >12 months of teriparatide (average 23 months) improved mean HU by 25% from 106 to 132 (p=0.039). Compared to mean baseline HU, there was no significant difference after treatment with 3 to 12 months of teriparatide (110 to 119, p=0.48), denosumab (105 to 107, p=0.68), or alendronate (111 to 113, p=0.80).

Conclusion

Patients treated with an average of 10.5 months of romosozumab and 23 months of teriparatide improved spinal bone mineral density as estimate by CT based opportunistic HU. Given the shorter duration of effective treatment, romosozumab may be the preferred medication for optimization of osteoporotic patients in preparation for elective spine fusion surgery.

8:29 – 8:38 Development of Non-Invasive Perfusion MRI as a Prognosticating and Treatment tool in Spinal Cord Injury

Shekar Kurpad, MD, PhD

Introduction

Our laboratory is interested in the role of imaging biomarkers in spinal cord injury (SCI), with a particular attention to diffusion MRI markers of neuronal injury. Recently, we have also turned our attention to developing spinal cord perfusion MRI technology to gain the ability to monitor perfusion noninvasively and understand the dynamics after acute injury, first in preclinical models.

Objectives

We aimed to develop pseucontinuous arterial spin labeling (p-CASL) as a tool to continuously monitor perfusion after rat SCI. Our goal was to optimize perfusion labeling and measure blood flow to non invasively quantify blood flow in acute SCI and correlate with long term functional outcomes.

Methods

We determined cervical spinal cord vascular anatomy and configured pulse sequences to label blood water (inversion). We measured arterial mean transit times at several time points after acute injury (4h-48h). MR sequences were optimized to minimize pulsation and/or motion artifacts. We examined diffusion and perfusion with one another and to t2 and t1 mapping in the same animals across 2 early timepoints and a wide range of contusion injury severities.

Results

We were able to obtain high quality perfusion maps of the injured and intact spinal cord. Time-encoded ASL using multiple delay times enabled capturing the perfusion dynamics including transit times to each voxel in the cord, along with clear evidence of watershed zones that likely relate to the feeding arteries. A clear perfusion deficit at 24 hours post injury at the lesion site was confirmed, with clear individual and group level differences. No changes outside of the injury site were evident. Our data additionally indicate that perfusion was highly disrupted at 4 hours and was partially restored by 48 hours, replicating previous histological data

with non invasive methods. Across all contrasts, the extent of the perfusion deficit was the best predictor of long-term (12 week) functional outcomes.

Conclusion

Our results reveal that perfusion is one of the strongest MRI predictors of long-term functional outcomes across a wide range of severities. Work is ongoing to translate these methods to human SCI to optimize hemodynamic care in the early hours after injury and to add a reliable long term prognostic biomarker.

8:38 – 8:47	**Neuromuscular choristoma and circumferential nerve territory desmoid-type fibromatosis: a nerve-driven mechanism**

Robert Spinner, MD

Introduction

Neuromuscular choristoma (NMC) is a rare developmental malformation of peripheral nerve that is frequently associated with the development of desmoid-type fibromatosis (DTF). Both NMC and NMC-DTF typically contain pathogenic CTNNB1 mutations and NMC-DTF develop only within the NMC-affected nerve territory.

Objectives

The authors aimed to determine if there is a nerve-driven mechanism invovled in the formation of NMC-DTF from the underlying NMC-affected nerve.

Methods

Retrospective review was performed for patients evaluated in the authors' institution with a diagnosis of NMC-DTF in the sciatic nerve (or lumbosacral plexus). MRI and FDG PET/CT studies were reviewed to determine the specific relationship and configuration of NMC and DTF lesions along the sciatic nerve.

Results

Ten patients were identified with sciatic nerve NMC and NMC-DTF. All primary NMC-DTF lesions were located in the sciatic nerve territory. Eight cases of NMC-DTF demonstrated circumferential encasement of the sciatic nerve, and one abutted the sciatic nerve. One patient had a primary DTF remote from the sciatic nerve, but subsequently developed multifocal DTF within the NMC nerve territory. Five patients had a total of 8 satellite DTFs, 4 of which abutted the parent nerve and 3 that circumferentially involved the parent nerve.

Conclusion

Based on clinicoradiologic data, a novel mechanism of NMC-DTF development from soft tissues innervated by NMC-affected nerve segments is proposed, reflecting their shared molecular genetic alteration. We believe that DTF develops outward from the NMC in a radial fashion or it arises in the NMC and wraps around it as it grows. In either scenario, NMC-DTF develops directly from the nerve, likely arising from (myo)fibroblasts within the stromal microenvironment of the NMC and grows outward into the surrounding soft tissues. Clinical implications for patient diagnosis and treatment are presented based on the proposed pathogenetic mechanism.

8:47 – 9:00	**Discussion**

9:00 – 9:55	**Peer Reviewed Abstract Session VI: General Interest** Moderators: Arthur Day and Anil Nanda

9:00 – 9:09 Neuro-Oncology Trials in the United States over Five Decades: Analysis of Completions and Failures for the Path forward

Isabelle Germano, MD

Introduction

The unmet therapeutic needs in neuro-oncology remain significant due to the biological and clinical challenges. Clinical trials are important to close the gap between therapeutic unmet needs and scientific advances.

Objectives

This study aims at analyzing the landscape of neuro-oncology trials to identify completion and failures and guide strategies for the path forward.

Methods

US-registered adult neuro-oncology clinical trials were extracted from www.clinicaltrial.gov (1966-2019) to include funding source, trial type, scope, phase, and subjects' demographics. Trial failures comprised "terminated," "withdrawn," and/or "suspended" trials. Univariate and multivariate analysis were used to detect differences across factors and over time.

Results

Our search yielded 4522 trials, 1257 eligible for this study. In 25 US States, neuro-oncology trials availability is < 0.85/100,000 population. Over time, completed trials have decreased with a significant increased percentage of trial failures from 22% to 36% ($p<0.001$). Overtime, NIH funding decreased from 47% to 24% ($p< 0.001$). Inclusion of subjects > 65-year-old and women increased in the last decade ($p< 0.001$) while inclusion of Hispanic subjects has decreased ($p< 0.001$). The top two reasons for failure included accrual and operational difficulties. Industry-funded trials had a trend toward higher failure rate than NIH-funded. A larger proportion of women ($p< 0.001$), non-Hispanic subjects ($p=0.001$), and older adult ($p< 0.001$) patients were enrolled in completed trials than in failed trials.

Conclusion

Our study is the first report on the neuro-oncology clinical trial landscape in the US over time. The data support the concept that strategies to further the availability of clinical neuro-oncology trials within the US are necessary.

9:09 – 9:18 An update of NeurosurGen, the Neurosurgery Genealogy Project

Cargill Alleyne, MD

Introduction

While neurosurgical history is recorded in a variety of different platforms and websites, there is currently no single website that is capable of generating an academic family history for each neurosurgeon and each institution in the US.

Objectives

The objective of the NeurosurGen project is to chronicle an academic family tree for each neurosurgeon in the US and eventually, the world.

Methods

The website was constructed by an IT specialist with the intent of storing, displaying, and editing academic ancestry data. Data were modeled using a structured database. A fuzzy text indexing system allows for speedy and relevant search results. The website user interface was built using 'React' for a fluid experience. Data were collected on the Chair/Chief and Program Director lineage at each residency program (current and defunct). These data also included the ancestry for each Chair/Chief. A list of current and deceased neurosurgeons in the U.S (and their place and date of residency completion) was then mapped to the Chair/Chief at the time of their graduation to construct each neurosurgeon's ancestry.

Results
Examples of both individual academic family trees and institutional histories will be presented. Data analysis also included identification of the founders of neurosurgery in the US, statistics on the chairs/chief, and diversity data. Examples of historical trivia on the chairs/chiefs will also be presented.
Conclusion
NeurosurGen is a comprehensive living database which generates a geneaology for each neurosurgeon and training institution. It preserves our professional history on one website that could be updated in perpetuity.

9:18 – 9:27 NousNav: an open source low cost neuronavigation system for LMIC

Alexandra Golby, MD

Introduction
Neuronavigation can provida intra-operative guidance for cranial surgeries helping to localize lesions and landmarks, decreasing complication rates, and allowing surgeons to take on more complex cases safely and effectively. Contemporary navigation systems are not suitable for use in LMIC due to their very high cost, need for specialized technical support, and use of consummables.
Objectives
We built a protype low-cost navigation system which leverages consumer electronics technology, simplied workflows, easy-to-manufacture custom reusable parts, and open source software to create a simple, intuitive, inexpensive, portable, sustainable and robust navigation system to be deployed by neurosurgical colleagues in LMICs.
Methods
NousNav uses a commercial 3D tracking camera (Optitrack), commodity photography hardware, low cost custom manufactured parts, and custom software developed on the open source platform 3D Slicer. Measurements of accuracy were made against a commercial navigation system (BrainLab) in a head model for a total of 24 TRE measurements for each system. Collegues in Morocco, Rwanda and Senegal have received protype systems which are currently being used to teach navigation principles and for feedback on the system design. Training materials have been developed to guide new users.
Results
The average TRE for Brainlab was 2.63mm (SD 1.19mm), while the average TRE for NousNav was 3.24mm (SD 1.95mm). Prototype systems have been successfully deployed and iteratively refined based on feedback from users in LMIC. Training materials using slides and videos cover basic principles of neuronavigation, system set up, and step-by-step use of the system for planning, registration and navigation.
Conclusion
Using an open source hardware and software model built on readily available components, NousNav can achieve accuracies comparable to commercial systems. Working with colleagues in LMIC, the system is being refined so that it may be deployed clinically.

9:27 – 9:36 Conscious sedation versus monitored anesthesia care during mechanical thrombectomy: a propensity score-matched analysis

Kevin Cockroft, MD

Introduction
Controversy over anesthetic management in patients undergoing mechanical thrombectomy (MT) for acute ischemic stroke typically focuses on use of general anesthesia versus monitored anesthesia care (MAC). However, resource limitations may make nurse administered conscious sedation (NACS) a necessary alternative at many centers.

Objectives
The purpose of this study was to determine whether sedation type (MAC versus NACS) impacts MT outcome.
Methods
This retrospective cohort study used our prospectively maintained institutional stroke database. Patients undergoing MT with either MAC or NACS were propensity matched by age, sex, hypertension, hyperlipidemia, admitting NIHSS, site of LVO, stroke side, administration of IV thrombolytic, transfer type, and access site.
Results
There were 111 patients in each group. MAC patients had faster median door to puncture (12 versus 15 minutes, $p<0.001$) and longer median procedural time (88 versus 72 minutes, $p=0.002$). There was no difference in median puncture to first pass, or puncture to successful reperfusion (TICI2B, 3) times. There was no significant difference in discharge disposition/NIHSS/mRS, or functional independence (mRS 0-2) at either discharge or 90 days. More MAC patients had intra-operative vasoactive medication administration (49.5% versus 23.4%, $p<0.001$), but there was no difference in complications, including post-operative intracerebral hemorrhage.
Conclusion
Despite a slight difference in the time to intervention, clinical outcomes and complications were similar in patients undergoing ET with MAC or NACS. In resource constrained environments, NACS may be a reasonable alternative to MAC. However, in situations where anesthesia support is available, faster time to intervention and better blood pressure control probably make MAC the best option.

9:36 – 9:45 Development of a Percutaneous Endovascular Biomimetic Shunt (eShunt) for Treatment of Communicating Hydrocephalus

Adel Malek, MD, PhD

Introduction
Communicating hydrocephalus is caused by an imbalance in cerebrospinal fluid (CSF) production and absorption, resulting in increased pressure and enlarged brain ventricles, currently treated with ventriculo-peritoneal (VP) shunt surgery. Despite advancements, such as adjustable valves and antibiotic-impregnation, infection risk, siphon-related overdrainage, and failure rates remain.
Objectives
In an attempt to address VP shunt limitations, we sought a biomimetic device strategy inspired by arachnoid granulations, aiming to bridge CSF cisterns to the venous system.
Methods
Our approach involved the design of an endovascular valved shunt micro-implant (eShunt) that mimics natural CSF flow from the cerebello-pontine angle cistern to the inferior petrosal sinus. We developed the necessary delivery catheters and imaging pipeline for safe percutaneous transfemoral endovascular delivery in the angiography suite.
Results
After eight years of development, the first-in-human eShunt procedure was successfully performed in a patient with communicating hydrocephalus after aneurysmal subarachnoid hemorrhage followed by seven additional patients, all achieving primary endpoint of low intracranial pressure (<20 cmH2O), enabling drain removal. In a recent pilot study, elderly patients with normal pressure hydrocephalus were treated with eShunt. Patients were enrolled based on a >20% improvement in gait after a high-volume lumbar tap. Analysis of the first six patients showed improved gait, bladder symptoms, and cognitive function at 30-180 days.
Conclusion
Our novel approach, utilizing an imaging pipeline, catheter design, and biomimetic endovascular eShunt implant, provides a less invasive treatment for communicating hydrocephalus. The early favorable clinical

experience is encouraging with longer follow-up needed to define the role of this innovative approach for hydrocephalus patients.

9:45 – 9:55 Discussion

9:55 – 10:10 Break

10:10 – 10:40 Special Debate Session II: Social Media in Medicine and Neurosurgery - Blessing or Curse?
Moderators: Bob Carter and Isabelle Germano

10:10 – 10:11 Introduction
Bob Carter, MD, PhD and Isabelle Germano, MD

10:11 – 10:20 It's a blessing
Brian Hoh, MD

10:20 – 10:29 It's a curse
Allan Levi, MD, PhD

10:29 – 10:40 Discussion

10:40 – 11:55 Peer Reviewed Abstract Session VII: Tumor Basic Science
Moderators: Peter Dirks and Michael Lim

10:40 – 10:49 CD8+ T cells maintain killing of MHC-I-negative tumor cells through the NKG2D-NKG2DL axis
Peter Fecci, MD, PhD

Introduction
The accepted paradigm for both cellular and antitumor immunity relies upon tumor cell kill by CD8+ T cells recognizing cognate antigens presented in the context of target cell major histocompatibility complex class I (MHC I) molecules. Likewise, a classically described mechanism of tumor immune escape is tumor MHC-I downregulation.
Objectives
Here we reveal a novel mechanism of MHC-independent tumor killing by CD8+ T cells that disrupts the long-held paradigm for antitumor immunity.

Methods
In vitro tumor cytotoxicity studies were conducted with both murine and human cells, while in vivo studies were conducted in mice. RNA sequencing data were obtained from both humans and mice.
Results
Here, we report that CD8+ T cells maintain the capacity to kill tumor cells that are entirely devoid of MHC-I expression. This capacity proves to be dependent instead on interactions between T cell NKG2D and tumor NKG2D ligands (NKG2DL), the latter of which are highly expressed on MHC-loss variants. Necessarily, tumor cell kill in these instances is antigen-independent, although prior T cell antigen-specific activation is required and can be furnished by myeloid cells or even neighboring MHC-replete tumor cells. In this manner, adaptive priming can beget innate killing. These mechanisms are active in vivo in mice, as well as in vitro in human tumor systems, and are obviated by NKG2D knockout or blockade.
Conclusion
These studies challenge the long-advanced notion that downregulation of MHC-I is a viable means of tumor immune escape, and instead identify the NKG2D/NKG2DL axis as a therapeutic target for enhancing T cell-dependent anti-tumor immunity against MHC loss variants.

10:49 – 10:58 Altered non-neoplastic plasma extracellular vesicle phenotype in glioblastoma patients

Ian Parney, MD, PhD

Introduction
Extracellular vesicles (EVs) are lipid bilayer-encapsulated nanoparticles released by all cells. While tumor cell-derived EVs have been the subject of intense investigation as a source of biomarkers for glioblastoma (GBM), true GBM-derived EVs are rare in body fluids. Non-neoplastic EVs are much more abundant.
Objectives
To determine if non-neoplastic plasma EV phenotype differs in GBM patients from patients with other brain tumors or normal donors and is correlated with tumor volume or survival.
Methods
Plasma EV phenotype based on EV-associated tetraspanins (CD9, CD63, CD81) and markers of non-neoplastic cells of origin (CD11b, CD31, CD41a, CD45) was determined by spectral flow cytometry in newly diagnosed GBM, Grade 2 glioma, and brain metastases patients and healthy donors and compared to tumor volume and overall survival.
Results
Plasma EV phenotype was distinct in GBM patients (increased CD9+, CD63+, CD81+, CD11b+; decreased CD41a+), had distinct multiparametric expression patterns, and an overall accuracy of 81.25% for identifying GBM using an artificial intelligence algorithm. Tumor volume was correlated with CD9+ (p=0.014), CD41a+ (p=0.037), and CD9+/CD63-/CD81- (p=0.007) EVs. Increased CD9+ (p=0.011), decreased CD9+CD63-CD81- (p=0.009) and decreased CD9+CD11b+ (p=0.006) plasma EVs independently predicted longer overall survival along with clinical prognostic factors.
Conclusion
Non-neoplastic plasma EV phenotype at diagnosis distinguishes GBM from normal donors and other brain tumor patients, correlates with tumor volume, and independently predicts overall survival, underscoring the systemic nature of GBM. Efforts are ongoing to determine the source and biological significance of these findings but non-neoplastic plasma EVs are an attractive target for GBM liquid biopsies.

10:58 – 11:07 Magnetic Hyperthermia Therapy in Combination with Chemoradiation for the Treatment of Glioblastoma

Constantinos (Costas) Hadjipanayis, MD, PhD

Introduction

Glioblastoma (GBM) is an aggressive primary brain cancer with significant resistance to the current therapeutic approach of chemotherapy and radiotherapy (RT), jointly known as chemoradiation (CRT). Magnetic hyperthermia therapy (MHT) is a promising therapy for GBM that can be used to perform multiple sessions of non-invasive, localized hyperthermia by activating locally delivered magnetic iron oxide nanoparticles (MIONPs) with an external alternating magnetic field (AMF).

Objectives

In this study, MHT-mediated enhancement of CRT was evaluated in murine and human glioma cell lines both in cell culture and in rodents.

Methods

The heating profile of MIONPs was assessed in the test tube and mouse brain in vivo. Computed tomography scan and magnetic particle imaging were used to confirm intracranial MIONP localization after convection enhanced delivery. Cell viability assays were performed following treatment with MHT and/or radiation. MHT-induced alterations to the tumor microenvironment were assessed in a syngeneic murine glioma model, and a survival study was performed in a GBM patient-derived xenograft (PDX) model to investigate synergism between MHT and CRT.

Results

Significantly increased survival was observed in mice treated with MHT+CRT compared to CRT alone in a therapy-resistant GBM PDX model. In vitro studies demonstrated that MHT with radiation was more cytotoxic than radiation or MHT alone. Additionally, MHT with CRT significantly increased tumoral expression of biomarkers for DNA double-strand breaks (g-H2AX), CD8+ T cell recruitment (CD8), and inflammation (P-selectin) compared to CRT alone, suggesting MHT-mediated radio-sensitization and immune cell recruitment to the tumor. MIONP heating was confirmed in the test tube (93.3 oC) and intracranially (50.7 oC) within minutes of AMF exposure, and localization of MIONPs to the delivery site was verified with imaging.

Conclusion

Adjuvant MHT may induce tumor radio-sensitization, immune cell recruitment, and survival benefit when combined with CRT.

11:07 – 11:16 Seq-ing the SINEs of Central Nervous System Tumors in Cerebrospinal Fluid DNA

Chetan Bettegowda, MD, PhD

Introduction

Central nervous system (CNS) neoplasms comprise a heterogenous class of tumors that are either primary or metastatic. A pressing clinical challenge is the lack of reliable biomarkers for the diagnosis and monitoring of cancers involving the CNS. The current gold standard is cytology on cerebrospinal fluid (CSF), which has a sensitivity that ranges from 2% to 50%, depending on cancer type

Objectives

Liquid biopsies that detect tumor-derived DNA in plasma (circulating tumor DNA, called ctDNA) are now being widely explored to detect and monitor cancers of many types. Implementing analogous tests in CSF is challenging because the quantity of circulating DNA in CSF is considerably lower than in plasma. In the current study, we describe our efforts to develop a simple strategy, called Real-CSF, for the diagnosis and monitoring of several of the most common and debilitating brain cancers: glioblastomas, metastatic lesions, lymphomas, and medulloblastomas.

Methods

Real-CSF uses a single primer pair to PCR-amplify ~350,000 short interspersed nuclear elements (SINEs) from throughout the genome. As described in Methods, these PCR products of SINEs are assessed by next

generation sequencing, and machine learning is used to assess gains or losses of 39 chromosome arms, focal amplifications, and Apparent Somatic Mutations. Two independent cohorts of patients were evaluated in this study: a training set and a validation set. The training set was composed of CSF samples from 92 patients, 37 with GBM, 14 with metastasis from primary tumors outside the brain, 7 with lymphoma, and 34 without cancer. The validation set was composed of CSF samples from 190 patients, 27 with GBM (five of which were pediatric H3K27M diffuse midline gliomas), 52 with metastasis from primary tumors outside the brain, 27 with CNS lymphoma, 23 with medulloblastoma, and 61 without cancer.

Results

Real-CSF was applied to 282 CSF samples and correctly classified 71 % of 187 cancers and misclassified only 4.2% of 95 non-neoplastic lesions in the brain. Of the 123 cases in whom cytology was available, 70% were detectable by Real-CSF assay while only 23% were detectable by cytology. The individuals with detectable levels of CSF-tDNA had an odds ratio of 5.1 ($p = 0.02$) for disease progression when compared to those without CSF-tDNA detection

Conclusion

Real-CSF provides an off the shelf, inexpensive and broadly applicable approach for the diagnosis of several of the most common brain cancers. Future studies are required to bring this technology into the clinical realm.

11:16 – 11:25 Glioblastoma induces the recruitment and differentiation of hybrid neutrophils from skull bone marrow

Manish Aghi, MD, PhD

Introduction

While tumor-associated neutrophils (TANs) were regarded as passive bystanders due to the limited lifespan of peripheral blood neutrophils (PBNs), TAN effects on glioblastoma remain under-characterized.

Objectives

We defined TAN lineage and functionality in GBM.

Methods

TAN heterogeneity was interrogated using single-cell RNA-sequencing (scRNA-seq) of matched patient PBNs/TANs. Skull irradiation was performed with body shields. Intracalvarial treatments were administered stereotactically after outer table drilling.

Results

In scRNA-seq, TANs were more immature than PBNs, with non-circulating immature TANs yielding TAN subtypes: (1) conventional cytotoxic TANs expressing phagocytosis genes and (2) "hybrid" TANs expressing antigen-presenting cell (APC) genes like MHC-II. Cultured patient TANs outlived PBNs and exhibited hybrid dendritic features: morphological complexity, exogenous peptide processing, and stimulating MHCII-dependent T-cell activation. The hybrid TAN phenotype was inducible in skull marrow precursors grown in glioblastoma conditioned media but not in PBNs. Neutrophil depletion in immunocompetent mice accelerated glioblastoma growth with diminished CD8+ T-cell infiltrate, while neutrophil depletion in T-cell deficient mice slowed glioblastoma growth with downregulation of glioblastoma stem cell (GSC) markers. Through labeled skull flap transplantation, we characterized calvarial marrow as a potent contributor of antitumoral hybrid TANs. Targeted skull bone marrow irradiation and intracalvarial AMD3100 decreased and increased survival of glioblastoma-bearing mice, respectively with associated changes in hybrid TAN levels and cytotoxic T-cell responses correlating with survival.

Conclusion

Glioblastoma TANs exhibit context-dependent functionality, with anti-tumoral APC hybrid functionality in the presence of T-cells but GSC-promoting functionality in the absence of T-cells. Agents augmenting neutrophil egress from skull marrow present therapeutic potential.

11:25 – 11:34 Myeloid cell reprogramming via TREM2 inhibition triggers anti-tumor immunity in glioblastoma

Albert Kim, MD, PhD

Introduction

The prevailing view is that myeloid cells, i.e., macrophages and microglia, in the tumor microenvironment (TME) are immunosuppressive and promote glioblastoma (GBM) progression. However, myeloid cells have the functional plasticity to restrict or support tumor cell growth. TREM2 plays important roles in brain microglial function in neurodegenerative diseases, but the role of TREM2 in the GBM TME has not been examined.

Objectives

To characterize the expression and functional role of TREM2 in human glioblastoma tumors and mouse models of glioblastoma.

Methods

Human glioblastoma tumors and mouse models of glioblastoma (SB28, NPA C54B) were utilized for in vitro analyses and in vivo orthotopic transplantation experiments, including bulk and single cell RNA-sequencing, flow cytometry, immunohistochemistry, and animal survival studies. Primary mouse bone-marrow derived macrophages, microglia, and cell line models of myeloid cells (THP-1, BV2) were utilized for phenotypic analyses and for conditioned media and tumor cell co-culture experiments. TREM2 inhibition was performed through several orthogonal approaches including knockout mice, lentiviral RNA interference, antisense oligonucleotides, and blocking antibodies.

Results

We found TREM2 is highly expressed in macrophages and microglia in human and mouse GBM tumors and that high TREM2 expression correlates with poor prognosis in GBM patients. TREM2 loss of function in human macrophages and mouse myeloid cells increased IFNγ-induced immunoactivation, proinflammatory polarization, and direct tumoricidal activity in vitro and in vivo. In mouse GBM models, mice with chronic and acute TREM2 loss of function demonstrated decreased tumor growth and increased survival. TREM2 inhibition reprogrammed myeloid cell phenotypes and increased PD-1+CD8+ T cells in the TME. Finally, TREM2 deficiency enhanced the effectiveness of anti-PD-1 treatment in vivo.

Conclusion

TREM2 inhibition suppresses tumor cell growth through direct and indirect immune cell mechanisms--by reshaping myeloid subset and T cell functions. Thus, TREM2 inhibitory strategies, in combination with immune checkpoint blockade and potentially other high priority immunotherapies, may represent an attractive new approach for GBM therapy.

11:34 – 11:43 Delivery of MSC-D24 into the Resection Cavity Using Fibrin Scaffold for Glioblastoma Treatment

Frederick Lang, MD

Introduction

The oncolytic virus Delta-24-RGD (D24) is a novel treatment of glioblastoma (GBM). Prior studies have examined intra-tumoral injection of D24 and intra-arterial delivery of tumor-tropic human mesenchymal stem cells loaded with D24 (MSCs-D24) to treat unresected GBM. However, the optimal method for delivering oncolytic virus directly in the surgical resection cavity for treating residual disease in resected GBM remains unclear.

Objectives

We explore a novel strategy of using fibrin as a scaffold for delivering MSC-D24 into the surgical cavity in a mouse model of glioma xenograft resection and recurrence.

Methods

For in vitro studies, MSCs~D24 were suspended in a fibrin matrix or in PBS and placed in upper wells of transwell plates with U87 tumor cells placed below. U87 cell viability was determined after 7 days to confirm release of D24 from fibrin~seeded MSCs and compare rates of cellular killing. For in vivo studies, U87 cells and glioma stem cell line, MDA-GSC11, were transduced with mCherry-Luciferase and implanted into the brains of athymic mice. After fluorescence-guided surgical resection of glioma xenografts, MSCs or MSC-D24 were delivered into the resection cavity with or without fibrin as a scaffold. Serial bioluminescence imaging (BLI) was used to monitor tumor recurrence.

Results

In vitro, MSCs~D24 in fibrin were as effective in killing U87 cells as MSC~DNX~2401 alone, indicating fibrin did not impair viral release. In in vivo studies mimicking residual tumor after surgical resection, delivery of MSCs suspended in fibrin in the post-resection cavity facilitated retention of stem cells within the tumor bed. Treatment with Fibrin/MSC-D24 significantly increased survival in both U87- and MDA-GSC11-bearing mice compared with treatment with MSC-D24 without fibrin and control MSCs in fibrin. Median survival of U87-bearing mice was prolonged to 100 days compared with 54 days with MSC-D24 treatment without fibrin, 44 days in Fibrin/MSCs without D24, 40 days in resected controls, and 25.5 days without treatment ($p<0.001$). In MDA-GSC11-bearing mice, treatment with Fibrin/MSC-D24 increased median survival 106.5 days compared with 78 days for treatment with MSC-D24, 78.5 days for treatment with Fibrin/MSC, 80.5 days for resection alone, and 64 days without treatment ($p<0.001$).

Conclusion

Delivery of MSCs loaded with oncolytic virus D24 into the surgical resection cavity using fibrin as a scaffold is capable of eradicating residual GBM and prolonging overall survival in a mouse model of glioma resection. These studies support the clinical translation of this approach in patients undergoing surgical resection of GBM.

11:43 – 11:55 Discussion

11:55 – 12:40 Presidential Address

11:55 – 12:00 Introduction of the Academy President: Bob Carter

12:00 – 12:40 Presidential Address: "Neurosurgery in the misinformation age" By Fred Barker

2:00 – 5:00 Academy Emerging Investigators' Program

Program Director: Gregory Zipfel

2:00 – 2:15 Introduction

2:15 – 5:00 Meetings with Established Investigator Faculty

7:30 – 8:20 Special Abstract Session VIII: The Oldfield Session of Excellence
Moderators: James Rutka and Fred Meyer

7:30 – 7:35 Introduction and a sampling of Ed Oldfield's vast contributions

James Rutka, MD, PhD

7:35 – 7:44 GABAergic interneuron cell therapy for treatment of medically intractable mesial temporal lobe epilepsy

Kim Burchiel, MD

Introduction
It is known that implantation of human cortical-type GABAergic interneurons in the hippocampus of mice with kainate-induced mesiotemporal sclerosis can control focal seizures (Priest et al., 2021). This study extends these results to a series of NRTX-1001 implants in non-human primates and some early findings in a first-in-human Phase I/II clinical trial.
Objectives
This pre-clinical and clinical study is investigating whether one-time implantation of human GABAergic interneurons derived from allogeneic human stem cells (NRTX-1001) can lead to seizure control in drug-resistant mesial temporal lobe epilepsy (MTLE).
Methods
This report details the results with image-guided stereotactic implantation of NRTX-1001 in 25 non-human primates (M. mulatta) and the initial results of a first-in-human Phase I/II clinical trial (NCT05135091). NHP implantation was completed at the Oregon National Primate Research Center (OHSU). Human subjects were also implanted, including a subject at OHSU. Human subjects had unilateral mesial temporal lobe epilepsy (MTLE) with hippocampal sclerosis and focal seizures refractory to drug treatment. Human testing included EEG, imaging, tests of memory, mood, and assessment of visual fields. Both NHP and human subjects received immunosuppression beginning 1 week prior to surgery, tapering after 1 year in the human trial. Cells were implanted via image-guided stereotactic injection along the long axis of the hippocampus with intra-operative MRI imaging. NHP subjects had histologic analysis only. The primary endpoint for the on-going human trial is safety, and the secondary endpoint is seizure frequency at 1-year post-implant.
Results
Histologic data from the NHP study confirmed the accuracy of graft placement in the hippocampus with cellular migration and incorporation of the NRTX-1001 GABAergic interneurons into and around the dentate gyrus, without any overt effects on motor function. Data on the human trial are reported as of 01May2023. There have been no serious adverse effects in the human trial thus far. The OHSU subject is 7 months out from dosing and has had a >90% seizure reduction to date. Additionally, select memory scores are numerically improved for the OHSU subject.
Conclusion
This study of NRTX-1001 cell therapy demonstrated the procedure of image-guided stereotactic cell implantation was anatomically accurate in both NHP and human brain, that these cells locally disperse, survive, and are incorporated into the hippocampus. The human trial is under way, and preliminary results of the first-in-human study of GABAergic interneurons for focal epilepsy are encouraging. One-time implantation of NRTX-1001 cells offers the potential for seizure control in patients with MTLE without removal or ablation of brain tissue.

7:44 – 7:53 Robotics for endovascular neurosurgery

Ben Waldau, MD

Introduction

Neurointerventional robotic systems may reduce occupational radiation, improve procedural precision, and allow for future remote teleoperation. A limited number of single institution case reports and series have been published outlining the safety and feasibility of robot-assisted diagnostic cerebral angiography and carotid angioplasty and stenting.

Objectives

To describe our initial experience with robotic diagnostic angiography and carotid angioplasty and stenting in a multi-institution study.

Methods

A total of 114 patients underwent robot-assisted diagnostic cerebral angiography from September 28th, 2020 to October 27th, 2022 at three separate institutions - UCLA, UCD, and UCSF. 113 cases were analyzed given that one case was removed due to insufficient documentation. Eleven patients underwent carotid angioplasty and stenting at the three institutions.

Results

88 of 113 (77.9%) cases were completed successfully with the robotic system without unplanned manual conversion. Femoral access was conducted in 98 of 113 (86.7%) cases. 14 of 113 (12.4%) cases were conducted using the radial approach (one through a distal snuffbox radial access) and 1 case (0.9%) was conducted with the ulnar approach. Robotic success was achieved in 78 of 98 (79.6%) femoral cases and 10 of 15 (66.6%) radial+ulnar cases. The principal causes for unplanned manual conversion included challenging anatomy, technical difficulty with the bedside robotic cassette, trouble with wire/catheter movement, and hubbing out of the robotic system due to limited working length. For robotic operation, average fluoroscopy time was 13.2 minutes (interquartile range, 9.3 to 16.8 minutes) and average cumulative air kerma was 975.8 mGY (interquartile range, 350.8 to 1073.5 mGy). Eleven patients underwent successful robotic carotid angioplasty and stenting (100%). Not all steps of robotic carotid angioplasty and stenting cases could be performed with all devices. Only the SpiderFX filter and Precise or Enroute Carotid Stent could be maneuvered robotically sucessfully into position.

Conclusion

Robotic cerebral angiography and carotid angioplasty and stenting with the CorPath GRX Robotic System is safe. However, there are significant technical constraints such as working length and device compatibility which may limit its widespread adoption in clinical practice.

7:53 – 8:02 Neonatal Paenibacilliosis: Discovery of a New Disease as a Major Cause of Hydrocephalus in African Infants

Steven Schiff, MD, PhD

Introduction

Worldwide, the largest cohort of new cases of pediatric hydrocephalus appears to have acquired hydrocephalus after infection early in life. In most cases we do not know the causative agents, or the infectious history, prior to presentation with hydrocephalus. In Uganda, in 2020, we found that the most common organism associated with such postinfectious hydrocephalus at presentation was a novel strain of Paenibacillus thiaminolyticus. But we did not know whether this organism caused the hydrocephalus, when this infection was acquired, whether it was a primary or secondary infection, nor the nature of the predisposing disease.

Objectives

To determine the underlying infectious disease causing hydrocephalus in Uganda.

Methods
We performed a prospective case-control study in 100 maternal-newborn pairs, and a cohort study in 800 neonates with sepsis, half from the Mbarara and Mbale Regional Referral Hospitals respectively, representing western and eastern Ugandan populations. We linked these cases to a contemporaneous case-control study of 400 cases of infant hydrocephalus, 200 with congenital and 200 with postinfetious hydrocephalus. In these 1400 patients we employed unbiased DNA sequencing to identify all bacterial species, and then used targeted qPCR confirmation of both genus and species of P thiaminolyticus in 2578 samples.
Results
Of 100 maternal-newborn pairs, we found no evidence of P thiaminolyticus in specimens from vagina, placenta, maternal blood or cord blood. Of 800 neonates with sepsis, age less than 28 days, we identified P thiaminolyticus in blood and CSF in 6% of cases, and were able to demonstrate linkage of the organism from neonate, through sepsis treatment, and to later development of infectious hydrocephalus. We observed P thiaminolyticus in 44% of the 200 cases of postinfectious hydrocephalus. We then identified the characteristics of a new disease syndrome - Neonatal Paenibacilliosis - in 37 neonates, 19% of whom developed postinfectious hydrocephalus, in comparison with 1% from other organisms causing sepsis.
Conclusion
We have identified a new disease syndrome and novel agent as the dominant cause of infant hydrocephalus in an East African country. Funding: NIH Director's Pioneer Award 5DP1HD086071 and NIH Director's Transformative Award 1R01AI145057.

8:02 – 8:11 What Predicts the Best Outcomes From Surgery for CSM? Analysis of the QOD Prospective Cohort

Praveen Mummaneni, MD

Introduction
Predictors of Neck Disability Index (NDI) following CSM surgery are incompletely defined.
Objectives
We sought to evaluate the predictors of the best outcomes following surgery for cervical spondylotic myelopathy (CSM) by evaluating 1,141 patients from the prospective Quality Outcomes Database (QOD) CSM cohort.
Methods
The prospective QOD CSM cohort-containing 1,141 patients from 14 highest-enrolling QOD Cervical Module sites-was retrospectively analyzed. The primary outcome was 2-year NDI. Patients were included that had the best (top 20th percentile) and worst (bottom 20th percentile) NDI outcome. To determine the significant predictors of the best outcomes, a multivariable logistic regression model was constructed using backward stepwise elimination and included candidate variables reaching $p \leq 0.20$ on univariate analyses. Candidate variables included all baseline characteristics-including baseline VAS-neck/arm pain, NDI, EQ-5D, EQ-VAS, and mJOA-and surgical variables. The final model included only variables $p<0.05$.
Results
The 2-year follow-up rate was 83.1% (948 of 1,141 patients). Overall, 204 (17.9%) and 200 (17.5%) patients had the best and worst NDI outcomes, respectively. Factors predicting the best NDI outcomes included symptom duration less than 12 months (OR=1.4,95%CI[1.1-1.9],p=0.01), anterior surgical approach (OR=1.5,95%CI[1.03-2.1],p=0.03), higher preoperative VAS-neck pain (OR=1.2,95%CI[1.1-1.3],p<0.001), and higher baseline NDI (OR=1.06,95%CI[1.05-1.07],p<0.001).
Conclusion
Those with the best NDI outcomes had shorter symptom durations, higher preoperative VAS-neck pain, higher preoperative NDI, and anterior surgeries. This suggests that earlier surgery (<12 months from symptom

onset) may be beneficial for CSM patients. Those with worse baseline disability and higher neck pain have the largest capacity for improvement in NDI postoperatively.

8:11 – 8:20 Glioblastoma remodeling of neural circuits in the human brain decreases survival

Shawn Hervey-Jumper, MD

Introduction

Gliomas synaptically integrate into neural circuits. Prior work has demonstrated bidirectional interactions between neurons and glioma cells, with neuronal activity driving glioma growth and gliomas increasing neuronal excitability. These results to date have been limited to preclinical models of disease.

Objectives

In this study we sought to determine how glioma-induced neuronal changes influence neural circuits underlying cognition and whether these interactions influence patient survival.

Methods

Using intracranial brain recordings during lexical retrieval language tasks in awake humans in addition to site-specific tumor tissue biopsies and cell biology experiments.

Results

We found that gliomas remodel functional neural circuitry such that task-relevant neural responses activate tumor-infiltrated cortex, beyond cortical excitation normally recruited in the non-tumor regions of the brain. Site-directed biopsies from functionally connected regions within the tumor are enriched for a glioblastoma subpopulation that exhibits a distinct synaptogenic and neuronotrophic phenotype. Tumor cells from functionally connected regions secrete the synaptogenic factor thrombospondin-1, which contributes to the differential neuron-glioma interactions observed in functionally connected tumor regions compared to tumor regions with less functional connectivity. Pharmacological inhibition of thrombospondin-1 through the FDA-approved drug, gabapentin decreases glioblastoma proliferation. The degree of functional connectivity between glioblastoma and the normal brain negatively impacts both patient survival and language task performance.

Conclusion

These data demonstrate that high-grade gliomas functionally remodel neural circuits in the human brain, which both promotes tumor progression and impairs cognition.

8:20 – 8:30 Discussion

8:30 – 9:14 Academy Award Presentation and Lecture

8:30 – 8:35 Introduction of Academy Award Winner

Kendall Lee, MD, PhD

8:35 – 8:44 Proteomic Inflammatory Signatures Predict Cerebral Aneurysm Presence

Kamil W. Nowicki, MD, PhD

Introduction

Cerebral aneurysms affect 2-5% of the population and are believed to result from a hemodynamic inflammatory process. Despite significant advances in management, there is no blood-based test currently available to detect cerebral aneurysm presence.

Objectives

1) To identify circulating, signature inflammatory profiles in patients with cerebral aneurysms, and 2) to develop a panel to detect cerebral aneurysms.

Methods

A total of 233 patients were prospectively enrolled into the study including 143 patients with cerebral aneurysms (n=108 unruptured, n=11 ruptured, n=12 treated and secured, n=12 treated but with remnant) and 90 control patients (Chiari 1 malformation, meningiomas, angiographically-negative subarachnoid hemorrhage). Semi-quantitative cytokine arrays (Raybiotech) were used to test for 120 protein cytokines in duplicate. Samples were randomly split into 80%-20% training-validation cohort, secondary validation cohort, and sub-analysis. Initial predictive models were derived in R-package using LASSO. Models with cytokines of interest were then optimized using machine learning with AWS SageMaker and Autopilot.

Results

Convolutional neural network optimization resulted in a 40-cytokine cerebral aneurysm detection model with F1-score of 0.96, 93.6% sensitivity and 88% specificity. Ruptured cerebral aneurysm profile detection model resulted in 14-cytokine model with validation AUC 0.99, sensitivity 88% and specificity 100%.

Conclusion

Circulating inflammatory signatures in cerebral aneurysm patients can be reliably differentiated from control patients using a mini-proteomic panel. We show for the first time, that inflammatory cytokine profiles correlate with patient outcomes in a setting of aneurysmal rupture. Finally, we present evidence for differences in inflammatory profiles of patients with secured and unsecured cerebral aneurysms that could aid in decision making.

8:44 – 8:49	**Introduction of NREF Academy Winners (Natasha Ironside, Ryan Naylor, and Jonathan Parker)**

Gregory Zipfel, MD

8:49 – 9:04	**American Academy Young Clinician Investigator & Research Fellowship Grant Recipients**

Gregory Zipfel, MD

9:04 – 9:14	**Emerging Investigator Program**

Gregory Zipfel, MD

9:14 – 9:50	**Peer Reviewed Abstract Session IX: Pediatrics** Moderators: Gerald Grant and Jennifer Strahle

9:14 – 9:23	**PTEN mutations impair CSF dynamics and cortical networks via neuroprogenitor cell dysregulation**

Kristopher Kahle, MD, PhD

Introduction
Fetal ventriculomegaly, the most common antenatally-diagnosed brain abnormality, is the defining feature of congenital hydrocephalus (CH). Fetal ventriculomegaly is also an overlooked associated finding in neuropsychiatric disorders, including autism spectrum disorder (ASD), which is diagnosed at a 10-fold higher rate in CH patients than in the general population.
Objective
Given these associations, an improved genetic, molecular, and cellular understanding of ventriculomegaly could reveal a shared biological etiology between CH and ASD and aid in patient prognosis, diagnosis, and treatment stratification.
Methods
We subjected 2,978 parent-trio probands with primary ventriculomegaly, including shunted, sporadic CH, to whole exome sequencing (WES). Using mouse molecular genetics, we generated a novel CH mutant mouse model via prenatal, genetic deletion of a WES-identified CH gene. MRI, measurement of CSF secretion, electrophysiological recordings, and cortex-wide, mesoscopic Ca2+ imaging were performed in mice.
Results
We identify phosphatase and tensin homolog (PTEN), a tumor suppressor gene, to be the most frequently mutated gene in primary human ventriculomegaly. Integrative analysis of the human fetal brain revealed PTEN was most highly expressed in NKX2.1+ neuroprogenitor cells (NPCs) and their post-natal interneuron descendants. A Pten mutant mouse model with Nkx2.1-specific Pten deletion exhibited neonatal-onset obstructive hydrocephalus. Pten-mutant ventriculomegaly results from aqueductal stenosis due to mTor-activated hyperproliferation of NPCs and CSF hypersecretion due to inflammation-driven choroid plexus (ChP) hyperplasia. Hydrocephalic Pten mutants also exhibit autism-like hypersynchronization of the somatosensory cortices due to impaired activity of interneurons. Strikingly, genetic or pharmacologic mTORC1 inhibition (rapamycin analogs) corrects ventriculomegaly and rescues cortical pathology of Pten mutants.
Conclusion
Our data demonstrate that PTEN, a commonly mutated ASD gene, is also the most frequently mutated gene in primary ventriculomegaly. To attenuate the pathologically entangled enlargement of the ventricular system and deficits within the surrounding cortical mantle, the use of rapamycin analogs has potentially high translational value as an adjunct therapy to neurosurgical CSF diversion, preventing intrinsic brain parenchymal dysfunction in ventriculomegalic patients harboring PTEN mutations. Ventriculomegaly may also be a useful radiographic biomarker for early referral for exome sequencing and formal neurodevelopmental assessments.

9:23 – 9:32 Cerebrospinal fluid extracellular vesicles mediate recruitment and activation T-cells in post-hemorrhagic hydrocephalus

David Limbrick, MD, PhD

Introduction
Intraventricular hemorrhage (IVH) is the most common, severe neurological complication of preterm birth and is closely associated with post-hemorrhagic hydrocephalus of prematurity (PHH). IVH-related inflammation has been implicated in the pathogenesis of PHH but remains poorly characterized.
Objectives
The objective of this study was to determine whether cerebrospinal fluid (CSF) extracellular vesicles (EVs) mediate the recruitment of inflammatory cells and activation of CSF T-cells in PHH.
Methods
CSF EV and cellular profiles from human preterm neonates with PHH were compared to IVH grade 1-2, congenital hydrocephalus (CH), and controls (no known neurological injury). CSF EVs were isolated and

analyzed by mass spectrometry-based high-throughput proteomics. CSF cells were analyzed by single-cell RNA sequencing and flow cytometry. T-cell activation after EV exposure was studied in vitro by bulk RNA sequencing, flow cytometry, and ELISA. Post-mortem human brain samples were analyzed using immunofluorescence.

Results

PHH CSF samples demonstrated a significant increase in EV pro-inflammatory proteins compared to control and CH. Robust populations of activated T-cells and myeloid cells were detected in the CSF of PHH. PHH EV-activated T-cells produced the pro-inflammatory interleukins IL1b, IL6, and tumor necrosis factor-alpha (TNFa) through the nuclear factor-κB (Nf-kB) pathway. T-cell recruitment and cytokine production were detected in the choroid plexus of post-mortem IVH/PHH samples.

Conclusion

These data strongly support the role of EV-mediated inflammation in the pathogenesis of PHH. T-cell activation occurred through the Nf-kB pathway and resulted in robust production of several cytokines implicated in PHH. Further delineating CSF EV-mediated inflammation and CSF cell profiling may inform targeted treatments to prevent the debilitating, lifelong sequelae of PHH.

9:32 – 9:41 HIF2alpha Modulation Reduces Neurological Sequelae of Existing Posthemorrhagic Hydrocephalus in Rats

Shenandoah Robinson, MD

Introduction

Children with posthemorrhagic hydrocephalus of prematurity (PHHP) are predisposed to epilepsy and cerebral palsy. Some recover from intraventricular hemorrhage (IVH) without sequelae, suggesting possible recovery. We hypothesize chronic modulation of persistent inflammation ameliorates failed recovery that leads to hydrocephalus and co-morbidities.

Objectives

Test if hypoxia-inducible-factor-2-alpha (HIF2alpha) modulation restores function after IVH.

Methods

To induce preterm injury, dams underwent laparotomy and intrauterine insult. On postnatal-day 1 (P1), pups (both sexes) were coded and underwent IVH. Shams underwent anesthesia with laparotomy only. On P21, PHHP rats were randomized to HIF2alpha agonism with FG4592 plus melatonin or vehicle (P21-P30 then qMWF). Digital gait analyses, touchscreen cognitive testing and seizure threshold using pentylenetetrazol were performed. Group differences were tested for normality, and compared with two-way ANOVA or Kruskal-Wallis with posthoc corrections; $p<0.05$ was considered significant.

Results

At P30, vehicle-treated PHHP rats (n=9) show elevated ICP compared to shams (n=17) and HIF2alpha agonism-treated PHHP rats (n=7, $p<0.05$). Vehicle-treated PHHP rats (n=10) also exhibit abnormal gait, compared to shams (n=17) and HIF2alpha-treated PHHP rats (n=10, all $p<0.05$). In visual discrimination, vehicle-treated PHHP rats (n=24, 71%passed) perform worse than shams (n=32, 91%passed) and HIF2alpha-treated PHHP rats (n=24, 92%passed). Cognitive flexibility shows improvement with HIF2alpha agonism. Vehicle-treated PHHP rats exhibit a lower seizure threshold than shams that normalizes with HIF2alpha treatment.

Conclusion

Our preclinical results suggest that HIF2alpha agonism begun at toddler-equivalent age can improve hydrocephalus, gait and epilepsy. Persistent inflammation from IVH may preclude endogenous neural cell repair, and HIF2alpha modulation offers a pharmacologic strategy to reduce shunt dependence and related sequelae.

9:41 – 9:50 Discussion

9:50 – 10:05 Break

10:05 – 11:40 Peer Reviewed Abstract Session X: Tumor Clinical Science
Moderators: Alfredo Quinones-Hinojosa and Nader Sanai

10:05 – 10:14 Prognostication: Meningioma methylation risk groups and molecular groups correlate with progression free survival

Mitesh Shah, MD

Introduction
Meningioma are common and usually benign. However, 25% behave aggressively despite resection and radiation. Meningiomas may behave aggressively despite benign appearing histology. Recently, methylation profiles and molecular markers have been associated with early recurrence.
Objectives
We aimed to stratify risk groups of patients with meningiomas that correspond with shorter progression free survival based on methylation and molecular profiling.
Methods
All meningiomas harvested underwent DNA methylation analysis and RNA sequencing. Clinical recurrence data was obtained from the electronic medical records. Methylation risk groups were stratified as low or high risk based on their calculated methylome recurrence risk. Molecular groups (MG) were identified and stratified from 1 to 4. Classification was completely blinded to clinical outcome. We then correlated methylation and MG with progression free survival (PFS) based on radiographic follow up.
Results
Among the 365 meninigioma samples (avg. follow up 23.3 months), MG4 conferred the largest risk of recurrence when compared with MG1-3 (HR 6.68). High-risk methylation groups were also significantly associated with recurrence when compared with low-risk methylation meningiomas (HR4.67). Although 90.5% of WHO 1 meningiomas were methylation low risk, 9.5% were considered methylation high risk. MG classification of WHO 1 meningiomas fit the following profile: 23.0% MG1,48.2% MG2,23.9%MG3, 5% MG4. 44.2% of WHO 2 meningiomas were considered methylation low risk and 55.8% were high risk (14.3% MG1,26.0%MG2, 41.6% MG3, 18.2% MG4). All WHO 3 meningiomas were methylation high risk (55.6% MG3, 44.4% MG4). High-fisk methylation profile was assiciated with median PFS 5.1 years whereas low-risk methylation was assiciated with 7.6 year median PFS ($p<0.0001$). Similarly, there was a stepwise decrease in 5-year PFS prevalence as MG increased (MG1 87.5%, MG2 80.5%, MG3 61.4%, MG4 42.6%; p0.0002).
Conclusion
Meningioma methylome analysis and MG stratification are associated with recurrence risk and may aid clinicians in planning optimal adjuvant therapy. Many histologically benign appearing meningiomas have more aggressive methylation and molecular profiles that are associated with earlier recurrence.

10:14 – 10:23 DNA Methylation Provides Diagnostic Value for Meningioma Recurrence in Clinical Practice

Ketan Bulsara, MD

Introduction

Meningiomas were classified into 3 grades and 15 subtypes, with three grades of malignancy based on morphological features. • Recent advancements in the genetic profiling of tumors have allowed information - including DNA copy number analysis, mutational analysis, and RNA sequencing - to be more frequently reported, in turn allowing better characterization of meningiomas. Analysis of DNA tumor methylomes that reflect both cell-origin methylation signatures and somatically-acquired DNA methylation alterations have been utilized to better classify meningiomas with great success. DNA methylation profiling is now coupled with genomic, transcriptomic, and proteomic information in order to stratify meningioma cases into clinically-meaningful classes for better characterization of disease progression, biological drivers, and therapeutic options. Few centers in the United States have incorporated the use of DNA methylation information into routine clinical practice for disease diagnosis and prognosis.

Objectives

Evaluate the benefit of clinical DNA methylation in predicting patient clinical course.

Methods

Brain tumor samples were de-identified and extracted using the Qiagen AllPrep DNA/RNA FFPE kit. Genomic profiling was conducted at the Jackson Laboratory for Genomic Medicine. Samples underwent final preparation using Infinium MethylationEPIC reagents and were loaded onto Infinium MethylationEPIC arrays. Classifier output consisted of assigned methylation classifications along with confidence scores, with scores ≥0.84 classified as "high confidence." • Unsupervised clusterings of meningiomas were grouped into six "methylation classes." They were designated as "Benign-1," "Benign-2," "Benign-3," "Intermediate-A," "Intermediate-B," and "Malignant."

Results

In our case series, we report DNA methylation profiling on 18 meningioma samples from 17 patients. In accordance with prior reports, more "malignant" methylation classes were identified in tumors with higher WHO histological grades and in patients with more aggressive clinical courses. In addition, DNA methylation profiling identified biologically and clinically distinct subclusters among tumors with the same WHO histology grade. • Our case series shows that DNA methylation combined with WHO histology classification can more accurately predict tumor behavior than WHO histology classification alone.

Conclusion

Our case series shows that DNA methylation combined with WHO histology classification can more accurately predict tumor behavior than WHO histology classification alone.

10:23 – 10:32 Correlation of Clinical Features to DNA Methylation-based Prognostic Subtypes in Chordoma Patients

Gelareh Zadeh, MD, PhD

Introduction

Chordomas are rare aggressive primary bone cancers affecting the skull-base and spine. We have previously identified robust DNA methylation-based prognostic groups, immune infiltrated and cellular subtypes.

Objectives

Here we sought to further characterize these prognostic subtypes with an extensively annotated clinical database to identify factors that correlate with subtype, and investigate methylation patterns between existing clinical scoring systems groups.

Methods

68 patients from a multi-institutional 20-year series were identified. These patients' tumor samples had undergone whole genome DNA methylation profiling on the Illumina EPIC array. Baseline clinical features, including clinical features, treatment details, outcomes parameters and imaging were analyzed using chi-squared or kruskal-wallis test, and differential methylation patterns were examined between clinically distinct groups based on the Sekhar scoring system.

Results

Of all the variables tested, age of onset (p-value 0.012), location (skull base vs spine vs sacral: p-value 0.0365) and histological subtype (classical vs chondroid: p-value 0.0132) were the only significant predictors of subgroup placement; older age, spinal location, and classical histological typing were predictors of immune infiltrated chordoma subtype, which has a poorer clinical performance. As expected, death from chordoma was significantly different between subtypes (p-value 0.0056). Patients survival stratified based on Shakur grading, and clustered together on unsupervised hierarchical analysis on methylation.

Conclusion

Overall, there are limited variables that correlate with methylation subtype, meaning that the epigenetic chordoma subtypes cannot be reliably identified using clinical or imaging features in the absence of molecular data. However clinical grading systems remain a valuable tool for prognostication, and display distinct methylation patterns.

10:32 – 10:41 High-Fidelity Carotid Injury Simulation: Analysis of Training Outcomes by Expert Surgeons vs. Computer-Vision Algorithms

Gabriel Zada, MD

Introduction

Benefits of simulation training are becoming increasingly realized in neurological surgery. We developed and nationally deployed a standardized cadaveric perfusion-based model to replicate internal carotid artery injury (ICAI) management during endoscopic endonasal approaches.

Objective

To evaluate simulation training outcomes and ability of a computer vision (CV)-based algorithm to predict outcomes using standardized simulation video.

Methods

Prospective data derived from repeated trials (T1, T2) in the validated ICAI model (n=177) were analyzed (trial success rate, time to hemostasis (TTH), blood loss (BL), and surgeon heart rate). Video data (147 trials) were hand-annotated (29,151 frames) to train a CV-based deep-learning neural network algorithm (SOCALNet). Expert neurosurgeon versus SOCALNet predictions of trial outcomes using the first minute of video (20 additional trials) were compared.

Results

Trial success (ICAI control) improved from 56% to 90% ($p < 0.0001$) from T1 to T2. BL and TTH decreased by 37% and 38%, respectively ($p < 0.0001$). The most improved participant quartile demonstrated trial success improvement from 25.6% to 100% ($p < 0.0001$). Tachycardia occurred in 57% of surgeon participants, but attenuated during T2, consistent with development of resiliency. Experts correctly predicted 14/20 trials (Sensitivity: 82%, Specificity: 55%, NPV: 71%, inter-rater reliability 0.95). SOCALNet correctly predicted 17/20 trials (Sensitivity 100%, Specificity 66, NPV 100%), had superior performance, and identified all successful attempts.

Conclusion

Simulated intervention promoted surgeon performance, development of cognitive skills and resiliency. Rare, life-threatening intraoperative complications may be optimal targets for simulations. CV analytics predicted outcomes as favorably as experts, demonstrating meaningful surgical video assessment and virtual coaching potential.

10:41 – 10:50 Intraoperative Radiotherapy (IORT) in Neuro-Oncology: Lessons Learned in Brain Metastases

Christopher Cifarelli, MD, PhD

Introduction

While adjuvant radiation remains critical in the management of many intracranial tumors treated via surgical resection, the optimal modality and timing of radiotherapy remains the subject of considerable debate. Brain metastases (BMs) requiring surgical resection based on size, symptomology, or need for pathological diagnosis routinely undergo post-operative treatment via either SRS or fractionated radiotherapy techniques.

Objective

The recent emergence of intraoperative radiotherapy (IORT) offers another option for management with the potential for improvement in local control via elimination of time to initiation of radiation from surgery, dose escalation beyond SRS or fSRT, and improved target delineation.

Methods

Utilizing IORT in conjunction with surgical resection for brain metastases, we have developed an international data registry to monitor outcomes including local control, distant brain failure (DBF), dosimetry analysis of organs at risk, seizure risk, radiation necrosis (RN), and overall survival.

Results

Between 2017 and 2023, 120 unique patients received IORT for BMs over five institutions in Germany, Brazil, and the USA. 1-yr local control rate was 88% with cavity wall doses between 20Gy and 30Gy. Dosimetric comparison in a subset of patients revealed superior homogeneity indices for single fraction IORT (0.56) compared to single session SRS (0.77) with a higher dose delivery of 30Gy to the margin in the IORT cohort. RN rates were <8% including patients receiving additional radiation treatment for DBF sites.

Conclusion

Registry data reporting for IORT in BMs indicate safety and efficacy in patients requiring surgical management of BMs.

10:50 – 10:59 How Patients with Brain Metastases Die

Douglas Kondziolka, MD

Introduction

Targeted therapies and a wider role for stereotactic radiosurgery (SRS) have resulted in significantly longer survival for patients with brain metastases. But there remains limited data on which aspects of disease and which mechanisms primarily cause these patients to die in the modern treatment era.

Objective

This study establishes new definitions for cause-of-death analyses and characterizes the frequencies of causes of terminal decline in patients with brain metastases.

Methods

NYUMets-Brain - the largest, longitudinal, real-world, open dataset of patients with brain metastases - and review of electronic health records allowed for the determination of primary causes of death in patients with brain metastases while treated at NYU with SRS between 2012 and 2021. Causes were classified in mutually exclusive, but collectively exhaustive categories. Multilevel models evaluated for differences in dynamics of intracranial tumors, including changes in volume and number.

Results

Of 440 patients that died during the study period, 73.2% died secondary to systemic disease, 10.2% secondary to CNS disease, and 16.6% due to other causes (including thrombotic events, infections, and other acute or

chronic diseases). CNS deaths were driven by acute increases in intracranial pressure (11%), development of focal neurologic deficits (18%), treatment-resistant seizures (11%), and global decline driven by increased intracranial tumor burden (60%). Rate of influx of new intracranial tumors was almost twice as high in patients that died compared to those that survived ($p < 0.001$), but there was no difference in rates of volume change per intracranial tumor ($p = 0.95$).

Conclusion

With modern treatments, most patients with brain metastases die from systemic disease progression. Even for the patients that die from neurologic disease, tumor dynamics and cause-of-death mechanisms suggest that death is most often due to unrelenting spread of new tumors to the CNS from unchecked systemic disease rather than failure of local control.

10:59 – 11:08 NRG-BN002: Phase I Study of Ipilimumab, Nivolumab, and the Combination in Patients with Newly Diagnosed GBM

Andrew Sloan, MD

Introduction

NRG-BN002: Phase I Study of Ipilimumab, Nivolumab, and the Combination in Patients with Newly Diagnosed GBM.

Objective

This study evaluated the safety of anti-CTLA-4 and anti-PD-1 ICIs alone or in combination in newly diagnosed GBM after completion of standard radiochemotherapy with the subsequent intent to test combinatorial ICIs in this setting.

Methods

Phase I study with endpoint of dose limiting toxicity (DLT) for adults with unifocal, supratentorial newly diagnosed GBM after resection and chemoradiation. Ipilimumab and nivolumab were tested separately and in combination with a planned expansion cohort dependent upon DLT results.

Results

Thirty-two patients were enrolled at 9 institutions; 6 to each DLT assessment cohort and 14 to the expansion cohort. Median age: 55 years, 67.7% male, 83.9% white. Treatment was well tolerated with a 16% Grade 4 events; the combination did not have unexpectedly increased toxicity, with no Grade 5 events. One DLT was seen in each single-agent treatment; none were observed in the combination, leading to expanded accrual of the combined treatment. Median follow-up was 19.6 mo. For all patients receiving combination treatment, median overall survival (OS) and progression-free survival (PFS) were 20.7 mo. and 16.1 mo., respectively.

Conclusion

IPI and NIVO are safe and tolerable with toxicities similar to those noted with other cancers when given in combination with adjuvant TMZ for newly diagnosed GBM. Combination IPI+NIVO is not substantially more toxic than single agents. These results support a subsequent efficacy trial to test the combination of ICIs in a phase II/III for patients with newly diagnosed GBM (NRG BN-007) which is ongoing.

11:08 – 11:17 Re-purposing deep brain stimulators as electric field therapy (EFT) as treatment for glioblastoma

Clark C Chen, MD, PhD

Introduction

Though alternating electric field therapy (EFT) for glioblastoma received FDA approval, biophysical modeling suggests that field strength generated by scalp electrodes may not sufficiently extend to deep, subcortical regions.

Objective
We explore the anti-tumor activity of electric field (EF) generated by electrode directly implanted into glioblastomas, with the goal of repurposing deep brain stimulators as a therapeutic platform.
Methods
Laboratory characterization and murine modeling.
Results
In vitro, activation of leads of a deep brain stimulator induced tumoricidal activity within the region encompassed by the EF. To further characterized this tumoricidal activity, a customized two-electrode array was designed and fabricated to allow study of glioblastoma cells seeded at the center of the EF. Consistent with the observations made using the deep brain stimulator electrode, electric field therapy (EFT) induced both necrosis and apoptosis of glioblastoma cells. To characterize this effect in vivo, a four-electrode array was designed and fabricated such that tumor cells can be implanted through a center channel equidistant the electrodes. Mice were implanted with this array, followed by luciferase labelled murine glioblastomas through the center channel. After tumor engravement, mice were randomized to EFT or placebo. EFT was associated with significant diminishment of tumor growth (measured by bio- bioluminescence) and prolonged survival. Analysis of brain sections following EFT showed a notable increase in peri-tumoral microglia accumulation, suggesting potential of EFT as an immune-modulation platform.
Conclusion
Our results suggest therapeutic potential for repurposing of deep brain stimulator as glioblastoma therapy, with opportunities for therapeutic enhancement through novel electrode design and stimulation parameter modulation.

11:17 – 11:26 Low-grade glioma imaging volumes and survival: A single-institution analysis of 103 patients after resection using iMRI

Randy Jensen, MD

Introduction
Intraoperative magnetic resonance imaging (iMRI) is a tool for maximizing resection of low-grade gliomas (LGGs) but the impact of this on patient outcome is not completely understood
Objective
In this single-institution study of patients with LGGs who underwent resection using iMRI, the we present a volumetric-based survival analysis to evaluate progression-free survival (PFS) and overall survival (OS) with a particular emphasis on intial tumor volume, impact of extent of resection and additional resection after iMRI on patient outcome.
Methods
This retrospective analysis included patients with LGGs who underwent resection using iMRI from 2011 to 2021. Volumetric analyses of T2-weighted (T2W), and T2W fluid-attenuated inversion recovery (FLAIR) MRI sequences were assessed at preoperative, intraoperative, immediate postoperative, and three-month postoperative timepoints. Statistical analyses were carried out using log-rank and multivariable Cox proportional hazard regression analyses.
Results
A total of 103 patients (median age 36.0 years) were treated. We found statistically significant associations between greater EOR of both T2 and FLAIR volumes and longer PFS and OS on both univariate and multivariate analysis (p=0.03 and p=0.04, respectively). Median EOR was 91%. Further resection was performed 52% of the time with 85% of the tissue from additional surgery demonstrating tumor. There was no observed association in either PFS or OS for patients undergoing additional resection after initial iMRI scan (p=0.67 and p=0.98). The results demonstrated significant associations between lower volume of

preoperative T2W/FLAIR , intraop T2W/FLAIR, post op T2W/FLAIR and 3-month postoperative T2W FLAIR volumes with longer PFS and OS (p=0.016-0.001).

Conclusion

Intraoperative MRI for low grade gliomas may help achieve high rates of extent of resection however further resection after MRI doe s not predict improved outcomes. Extent of resection and lower T2 and FLAIR volumes at all phases of preop, intraop and post op imaging were significant prognosticators with respect to PFS and OS.

11:26 – 11:40 Discussion

11:40 – 12:43 Peer Reviewed Abstract Session XI: Epilepsy/Functional/Pain Clinical Science
Moderators: Aviva Abosch and Andres Lozano

11:40 – 11:49 Speech arrest redefined: premotor cortex function for active inhibition of speech

Edward Chang, MD

Introduction

Natural speech is full of starts and stops. Here, we studied the neural mechanisms that underlie the inhibitory control of speech, specifically the ability to stop speaking on demand.

Objectives

To probe the mechanisms of active speech inhibition.

Methods

We recorded direct cortical activity while participants spoke sentences and were given a visual cue to stop speaking. We used high-density electrocorticography (ECoG) to record cortical regions across frontal, parietal, temporal, and medial areas. This methodology provided extensive spatial sampling and fine temporal resolution to track millisecond level dynamics that are essential for both speech production and stopping. Participants performed a task where they were required to immediately start and stop speaking in response to visual cues.

Results

Neural recordings revealed activity in the premotor frontal cortex associated with speech stopping. Cortical sites showing stop activity were largely distinct from sites involved in active speech production or, more specifically, encoding articulatory movements. Electrocortical stimulation mapping at many premotor sites with stop activity caused involuntary speech arrest, an immediate inability to speak or vocalize. Furthermore, many speech arrest sites did not co-localize with neural activity correlating with speech motor planning or execution, contrary to this long-assumed function in clinical brain mapping.

Conclusion

Together, these results suggest a novel premotor cortical network that underlies the inhibitory control of speech, which has significant implications for understanding the dynamics of normal and altered speech production, as well as clinical brain mapping.

11:49 – 11:58 Trial of Globus pallidus Focused Ultrasound Ablation in Parkinsons Disease

Vibhor Krishna, MD

Introduction

Unilateral focused ultrasound ablation of the globus pallidus improved motor symptoms of Parkinson's disease (PD) in open-label trials.

Objectives

We tested its safety and efficacy in a multicenter, double-blind, sham-controlled randomized trial.

Methods

PD subjects with significant motor complications of medical treatment (characterized by dyskinesias or motor fluctuations) were enrolled and randomly assigned in a 3:1 ratio to focused ultrasound or sham treatment. Subjects were confirmed to have a motor impairment score ≥20 using the Movement Disorders Society Unified Parkinson's Disease Rating Scale subscale III (MDS UPDRS III) and levodopa responsiveness (defined as a 30% decline in MDS UPDRS III score after levodopa). The primary outcome was the number of responders at three months, defined by a pre-specified composite score measuring clinically meaningful reduction in either dyskinesia (defined as ≥3 points decline in the unified dyskinesia rating score (UDysRS) and/or improvement in motor impairment (defined as ≥3 points decline in the MDS UPDRS III score).

Results

Ninety-four subjects were randomly assigned to unilateral globus pallidus focused ultrasound ablation (n=69) or sham treatment (n=25). Sixty-five focused ultrasound and 22 sham subjects completed the primary outcome assessment. Forty-five subjects (69.2%) in the focused ultrasound group were responders in contrast to 7 (31.8%) in the sham group (Odds ratio: 4.8, 95%CI: 1.7-13.6, p=0.003). After focused ultrasound ablation, MDS UPDRS III improved in 19 (29.2% subjects, mean improvement: 49.2%), UDysRS in 8 (12.3% subjects, mean improvement: 66.7%), and both MDS UPDRS III and UDysRS improved in 18 (27.7% subjects, mean improvements: 39.5% and 70.3% respectively). Pallidotomy-related adverse events were mild or moderate and transient.

Conclusion

We report significant improvement in dyskinesia and motor impairment in subjects with Parkinson's disease undergoing unilateral focused ultrasound ablation of the globus pallidus.

11:58 – 12:07 Phase 1 trial of human ES-derived dopamine neurons for Parkinson's disease

Viviane Tabar, MD

Introduction

Advances in human stem cell technology have led to great scientific discovery but the path to the clinic has been challenging. Parkinson's disease (PD) has long been a target for cell replacement therapy but progress has stalled due to challenges with cell sources among others. Here we will provide the results (currently embargoed until July) of a first-in-human clinical trial of an investigational cell product consisting of dopaminergic neurons derived from human embryonic stem cells, for cell replacement therapy in PD.

Objectives

This first-in-human Phase 1 study aims to assess the safety, tolerability, clinical efficacy, and functional imaging measures of bemdaneprocel in subjects with PD.

Methods

In this open-label, non-controlled study, 12 subjects have received 1 of 2 doses of dopamine neurons delivered stereotactically to the post-commissural putamen bilaterally, along with a 1-year immunosuppression regimen. Safety and tolerability have been assessed, along with assessments of engraftment and clinical impact.

Results

At screening, the average age was 66.4 yrs (57-77) and the mean time since diagnosis was 9.1 yrs (5-14). All subjects presented at screening with a Hoehn and Yahr stage of 2 in the on-medication state. The mean MDS-UPDRS part III score was 46.6 (15-73) when assessed in the off-medication state, and patients presented with 4.3 (1.4-6.2) average daily hours of OFF time as assessed by PD diaries. In both cohorts, the safety profile is favorable with the vast majority of reported treatment-emergent adverse events (AEs)being mild to moderate

in nature. There were no AEs reported as possibly related to the cell therapy. Clinical assessments post surgery included MDS-UPDRS, PD Diaries, PDQ-39 and others. Patients also underwent 18-fluoro-Dopa PET imaging to detect evidence for graft survival and function.

Conclusion

Full data will be discussed at the meeting as it is currently embargoed until July. We are very optimistic about the potential for a sustained disease-modifying impact of cell replacement therapy on PD. Future directions include addressing additional challenges to cell survival and integration in the PD microenvironment, among others. PD may represent an excellent stepping stone for other applications of stem cell therapy in CNS disorders.

12:07 – 12:16 Safety and early efficacy of convective delivery of AAV2-GDNF gene therapy for Parkinsons disease

Russell Lonser, MD

Introduction

Dopaminergic cell loss underlies the pathobiology of Parkinson's disease (PD). Glial cell line-derived neurotrophic factor (GDNF) plays critical role in the development and maintenance of dopaminergic neurons. Consequently, sustained and augmented production of intratriatal GDNF could have regenerative properties in PD.

Objective

To define the safety and early efficacy of direct convective delivery of adeno-associated virus (serotype 2, [AAV2]) containing the GDNF gene (AAV2-GDNF) for regenerative gene therapy in PD.

Methods

PD patients (early- [n=4] or moderate-stage [n=6]) enrolled in a Phase 1b study underwent bilateral putaminal perfusion with AAV2-GDNF (upto 1.8 milliliters of AAV2-GDNF [3.0x1012 vg/mL] with gadoteridol [2mM]). Clinical findings, Unified Parkinson's Disease Rating Scale (UPDRS) scores, levodopa equivalent dose (LED) and imaging were analyzed.

Results

Ten patients were included (follow-up greater than 9 months). Mean duration from PD diagnosis in patients was 1.95±0.44 years (early-stage) and 8.0±0.71 years (moderate-stage). Early-stage patient mean baseline UPDRS III score was 19.5±3.25 points (OFF) and 7.67±0.99 points (ON) with a mean LED of 541 mg/day. Early-stage patient 6-month post-treatment UPDRS III scores revealed stability (mean change, -2.67±2.28 [OFF] and -1.6±1.21 [ON]). Moderate-stage patient mean baseline UPDRS III (OFF) was 40.75±3.71 points and 24.0±3.44 points (ON) with a mean LED of 840 mg/day. Moderate-stage patient 6-month UPDRS III scores revealed significant improvement (mean change, -12.3±4.13 [OFF] and -6.8±5.44 [ON]). LED requirements remained stable in both cohorts. Putaminal coverage was similar in both cohorts (mean, 62.5%±3.09%). All participants tolerated the infusions without complication.

Conclusion

MR-imaging guided convective perfusion of the bilateral putamina with AAV2-GDNF was safe and well-tolerated in PD patients. There were PD-stage dependent clinical improvements to AAV2-GDNF gene therapy that was associated with LED stability.

12:16 – 12:25 Explantable endocisternal neural interfaces for wireless bi-directional neuromodulation

Peter Kan, MD

Introduction

Minimally invasive neural interfaces significantly decrease the risks of surgical complications and can be used to treat many disorders. Existing neurotechnologies rely on invasive surgeries with penetrating electrodes or, more recently, endovascular approaches. However, endovascular neural interfaces will require a lifetime prescription of anti-thrombotic medication, and the endothelialization of vascular implants makes it challenging to explant any devices.

Objectives

Here, we demonstrate a chronic endocisternal neural interface that can stimulate and record cortical brain activity within the subarachnoid space over the brain convexity, deep brain structures within the ventricles, and the spinal cord from the spinal subarachnoid space.

Methods

Taking advantage of magnetoelectric materials for miniaturization, the entire wireless system is deployable through a percutaneous procedure, and the electrode interface is introduced through a lumbar puncture in a large animal model.

Results

The flexible catheter electrodes can be freely navigated throughout the body from the spinal to cranial subarachnoid space, and also from the cranial subarachnoid space to the ventricles. We can also explant the neural interface after chronic implantation.

Conclusion

This enables applications in therapies that require transient or permanent brain/machine interface such as stroke rehabilitation and epilepsy monitoring and opens up a new class of minimally-invasive intraventricular bioelectronics.

12:25 – 12:34 Expansion Of Stereotactic Work Envelope Using Transformation Matrix And Geometric Algebra For Neurosurgery

Kendall Lee, MD, PhD

Introduction

Stereotactic systems have used cartesian coordinate systems and linear algebraic mathematical models to navigate the brain. Previously the Mayo Neural Engineering Labs have developed the NaviNetics stereotactic system that allows for improved patient comfort, reduced size, and carries through the intuitive interface for users. However, the system was designed with a work envelope and trajectory range optimized for DBS applications.

Objectives

Here we developed a system of translational and rotational adapters with the principle of geometric algebra that would allow total brain navigation capabilities.

Methods

The adapter was designed using Solidworks™ and fits onto the skull anchor key of the NaviNetics frame, allowing for both rotation and translation of the work envelope. We then developed the mathematical formulas for the transformation matrix, allowing new coordinate determination for each of the skull anchor key adapters, using both traditional transformation matrix and geometric algebra. We tested the operational mechanics, as well as examined the system's mechanical and image-guided accuracy using ground truth fixture. The system's clinical workflow and its ability to reliably and accurately be used in a mock surgical scenario was investigated using a cadaver head, CT guidance and Medtronic Stealth software.

Results

We designed and 3D-printed a total of 8 adapters that allowed the work envelope to be expanded to the total head. The mathematical transform formulae using both transformation matrix and geometric algebra generated identical results that accurately reflected the expanded work envelope. The mechanical accuracy

test using ground truth fixture was 1.75 ± 0.20 mm (n=29 targets) and the cadaver study was 1.05 ± 0.28 mm (n=7 implantations).

Conclusion

Here, we demonstrate a novel application using conventional and geometric algebra in conjunction with hardware modifications to expand the work envelope of the NaviNetics stereotactic system to the entire cranial cavity, thereby expanding the clinical applications and the use of stereotactic navigation beyond that of DBS targeting.

12:34 – 12:43 Discussion

12:43 – 12:45 Closing Remarks & Meeting Adjourn

Shenandoah Robinson

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JUAN URIBE Barrow Neurological Institute juansuribe@gmail.com	2022	ACTIVE

ALEX B. VALADKA (Patti) Seton Brain and Spine Institute avaladka@gmail.com	2007	SENIOR
HARRY R. VAN LOVEREN (Jeffrie) University of South Florida hvanlove@health.usf.edu	1995	SENIOR
MICHAEL A. VOGELBAUM (Judith Rosman) Moffitt Cancer Center Michael.Vogelbaum@moffitt.org	2012	ACTIVE
DENNIS G. VOLLMER (Dorothy) University of Virginia Health System dv2k@hscmail.mcc.virginia.edu	2001	SENIOR
RAND M. VOORHIES (Terry) Southern Brain and Spine branemd@aol.com	1996	SENIOR | RETIRED
TOSHIHIKO WAKABAYASHI (Midori) Nagoya University Graduate SOM wakabat@med.nagoya.u.ac.jp	2013	CORRESPONDING
M. CHRISTOPHER WALLACE (Katie) University of Toronto wallacec@kgh.kari.net	2003	SENIOR | RETIRED
HOWARD L. WEINER (Barbara) Texas Children's Hospital hlweiner@texaschildrens.org	2020	ACTIVE
BRYCE K. A. WEIR (Mary Lou) University of Alberta & Chicago brycekeithweir@gmail.com	1984	SENIOR | RETIRED

MARTIN H. WEISS (Debby) University of Southern California weiss@email.usc.edu	1981	SENIOR | RETIRED
H. RICHARD WINN (Deborah) Mount Sinai School of Medicine HRWinn64@gmail.com	1993	SENIOR | RETIRED
FREMONT P. WIRTH (Lynn) Neurological Institute of Savannah fpwirth1@att.net	1993	SENIOR | RETIRED
JEFFREY H. WISOFF (Deborah) NYU Langone Medical Center jhw1@nyulangone.org	2012	SENIOR
GRAEME F. WOODWORTH University of Maryland gwoodworth@som.umaryland.edu	2021	ACTIVE
M. GAZI YASARGIL (Dianne) University of Arkansas dianne9182@gmail.com	1975	SENIOR CORRESPONDING
DANIEL YOSHOR (Shira) University of Pennsylvania Daniel.yoshor@pennmedicine.upenn.edu	2016	ACTIVE
A. BYRON YOUNG (Judy) University of Kentucky Medical Center byoung9560@aol.com	1989	SENIOR | RETIRED
HAROLD F. YOUNG (Theresa) Medical College of Virginia hfyoung@vcu.edu	1994	SENIOR

GELAREH ZADEH Toronto Western Hospital gelareh.zadeh@uhn.ca	2017	ACTIVE
ERIC L. ZAGER (Marirosa Colon) University of Pennsylvania Hospital Eric.Zager@pennmedicine.upenn.edu	2006	SENIOR
NICHOLAS T. ZERVAS Massachusetts General Hospital nzervas@partners.org	1972	SENIOR | RETIRED
GREGORY J. ZIPFEL (Mary Jo) Washington University School of Medicine zipfelg@wustl.edu	2013	ACTIVE

IN MEMORIAM
DECEASED MEMBERS

	ELECTED	DECEASED
EBEN ALEXANDER, JR.	1950	2004
JOAO (JOHN) L. ANTUNES	2001	2016
JAMES R. ATKINSON	1970	1978
PERCIVAL BAILEY (Honorary)	1960	1973
GEORGE BAKER	1940	1993
H. THOMAS BALLANTINE, JR	1951	1996
DONALD P. BECKER	1990	2020
GILLES P. BERTRAND	1967	2019
WILLIAM F. BESWICK	1959	1971
EDWIN B. BOLDREY	1941	1988
E. HARRY BOTTERELL	1938	1997
ROBERT BOURKE	1983	1996
SPENCER BRADEN, Founder	1938	1969
F. KEITH BRADFORD	1938	1971
JEAN BRIHAYE	1975	1999
JERALD S. BRODKEY	1977	2014
HOWARD BROWN	1939	1990
KARL-AUGUST BUSHE	1972	1999
FERNANDO CABIESES	1966	2009

LUC CALLIAUW	1988	2021
JUAN Y. CARDENAS	1966	1996
HARVEY CHENAULT	1949	2006
SHELLEY CHOU	1974	2001
JUAN CARLOS CHRISTENSEN	1970	2003
GALE CLARK	1970	1996
W. KEMP CLARK	1970	2007
DONALD COBURN	1938	1988
WILLIAM FRANCIS COLLINS JR.	1963	2009
EDWARD S. CONNOLLY	1972	2014
JAMES W. CORRELL	1966	2004
WINCHELL McK. CRAIG (Honorary)	1942	1960
EDWARD DAVIS	1949	1988
COURTLAND HARWELL DAVIS, JR.	1967	2018
EVANDRO DE OLIVEIRA	2002	2021
JACQUES C. DE VILLIERS	1986	2015
RICHARD L. DESAUSSURE, JR.	1962	2008
HERMANN DIETZ	1980	2016
PEARDON DONAGHY	1970	1991
CHARLES DRAKE	1958	1998
FRANCIS ECHLIN	1944	1988
DEAN ECHOLS, Founder	1938	1991
GEORGE EHNI	1964	1986
ARTHUR ELVIDGE	1939	1985
THEODORE ERICKSON	1940	1986
JOSEPH EVANS, Founder	1938	1985
WILLIAM H. FEINDEL	1959	2014
ROBERT G. FISHER	1955	2003
ELDON L. FOLTZ	1960	2013
RICHARD A. R. FRASER	1976	2017
JOHN FRENCH	1951	1989

LYLE A. FRENCH	1954	2004
JAMES GALBRAITH	1947	1997
HENRY GARRETSON	1973	2007
F. JOHN GILLINGHAM	1962	2020
SIDNEY GOLDRING	1964	2004
PHILIP GORDY	1968	2014
EVERETT G. GRANTHAM	1942	1997
JOHN WILLIS GREEN	1953	1990
JAMES GREENWOOD, JR.	1952	1992
ROBERT G. GROSSMAN	1984	2021
WESLEY A. GUSTAFSON	1942	1975
WALLACE B. HAMBY	1941	1999
HANNIBAL HAMLIN	1949	1982
JOHN WILLIAM HANBERY	1959	1996
JOHN HANKINSON	1973	2007
GRIFFITH R. HARSH, III	1980	2019
GEORGE HAYES	1962	2002
MARK PETER HEILBRUN	1984	2010
E. BRUCE HENDRICK	1968	2001
JESS D. HERRMANN	1938	1944
HENRY L. HEYL	1951	1975
JULIAN T. HOFF	1975	2007
HAROLD J. HOFFMAN	1982	2004
EDGAR M. HOUSEPIAN	1976	2014
WILLIAM E. HUNT	1970	1999
OLAN HYNDMAN	1942	1966
FABIAN ISMAT	1989	2019
SHOZO ISHII	1975	2012
KENNETH JAMIESON	1970	1976
JOHN A. JANE, SR.	1982	2015
PETER J. JANNETTA	1994	2016

SIR GEOFFREY JEFFERSON (Honorary)	1951	1961
HANS-PETER JENSEN	1980	2000
RICHARD JOHNSON	1974	1997
ELLIS B. KEENER	1978	2021
WILLIAM KEITH, Founder	1938	1987
GLENN W. KINDT	1977	2022
ROBERT B. KING	1958	2008
KATSUTOSHI KITAMURA	1970	2005
ROBERT KNIGHTON	1966	2004
RICHARD KRAMER	1978	2001
HUGO KRAYENBUHL (Honorary)	1974	1985
KRISTIAN KRISTIANSEN	1967	1993
THEODORE KURZE	1967	2002
LAURI LAITINEN	1972	2007
THOMAS LANGFITT	1971	2005
SANFORD LARSON	1989	2012
GUY LAZORTHES (Honorary)	1973	2014
WALPOLE LEWIN	1973	1980
RAEBURN LLEWELLYN	1963	2009
VALENTINE LOGUE (Honorary)	1974	2000
H.C. RUEDIGER LORENZ	1998	2008
HERBERT LOURIE	1965	1987
ALFRED LUESSENHOP	1977	2009
WILLEM LUYENDIJK	1973	1995
ROBERT MACIUNAS	1999	2011
ERNEST MACK	1956	2000
STEPHEN MAHALEY	1972	1992
LEONARD MALIS	1973	2005
GEORGE MALTBY	1942	1988
FRANK MARGUTH	1978	1991
DONALD MATSON	1950	1969

ROBERT E. MAXWELL	1992	2022
FRANK MAYFIELD, Founder	1938	1991
AUGUSTUS McCRAVEY	1944	1989
KENNETH McKENZIE (Honorary)	1960	1964
ROBERT L. McLAURIN	1955	2015
J. MICHAEL MCWHORTER	1989	2004
WILLIAM MEACHAM	1952	1999
JAMES MEREDITH	1946	1962
J. DOUGLAS MILLER	1988	1995
W. JASON MIXTER (Honorary)	1951	1968
EDMUND MORRISSEY	1941	1986
JOHN F. (SEAN) MULLAN	1963	2015
FRANCIS MURPHEY, Founder	1938	1994
BLAINE NASHOLD, JR.	1967	2014
GOSTA NORLEN (Honorary)	1973	1992
FRANK NULSEN	1956	1994
SIXTO OBRADOR (Honorary)	1973	1978
GUY ODOM	1946	2001
ROBERT OJEMANN	1968	2010
EDWARD OLDFIELD	1975	2017
PIETRO PAOLETTI	1989	1991
ANDREW T. PARSA	2012	2015
WILDER PENFIELD (Honorary)	1960	1979
HELMUT PENZHOLZ	1978	1985
PHANOR PEROT, JR.	1970	2011
BERNARD PERTUISET (Honorary)	1986	2000
BYRON CONE PEVEHOUSE	1964	2010
HANS-WERNER PIA	1978	1986
J. LAWRENCE POOL	1940	2004
ROBERT W. PORTER	1962	2021
ROBERT PUDENZ	1943	1998

JOHN E. RAAF, Founder	1938	2000
B. RAMAMURTHI	1973	2003
AIDAN RANEY	1946	2002
RUPERT B. RANEY	1939	1959
JOSEPH RANSOHOFF	1965	2001
THEODORE RASMUSSEN	1947	2002
BRONSON RAY (Honorary)	1992	1993
DAVID REEVES	1939	1970
DAVID REYNOLDS	1964	1978
ALBERT RHOTON, JR.	1984	2016
HUGO RIZZOLI	1973	2014
THEODORE ROBERTS	1976	2007
JAMES T. ROBERTSON	1971	2019
R. C. L. ROBERTSON	1946	1985
STEWART ROWE	1938	1984
KEIJI SANO (Honorary)	1975	2011
RICHARD SCHNEIDER	1970	1986
KURT-FRIEDRICH SCHURMANN	1978	2005
HENRY SCHWARTZ	1942	1998
R. MICHAEL SCOTT	1991	2023
WILLIAM SCOVILLE	1944	1984
EDWARD L. SELJESKOG	1992	2022
R. EUSTACE SEMMES (Honorary)	1955	1982
C. HUNTER SHELDEN	1941	2003
FREDERICK A. SIMEONE	1981	2022
JAMES C. SIMMONS	1975	2019
ROBERT SMITH	1989	2003
SAMUEL SNODGRASS	1939	1975
GLEN SPURLING (Honorary)	1942	1968
BENNETT M. STEIN	1970	2022
C. WILLIAM STEWART	1948	1948

KENICHIRO SUGITA	1988	1994
THORALF SUNDT, JR.	1971	1992
ANTHONY SUSEN	1965	2008
HENDRIK SVIEN	1957	1972
HOMER SWANSON	1949	1987
WILLIAM SWEET	1950	2001
LINDSAY SYMON	1982	2019
SUZIE CUNNINGHAM TINDALL	1990	2016
RUSSELL L. TRAVIS	1994	2022
JOHN S. TYTUS	1967	2011
ALFRED UIHLEIN	1950	1990
KJELD VAERNET	1970	2006
JOHN VAN GILDER	1980	2007
A. EARL WALKER	1938	1995
EXUM WALKER	1938	2001
ARTHUR WARD, JR.	1953	1997
E. SYDNEY WATKINS	1975	2012
THOMAS WEAVER, JR.	1943	1985
W. KEASLEY WELCH	1957	1996
BENJAMIN WHITCOMB	1947	1998
LOWELL E. WHITE, JR.	1971	2018
ROBERT WILKINS	1973	2017
CHARLES B. WILSON	1966	2018
BARNES WOODHALL	1941	1985
FRANK WRENN	1973	1990
DAVID YASHON	1972	2016