THE AMERICAN ACADEMY OF NEUROLOGICAL SURGERY

76th Annual Meeting
WaterColor Inn & Resort
Santa Rosa Beach, Florida
September 17 - 20, 2014

American Association of Neurological Surgeons

Jointly Provided by the AANS

Future Meetings

2015

Joint Meeting with the German Neurosurgical Society

European Hotel
Heidelberg, Germany

October 7-10, 2015

Mark your calendars now!

GENERAL INFORMATION

HOTEL INFORMATION

The WaterColor Inn & Resort
34 Goldenrod Circle
Santa Rosa Beach, Florida 32459
Phone: 850.534.5000
Website: www.watercolorresort.com/

REGISTRATION DESK LOCATION & HOURS:

Wednesday, September 17	12:00 pm – 6:00 pm
Thursday, September 18	6:00 am – 12:00 pm
Friday, September 19	6:00 am – 12:00 pm
Saturday, September 20	7:00 am – 12:00 pm

Program Summary

PROGRAM SUMMARY

WEDNESDAY, SEPTEMBER 17, 2014

Events	Time	Location
Registration	12:00 pm - 6:30 pm	WaterColor Inn Lobby
AAcNS Executive Committee Meeting	3:00 pm - 6:00 pm	Room Two
Welcome Reception *Music by the Neurosurgery Jazz Quartet*	6:30 pm - 9:30 pm	The Inn Green & Patio

THURSDAY, SEPTEMBER 18, 2014

Events	Time	Location
Registration	6:00 am - 1:00 pm	The LakeHouse Lobby
Members Breakfast & Business Meeting	6:30 am - 7:30 am	Room One
Spouse & Guest Breakfast	6:30 am - 9:30 am	The Gathering Spot
General Scientific Session	7:30 am - 1:05 pm	The LakeHouse
Spouses Program	10:00 am	Room Two
Lunch	At Your Leisure	
Golf Tournament	1:30 pm Shotgun Start	Shark's Tooth Golf Club
Afternoon Activities	See Concierge to Schedule	
Cocktail Reception & Dinner	7:00 pm - 10:00 pm	Fish Out of Water

FRIDAY, SEPTEMBER 19, 2014

Events	Time	Location
Registration	6:00 am - 1:00 pm	The LakeHouse Lobby
Members Breakfast & Business Meeting	6:30 am - 7:20 am	Room One
Members Photo	7:20 am	The Inn Green
Spouse & Guest Breakfast	6:30 - 9:30 am	Room Two
General Scientific Session	7:30 am - 12:20 pm	The LakeHouse
Spouses Program	10:00 am	Room Two
Presidential Address *"Triple Threat"*	12:20 - 1:00 pm	The LakeHouse
Lunch	At Your Leisure	
Golf	1:30 pm Shotgun Start	Camp Creek Golf Club
Tennis Tournament	2:00 pm	
Afternoon Activities	See Concierge to Schedule	
Cocktail Reception & Dinner *Black Tie Optional*	7:00 - 11:00 pm	The LakeHouse
Dancing with Music Garden		

SATURDAY, SEPTEMBER 20, 2014

Events	Time	Location
Registration	7:00 am - 12:00 pm	The LakeHouse Lobby
General Scientific Session & Breakfast	7:00 am - 11:15 am	The LakeHouse
Meeting Adjourned!		

About the AAcNS

AMERICAN ACADEMY OF NEUROLOGICAL SURGERY
2014 OFFICERS

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Mitchel S. Berger, MD

VICE PRESIDENT
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SECRETARY
Daniel L. Barrow, MD

TREASURER
E. Antonio "Nino" Chiocca, MD

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Daniel L. Barrow, MD
E. Antonio "Nino" Chiocca, MD
Griff Harsh IV, MD
Robert R. Harbaugh, MD

HISTORIAN
Donald Quest, MD

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2013 - 2014 COMMITTEES

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Matthew Howard III, MD
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Daniel L. Barrow, MD
E. Antonio "Nino" Chiocca, MD
James Markert (2013-2015)
Karin Muraszko (2014-2016)

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Nelson M. Oyesiku, MD
James Rutka, MD

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Fredric Meyer, MD
Mitchel Berger, MD

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Douglas Kondziolka, MD
Robert Spinner, MD

ROUND ROBIN EDITOR
Daniel L. Barrow, MD

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Robert Spinner, MD

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Robert Spetzler, MD – Senior Delegate
Jacques Morcos, MD – Second Delegate

RESEARCH ADVISORY COMMITTEE
Robert Friedlander, MD – Chair
Sander Connolly, MD
Murat Gunel, MD
Richard Ellenbogen, MD

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

PAST VICE-PRESIDENTS

Francis Murphey	1941	Ernest W. Mack	1975
William S. Keith	1942	Frank E. Nulsen	1976
John Raaf	1943	Robert S. Knighton	1977
Rupert B. Raney	1944	Robert G. Fisher	1978
Arthur R. Elvidge	1946	H Thomas Ballantine, Jr.	1979
F. Keith Bradford	1949	George Ehni	1980
David L Reeves	1950	Courtland H. Davis, Jr.	1981
Henry G. Schwartz	1951	John F. Mullan	1982
J. Lawrence Pool	1952	Hugo V. Rizzoli	1983
Rupert B. Raney	1953	James W Correll	1984
David L. Reeves	1954	E. Bruce Hendrick	1985
Stuart N. Rowe	1955	Griffith R Harsh, III	1986
Jess D. Hermann	1956	Ellis B Keener	1987
George S. Baker	1957	Robert Grossman	1988
Samuel R. Snodgrass	1958	Jim Story	1989
C. Hunter Shelden	1959	John Jane, Sr.	1990
Edmund Morrissey	1960	Stewart Dunsker	1991
Donald F. Coburn	1961 - 62	Burton M Onofrio	1992
Eben Alexander, Jr.	1963	Martin H Weiss	1993
George L Maltby	1964	John M. Tew, Jr.	1994
Robert Pudenz	1965	John C. VanGilder	1995
Francis A. Echlin	1966	Edward Connolly	1996
Benjamin Whitcomb	1967	George Ojemann	1997
Homer S. Swanson	1968	Charles H. Tator	1998
Augustus McCravey	1969 - 70	Donald O. Quest	1999
Edward W. Davis	1971	Howard M. Eisenberg	2000
John R. Green	1972	Richard B. Morawetz	2001
George J. Hayes	1973	Martin B. Camins	2002
Richard L. DeSaussure	1974	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

Past Secretary-Treasurers

Francis Murphey	1938 - 40
A. Earl Walker	1941 - 43
Theodore C. Erickson	1944 - 47
Wallace B. Hamby	1948 - 50
Theodore B. Rasmussen	1951 - 53
Eben Alexander	1954 – 57
Robert L. McLaurin	1958 - 62
Edward W. Davis	1963 - 65
Robert G. Fisher	1966 - 68
Byron C. Pevehouse	1969 - 72

Past Secretaries

Byron C. Pevehouse	1973
Russel H. Patterson, Jr	1974 - 76
Phanor L. Perot, Jr	1977 - 80
John T. Garner	1981 - 83
James T. Robertson	1984 - 86
Nicholas T. Zervas	1987 - 89
William A. Buchheit	1990 - 92
Julian T. Hoff	1992 - 95
Roberto C. Heros	1995 - 98
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

PAST TREASURERS

Russel H. Patterson, Jr.	1973
Phanor L. Perot, Jr	1974 - 76
John T. Garner	1977 - 80
James T. Robertson	1981 - 83
Nicholas T. Zervas	1984 - 86
William A. Buchheit	1987 - 89
Julian T. Hoff	1990 - 92
Roberto C. Heros	1992 - 95
David G. Piepgras	1996 - 98
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

Paul M. Lin	1955
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Byron C. Pevehouse	1957
Norman Hill	1958
Jack Stern	1959
Robert Ojemann	1960
Lowell E. Ford	1962
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Earle E. Crandall	1964
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Howard W. Blume	1977
Howard J. Senter	1978
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Dennis A. Turner	1981
Marc R. Mayberg	1982
David S. Baskin	1983
Kevin J. Kiwak	1984
Terry Lichtor	1985
Michael G. Nosko	1986
Joseph R. Madsen	1987
James T. Rutka	1988
Christopher D. Heffner	1989
Scott I. Gingold	1990
Mary Louise Hlavin	1991
Adam P. Brown	1992
Michael Tymianski	1993
David Garrett, Jr.	1994
L. Brannon Thomas	1995
John S. Yu	1996
Gregory Canute	1997
Nathan R. Selden	1998
Robert M. Friedlander	1999
Tien T. Nguyen	2000
Peng Chen	2001
Ganesh Rao	2002
Gelarch Zadeh	2003
Eric C. Leuthardt	2004
Manish Aghi	2005
Alfred T. Ogden	2006
Paul Kongkham	2007
Elias Rizk	2008
Costas Hadjipanayis	2009
Scellig Stone	2010
Paul S.A. Kalanithi	2011
Derek G. Southwell	2012
Nader Sanai	2013
Hani Malone	2014

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	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

A Special Thank You to the
following companies for providing educational grants
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AMERICAN ACADEMY OF NEUROLOGICAL SURGERY
76TH ANNUAL MEETING

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Mission & Objectives

MISSION STATEMENT:

The purpose of the live 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.

AMERICAN ACADEMY OF NEUROLOGICAL SURGERY

American Association of Neurological Surgeons

Jointly Provided by the AANS

LEARNING OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- Describe recent advances in techniques and basic biology of cerebrovascular disease
- Understand new concepts in brain and spinal trauma treatment
- Describe recent advances in brain tumor biology
- Identify novel translational approaches for glioma therapy
- Understand the complexity of new advances in spinal instrumentation
- Understand the advantages and disadvantages of randomized clinical trials compared with prospective databases in neurosurgery
- Discuss uses of stem cell and cellular transplantation in neurosurgery
- Describe novel imaging techniques and biomarkers in neurosurgery
- Understand recent basic and translational science and advances in functional and pediatric neurosurgery

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 AANS and the American Academy of Neurological Surgery. The AANS is accredited by the ACCME to provide continuing medical education for physicians.

DESIGNATION STATEMENT

The AANS designates this live activity for a maximum of **14.50** *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

INTENDED AUDIENCE/BACKGROUND REQUIREMENT

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

AANS JOINT PROVIDERSHIP DISCLAIMER STATEMENT

The material presented at the 76th Annual Meeting of the American Academy of Neurological Surgery has been made available by the American Academy of Neurological Surgery and the AANS 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 AANS, or its Committees, Commissions, or Affiliates.

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Disclosure Information

The AANS 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.

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.

Those who have disclosed a relationship with commercial interests are listed below:

NAME	DISCLOSURE	TYPE OF RELATIONSHIP
Christopher Ames	Consultant Fee	DePuy; Stryker; Medtronic
	Stock or Shareholder	Doctors Research Group; Visualase; Baxano Surgical
	Other Financial or Material Support	Biomet Spine (royalties); Aesculap (royalties); Fish & Richardson, P.C. (patent)
Ali Baaj	University Grants/ Research Support	DePuy
	Consultant Fee	DePuy; Ulrich
Gene Barnett	Consultant Fee	Monteris Medical
	Stock or Shareholder	Monteris Medical
Tracy Batchelor	Industry Grant Support	Pfizer; Astra Zeneca; Millenium
	Consultant Fee	Merck & Co., Inc.; Kirin Pharmaceuticals; Proximagen; Agenus
	Speaker's Bureau	Up To Date, Inc.; Research To Practice; Oakstone Medical Publishing; Imedex
Kristen Batich	Other Financial or Material Support	Provisional Patent (Use of Td Pre-Conditioning as a Method to Improve Immunization Efficacy)
Mitchel Berger	Consultant Fee	Ivivi; Pharmaco-Kinesis
	Stock or Shareholder	Ivivi

Shay Bess	University Grants/ Research Support Industry Grant Support Consultant Fee Honorarium	DePuy Synthes Spine; Medtronic DePuy Synthes Spine; Medtronic K2M; AlloSource K2M
Jeff Biernaskie	University Grants/ Research Support	Alberta Innovates Health Solutions; Canadian Institutes of Health Research
Gregory Bix	University Grants/ Research Support	University of Kentucky Research Support
Ennio Chiocca	Consultant Fee	Alcyone Biosciences; Stemgen; DNAtrix
Charles Conrad	Consultant Fee Stock or Shareholder	DNAtrix, Inc. DNAtrix, Inc.
Andrew Dailey	Industry Grant Support Consultant Fee Honorarium	Biomet Biomet AOSpine; DePuy Synthes
Annick Desjardins	Honorarium	Genentech USA, Inc.; EMD Serono, Inc.; Celldex Therapeutics; Eli Lilly and Company, LLC

Kevin Foley	Consultant Fee	Medtronic
	Stock or Shareholder	Bio-D; DiscGenics; Medtronic; Nuvasive; Spine Wave; TrueVision
	Fiduciary Position (outside AANS)	Bio-D; DiscGenics; Semmes-Murphey Clinic; TrueVision
	Other Financial or Material Support	ArthroCare Corporation (royalties); Medtronic (royalties)
Justin Fraser	University Grants/ Research Support	University of Kentucky Start-up Funds; University of Kentucky CCTS Support
Mark Gilbert	Industry Grant Support	Genentech; GlaxoSmithKline
	Consultant Fee	AbbVie
	Honorarium	Merck; Genentech
Christopher Glielmi	Employee [any industry]	Siemens Healthcare
Mark Griswold	Industry Grant Support	Siemens Medical Systems, Inc.; Siemens Master Research Collaboration
Ziya Gokaslan	University Grants/ Research Support	AOSpine North America AOSpine International NREF DePuy Synthes
	Stock or Shareholder	Spinal Kinetics
	Honorarium	AO Foundation

Vikas Gulani	Industry Grant Support	Siemens Medical Systems, Inc.; Siemens Master Research Collaboration
Kavita Gupta	Employee [any industry]	DiscGenics, Inc.
Daniel Haber	University Grants/ Research Support Industry Grant Support Consultant Fee	Howard Hughes Medical Institute Massachusetts General Hospital Johnson & Johnson Center for CTC Technologies Cell Signaling; Life Technologies (scientific advisory board)
Costas Hadjipanayis	Industry Grant Support	NX Development Corporation
Randy Jensen	Consultant Fee Honorarium	Medtronic Varian Medical Systems; Pharmaco-Kinesis
Ranjan Kumar	University Grants/ Research Support	Alberta Innovates Health Solutions
Virginie Lafage	Industry Grant Support Consultant Fee Stock or Shareholder Honorarium Speaker's Bureau	DePuy; ISSG, SRS MSD Nemaris Inc. MSD; DePuy; K2M MSD; DePuy; K2M
Frederick F. Lang*	Industry Grant Support	DNAtrix, Inc.

Michael Lawton	Consultant Fee Other Financial or Material Support	Stryker Mizhuo America (royalties)
Eric Leuthardt	Industry Grant Support Consultant Fee Stock or Shareholder	Merck; Stryker Monteris Medical; Ascenscion Health Ventures; Intellectual Ventures; General Sensing Neurolutions; General Sensing; Osteovantage; Pear Therapeutics; Face to Face Biometrics
Allan Levi	Other Financial or Material Support	Medtronic (teaching honorarium)
Linda Liau	Industry Grant Support	Northwest Biotherapeutics, Inc.
Neil Malhotra	University Grants/ Research Support Consultant Fee	VA Merit Grant; McCabe Foundation; McKenna Scholar Trust Stryker Spine (unrelated)
Michael McDermott	Other Financial or Material Support	UCSF Medical Device (royalties, patent rights signed over to UCSF)
Rajiv Midha	University Grants/ Research Support Industry Grant Support	Alberta Innovates Health Solutions Integra Life Sciences
Duane Mitchell	Other Financial or Material Support	Provisional Patent (filed based on technology reported in current abstract)

Alon Mogilner	Industry Grant Support Consultant Fee	Boston Scientific Medtronic
Alireza Mohammadi	Consultant Fee	Monteris Medical Corp.
Jacques Morcos	Consultant Fee	Codman
Alexander Morgan	Consultant Fee Stock or Shareholder	Personalis, Inc. Carmenta Biosciences
Praveen Mummaneni	Stock or Shareholder Honorarium Other Financial or Material Support	Spinicity Globus; DePuy Thieme; QMP; DePuy
Christopher Ogilvy	Honorarium	UpToDate
David Okonkwo	Other Financial or Material Support	BioMet/Lanx (royalties)
Ronald Petersen	Consultant Fee Fiduciary Position (outside AANS)	Merck, Inc.; Roche, Inc.; Genentech, Inc. Alzheimer's Association
Mark Preul	Industry Grant Support	Carl Zeiss AG; Neomend; Capstone Therapeutics; Stryker
Daniel Resnick	Consultant Fee	Asterias
John Sampson	Other Financial or Material Support	Provisional Patent (filed based on technology reported in current abstract)
Michael Schulder	Honorarium	Varian

Frank Schwab	Industry Grant Support Consultant Fee Stock or Shareholder Honorarium Speaker's Bureau	DePuy; MSD; AO MSD DePuy; K2M Nemaris Inc. MSD; K2M MSD; K2M
Theodore Schwartz	Stock or Shareholder	Visionsense
Christopher Shaffrey	University Grants/ Research Support Industry Grant Support Consultant Fee Stock or Shareholder Other Financial or Material Support	Department of Defense; NACTN AO; ISSG DePuy Biomet; Globus; Medtronic; Nuvasive; Stryker Nuvasive Biomet; Medtronic; Nuvasive (royalties, patent holder)
Lara Silverman	Stock or Shareholder Employee [any industry]	DiscGenics DiscGenics

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Costas Hadjipanayis	Atlanta, GA	Douglas Kondziolka
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Amy Heimberger	Houston, TX	Franco DeMonte
Brian Hoh	Gainesville, FL	William Freidman
Judy Huang	Baltimore, MD	Rafael Tamargo
Randy Jensen	Salt Lake City, UT	William Couldwell
John Kuo	Madison, WI	Daniel Resnick
Nandan Lad	Durham, NC	John Sampson
Giuseppe Lanzino	Rochester, MN	Robert Spinner
James Levine	Scottsdale, AZ	Fredric B. Meyer
Linda Liau	Los Angeles, CA	Jeffrey Bruce
Michael Link	Rochester, MN	Fredric Meyer
Neil Malhotra	Philadelphia, PA	M. Sean Grady
Hani Malone	New York, NY	Academy Award Winner
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Scientific Program

AMERICAN ACADEMY OF NEUROLOGICAL SURGERY

2014 SCIENTIFIC PROGRAM
AGENDA

THURSDAY, SEPTEMBER 18, 2014

7:30-7:40 **Welcoming Remarks: Frederick F. Lang, MD**

7:40-8:50 **Peer Reviewed Abstract Session 1: Select Papers**
Moderators: Frederick F. Lang, MD, Doug Kondziolka, MD

Cerebrovascular		
7:40-7:50	Michael Lawton	Sentinel AVM hemorrhage: characterization of a clinical entity, surgical management, and pathological correlates
Functional		
7:50-8:00	Emad Eskandar	Insights into impulsive versus conservative decision-making from human microelectrode recordings and closed loop deep brain stimulation
Spine		
8:00-8:10	Neil Malhotra	Functional regeneration of the human degenerative disc
Trauma		
8:10-8:20	Nicholas Theodore	Cerebrospinal fluid drainage and induced hypertension improve spinal cord perfusion after acute spinal cord injury in pigs

Tumor		
8:20-8:30	Michael Taylor	The nucleotide is mightier than the scalpel: neurosurgical care for patients with ependymoma in the post-genome era
Pediatric		
8:30-8:40	Shenandoah Robinson	Post-injury erythropoietin treatment mitigates gait and cognitive deficits following prenatal hypoxia-ischemia in rats

8:40-8:50 **Discussion**

8:50-9:30 **Special Lecture 1**

8:50-9:00 Introduction of Dr. Petersen: Fredric B. Meyer, MD

9:00-9:30 Ronald Petersen, MD, PhD
Professor of Neurology, Mayo Clinic
Title: "How Early Can We Diagnose Alzheimer's Disease"

9:30-9:45 **Break**

9:45-10:25 **Point-Counterpoint Debate 1**
Moderator: Ziya Gokaslan, MD

Resolved: In "standard" degenerative multilevel lumbar spinal stenosis with loss of lordosis spinal instrumentation to establish normal sagittal balance is more important than decompression of the central canal and neural foramina for improving symptoms

For: Christopher Shaffrey, MD
Against: Vincent Traynelis, MD

10:25-11:35 Peer Reviewed Abstract Session 2:
Vascular; Clinical Studies and Basic Science
Moderator: Michael Lawton, MD

10:25-10:35	Christopher Ogilvy	Stratification of recanalization for patients with endovascular treatment of intracranial aneurysms
10:35-10:45	Felipe Albuquerque	Multimodality treatment strategies for complex cerebral arteriovenous fistulas in the pediatric population: contemporary case series at the Barrow Neurological Institute
10:45-10:55	Daniel Barrow	Resolution of oculomotor nerve palsy secondary to posterior communicating artery aneurysms: comparison between clipping and coiling
10:55-11:05	Gary Steinberg	Microsurgical resection of intracranial arteriovenous malformations following stereotactic radiosurgery treatment
11:05-11:15	Justin Fraser	Selective intra-arterial verapamil as an adjunct to thrombectomy is highly neuroprotective in animals and feasible in humans
11:15-11:25	Brian Hoh	Interleukin-17 blockade inhibits cerebral aneurysm formation and prevents cerebral aneurysm rupture

11:25-11:35 Discussion

11:35-1:05 Peer Reviewed Abstract Session 3:
Tumor: Translational Studies
Moderator: Fred Barker, MD

11:35-11:45	Amy Heimberger	Targeting the immune checkpoint network with miR-138 exerts therapeutic efficacy in murine models of glioma
11:45-11:55	Andrew Sloan	Magnetic resonance fingerprinting of brain tumors: initial clinical results
11:55-12:05	Brian Nahed	Circulating tumor cells in patients with glioblastoma
12:05-12:15	Costas Hadjipanayis	Use of volumetric MR spectroscopic imaging and 5-ALA fluorescence-guided surgery for resection of glioblastoma
12:15-12:25	John Kuo	Alkylphosphocholine analogs for broad spectrum cancer imaging and therapy
12:25-12:35	Ganesh Rao	Surviving transcript variant 2 drives angiogenesis and malignant progression in proneural gliomas
12:35-12:45	Jacques Morcos	A comparison of the sublabial microscopic and endoscopic endonasal resection of pituitary adenomas: a volumetric analysis on 272 cases
12:45-12:55	Michael McDermott	Transcortical transventricular and endoscopic removal of colloid cysts: single institution comparison of results and classification of operative zones
12:55-1:05	Theodore Schwartz	Long-term quality of life after endoscopic endonasal resection of craniopharyngiomas

1:05 – 1:15 Discussion

FRIDAY, SEPTEMBER 19, 2014

7:30-7:35 **Welcome: Frederick F. Lang, MD**

7:35-8:35 **Peer Reviewed Abstract Session 4: Clinical Trials in Neurosurgery**
Moderator: Robert Spinner, MD

7:35-7:45	Eric Leuthardt	The role of laser interstitial thermal therapy in enhancing progression-free survival of difficult-to-access high-grade gliomas: a multicenter study
7:45-7:55	Michael Schulder	Laser interstitial thermal therapy: lessons learned
7:55-8:05	Christopher Shaffrey	Outcomes of operative and nonoperative treatment for adult spinal deformity: a prospective, multi-center matched and unmatched cohort assessment with minimum 2-year follow-up
8:05-8:15	Praveen Mummaneni	Clinical and radiographic analysis of an artificial cervical disc: seven-year follow-up from the PRESTIGE prospective randomized controlled clinical trial
8:15-8:25	Mark Shaffrey	Cervical disc arthroplasty vs. ACDF: seven-year outcomes

8:25-8:35 **Discussion**

8:35-9:15 **Point-Counterpoint Debate 2**
Moderator: Frederick F. Lang, MD

Resolved: Prospective Databases Provide Better Insight into Clinical Therapies than do Randomized Controlled Phase III Trials

For: Douglas Kondziolka, MD
Against: Fred Barker, MD

9:15-9:30 **Break**

9:30-10:10 **Peer Reviewed Abstract Session 5:**
Cell Therapy in Trauma and Degenerative Disease
Moderator: Robert Friedlander, MD

9:30-9:40	Allan Levi	Transplantation of autologous schwann cells after sub-acute thoracic spinal cord injury
9:40-9:50	Rajiv Midha	Differential abilities of acutely and chronically denervated nerve derived and skin derived schwann cells to support axonal regeneration and remyelination
9:50-10:00	Lara Silverman	Non-immunogenic and anti-inflammatory properties of discogenic cells, a novel cell population used for the treatment of degenerative disc disease

10:00-10:10 **Discussion**

10:10-10:50 Special Lecture 2

10:10-10:20 Introduction of Dr. Futreal: Frederick F. Lang, MD

10:20-10:50 Andrew Futreal, PhD
Professor Genomic Medicine, MD Anderson Cancer Center
Title: "Tumor Heterogeneity"

10:50-12:20 Peer Reviewed Abstract Session 6:
Functional Neurosurgery, Imaging and Biomarkers
Moderator: Raymond Sawaya, MD

10:50-11:00	Mitchel Berger	Intraoperative mapping during repeat awake craniotomies reveals functional plasticity of the adult cerebral cortex
11:00-11:10	Nandan Lad	Circuit modulation: dissecting structure-function of deep brain stimulation (DBS) using diffusion tensor imaging (DTI)
11:10-11:20	David Okonkwo	The predictive ability and clinical utility of serum measurement of GFAP-BDP biomarker for the detection of traumatic brain injury
11:20-11:30	Charles Matouk	High-resolution, vessel wall MRI in the evaluation of ruptured /symptomatic intracranial aneurysms and AVMs
11:30-11:40	Robert Friedlander	Preliminary experience with longitudinal evaluation of corticospinal tract in patients with surgically resected brainstem cavernous malformations using high definition fiber tractography and diffusion connectometry analysis

11:40-11:50	Douglas Kondziolka	Identifying the thalamic nuclei using 3-T MRI track density imaging
11:50-12:00	Steven Schiff	Volumetric brain analysis for hydrocephalus and epilepsy in the developing world
12:00-12:10	Daniel Yoshor	Creating visual percepts with electrical stimulation of human visual cortex

12:10-12:20 Discussion

12:20-1:00pm Presidential Address

12:20-12:30 Presentation of the President: Alan R. Cohen, MD

12:30-1:00 Presidential Address
Fredric B. Meyer, MD
Title: "Tripe Threat"

SATURDAY, SEPTEMBER 20, 2014

7:00-7:05 **Welcome: Frederick F. Lang, MD**

7:05-7:30 **Peer Reviewed Abstract Session 7:**
Policy and Politics
Moderator: Douglas Kondziolka, MD

7:05-7:15	Stephen Haines	Holding policy makers accountable: what patient safety gains have duty hours regulations produced?
7:15-7:25	Daniel Resnick	Divide and conquer: a history of organized neurosurgery and a blueprint for the future

7:25-7:30 **Discussion**

7:30-8:15 **Special Lecture 3: Academy Award Presentation and Lecture**

7:30-7:40 Introduction of Academy Award Winners: Daniel Fults, MD

Winner: Hani Malone, MD Columbia University 'Stereotactically Localized Biopsies Uncover Subtype – Specific Differences in Molecular and Cellular Composition at the Infiltrating Margins of Glioblastoma"

Honorable Mention: Terry Burns, MD, PhD Stanford University "Transcriptome of irradiated microglia."

7:40-8:05 Academy Award Winner Lecture
Hani Malone, MD

8:05-8:15 **Discussion**

8:15-9:45 **Peer Reviewed Abstract Session 8:**
Scientific Discoveries in Tumor & Spine
Moderator: Ennio Chiocca, MD

8:15-8:25	James Rutka	Transcriptional profiling of GBM invasion genes identifies effective inhibitors of the LIM kinase-Cofilin pathway
8:25-8:35	Terry Burns	Transcriptional signature of irradiated microglia: implications for cognition and tumor infiltration
8:35-8:45	Randy Jensen	RNA interference targeting HIF-1a via a novel multifunctional surfactant attenuates glioma growth in an intracranial mouse model
8:45-8:55	John Sampson	Activated CD4+ cell-induced CCL3 improves dendritic cell vaccine in mice and cancer patients
8:55-9:05	David Baskin	Novel selective mitochondrial based chemotherapy for glioblastoma: in vitro and in vivo studies
9:05-9:15	Marcus Mazur	Destabilization and restabilization of the occipitocervical junction after a far lateral transcondylar resection: a biomechanical analysis
9:15-9:25	John Boockvar	Durability of a single high dose of intra-arterial bevacizumab with blood-brain-barrier disruption for the treatment of recurrent glioblastoma
9:25-9:35	Robert Spinner	Perineural spread in pelvic malignancies

9:35-9:45 **Discussion**

9:45-9:55 **NREF Presentation: John Robertson, MD**

9:55-10:10 **Break**

10:10-11:10 **Peer Reviewed Abstract Session 9:**
Outcomes and Quality of Life
Moderator: Robert Spinner, MD

10:10-10:20	Raymond Sekula	Quality of life and referral patterns in hemifacial spasm patients undergoing microvascular decompression
10:20-10:30	Michael Link	Long-term dizziness handicap analysis in vestibular schwannoma patients. An international multicenter cross-sectional study comparing microsurgery, stereotactic radiosurgery, observation and non-tumor controls
10:30-10:40	Jeffrey Blount	Quality of life metrics from an initial 4 year experience in a transitional spinal dysraphism clinic
10:40-10:50	Anthony Sin	Three-year experience as a spine surgeon at Shriners Hospital: Neurosurgical perspective
10:50-11:00	Linda Liau	Quantitative imaging evaluation of tumor response in malignant glioma patients treated with dendritic cell vaccination

11:00-11:10 **Closing Remarks: Frederick F. Lang, MD**

THURSDAY, SEPTEMBER 18

7:40 – 7:50 SENTINEL AVM HEMORRHAGE: CHARACTERIZATION OF A CLINICAL ENTITY, SURGICAL MANAGEMENT, AND PATHOLOGICAL CORRELATES

***Michael T. Lawton, M.D.**, University of California San Francisco*

INTRODUCTION: Brain arteriovenous malformations (AVM) are often characterized dichotomously as unruptured or ruptured, based on a patient's clinical presentation with symptoms, signs, or radiological findings of hemorrhage. In a previous report, our group documented evidence of sentinel AVM hemorrhage, which we described then as "silent intralesional microhemorrhage." In the current study, we further characterize the clinical and radiological features, surgical management, and pathological correlates of this clinical entity of sentinel AVM hemorrhage.

METHODS: Patients with brain AVMs operated on since 1997 were identified from two prospectively maintained databases: 1) the University of California, San Francisco Brain AVM Study Project; and 2) the UCSF Neuropathology AVM database. Patients who underwent AVM surgery were included if their specimen contained brain tissue and AVM. Patients were categorized into four groups defined by their hemorrhagic presentation: (1) *unruptured AVM patients* (Group 1: no clinical history of hemorrhage, no radiographic EOOH, and hemosiderin negative); (2) *sentinel AVM hemorrhage patients* (Group 2: no clinical history of hemorrhage, radiographic EOOH, and hemosiderin positive); (3) *spontaneous AVM rupture patients* (Group 3: clinical history of hemorrhage, no radiographic EOOH, and hemosiderin negative); and *AVM re-rupture patients* (Group 4: clinical history of hemorrhage, radiographic EOOH, and hemosiderin positive).

RESULTS: 83 patients (31.6%) presented with unruptured AVMs (Group 1), 37 patients (14.1%) presented with sentinel AVM haemorrhage (Group 2), 59 patients (22.4%) presented with spontaneous AVM rupture (Group 3), and 84 patients (31.9%) presented with AVM re-rupture (Group 4). Significant differences were observed in patients' baseline and first postoperative mRS, and a borderline difference was observed in last postoperative mRS scores ($p<0.001$, $p<0.001$, and $p=0.060$). Significant differences were also demonstrated between the 4 groups in terms of deep venous drainage, lobar location, and infratentorial location. However, there were no significant differences in mRS scores between patients with unruptured AVMs and those with sentinel AVM haemorrhage, at baseline or any time postoperatively, indicating that microhemorrhage did not confer any measurable benefits in circumdissection and resection, as it does with frank rupture. 37 patients with sentinel AVM haemorrhage were more likely to have radiographic EOOH compared to unruptured AVM patients, consisting of hemosiderin in 31.2% of patients who underwent preoperative MRI, encephalomalacia in 31.8% of patients who underwent preoperative MRI and/or CT, calcifications in 47.1% of patients who had preoperative CT, and T2 signal in 63.

CONCLUSION: Improving the detection of sentinel AVM hemorrhage is important because it portends a more aggressive natural history. The diagnosis of sentinel AVM hemorrhage *pre factum*, without knowledge of surgical pathology findings, is possible using readily available MRI clues including encephalomalacia, hemosiderin staining or gradient echo hyperintensity, calcifications, and gliosis. Additionally, the nearly 1-to-1 correlation between macrophage infiltration and hemosiderin positivity allows imaging detection of one of these to essentially serve as direct evidence of the other, improving prediction of progression from unruptured AVM to overt hemorrhage. Sentinel AVM hemorrhage patients should be managed more aggressively than unruptured AVM patients and therapeutic options should be considered.

7:50 – 8:00 **INSIGHTS INTO IMPULSIVE VERSUS CONSERVATIVE DECISION-MAKING FROM HUMAN MICROELECTRODE RECORDINGS AND CLOSED LOOP DEEP BRAIN STIMULATION**

***Emad Eskandar, M.D.**, Massachusetts General Hospital*

INTRODUCTION: Impulse control disorders such as pathological gambling and addiction are major societal and public health problems and are also a side effect of continuous "open-loop" deep brain stimulation (DBS) in Parkinson Disease. Functional procedures provide a unique opportunity to study neuronal activity in awake-behaving humans to understand this process. We investigated the role of single neurons in the Nucleus Accumbens (NAcc) and Subthalamic Nucleus (STN) of human subjects undergoing DBS. The first hypothesis was that the NAcc and STN predict the subject's disposition under conditions of uncertainty. The second hypothesis was that intermittent closed-loop deep brain stimulation could bias the subjects' disposition toward less impulsive choices.

METHODS: DBS patients were prospectively enrolled in the study after informed consent following an approved IRB protocol. Microelectrode recordings are a standard part of DBS procedures to localize the nuclei of interest. In these studies, we intra-operatively recorded the activity of single neurons while subjects performed a simple gambling task, using traditional cards, intended to assess decision making under conditions of uncertainty. In this this task, patients viewed a computer monitor and indicated their choices using a joystick. In each trial of the task, the subjects first viewed their own card. They then placed a bet on whether their card was likely to be higher than the computer's card. The higher card won. We used a simplified deck with only the 2, 4, 6, 8, and 10 cards. Data were recorded from three electrodes per subject. Post-operatively, we used intermittent deep brain stimulation to investigate the effects on behavioral choices.

RESULTS: We successfully obtained intra-operative data from 13 patients, and post-operative stimulation data from 16 patients. There were several important findings. Both the NAcc and STN were particularly sensitive to unexpected wins and losses, consistent with the reinforcement-learning model of basal ganglia function. Interestingly, activity of neurons in both nuclei predicted the subjects' choices 1-3 seconds before the choice was actually made based on a receiver operating characteristic analysis (NAcc, $p = 0.003$; STN, $p = 0.03$). In the extra-operative experiments, we found that delivering brief trains of 1 sec stimulation in the STN during the same time period when the neurons were active, before subjects made their choice, significantly biased them toward more conservative and less impulsive choices (binomial fit; $p < 1x10^{-6}$).

CONCLUSION: Decision-making is a complex task requiring interaction of cortical and subcortical areas. These findings suggest that the NAcc and STN play a critical role in making decisions under conditions of uncertainty, and that their activity encodes the subjects' current disposition - whether they feel lucky or not. Interestingly, in contrast to continuous stimulation, intermittent stimulation appears, to induce a more conservative and less impulsive disposition. This insight could be used to modify DBS for Parkinson disease to reduce the common side-effects of impulse control disorders. More generally, the implication is that this type of stimulation could potentially be used to treat primary disorders of impulse control such as pathological gambling, drug addiction, and possibly even obesity, which can also be conceptualized as an impulse control disorder.

8:00 – 8:10 FUNCTIONAL REGENERATION OF THE HUMAN DEGENERATIVE DISC

Neil R. Malhotra, M.D.; *Lachlan J. Smith, Ph.D., University of Pennsylvania*

INTRODUCTION: Intervertebral disc degeneration is implicated as a major cause of low back pain. There is a pressing need for new regenerative therapies that restore native tissue structure and mechanical function. To address this need, we designed, constructed and investigated the therapeutic potential of an injectable hydrogel, a triple interpenetrating network comprised of dextran, chitosan and teleostean, for functional regeneration of the nucleus pulposus (NP) of the intervertebral disc in a series of ***biomechanical, drug delivery, cytotoxicity and tissue engineering studies***.

METHODS: *Biomechanical properties* (modulus and Poisson's ratio) were evaluated as a function of implant gelation time and between different batches of hydrogel. Implant impact on biomechanical function of injured cadaveric spinal motion segments (range of motion, creep strain, compression strain) was also determined. *Drug delivery capabilities* were assessed using a polymeric microsphere delivery system, for time frame of delivery, and ability to inhibit local inflammation and associated functional degradation both *in vitro* and *in vivo*. *Cytotoxicity and capacity for cell-mediated functional tissue regeneration* were studied via live dead and DAPI staining, and biochemical and biomechanical and analyses of 3D hydrogel constructs seeded with mesenchymal stem cells (MSCs) and native NP cells.

RESULTS: The prototype implant achieved ~90% of steady-state mechanical properties within 10 hours and demonstrated excellent inter-batch consistency in compression testing. Hydrogel mechanical properties, evaluated in both confined and unconfined compression, were statistically no different than native human NP properties. *In vitro* studies demonstrated reconstitution of normal range-of-motion of injured discs after implant treatment. All implants were contained within injured discs during 10,000 cycles of physiological loading, with gross analysis demonstrating no implant extrusion, and excellent

inter-digitation of the hydrogel material with the native NP tissue. Drug delivery from polymeric microspheres was sustained over 20 days and, in the presence of an inflammatory stimulant (IL-1β), resulted in preservation of mechanical properties (modulus), and biochemical composition (glycosaminoglycan (GAG) content) and reduced expression of inflammatory mediators (mRNA for ADAMTS4, MMP3 and INOS). *In vivo* microsphere treatment demonstrated retention of microspheres for up to 28 days and effective attenuation of the degradative inflammatory effects of IL-1β. To confirm cytocompatibility with the native NP cell population, hydrogel constructs were surface-seeded with NP cells and cultured for 14 days. Results showed that the hydrogel maintained NP cell viability and promoted proliferation. Constructs seeded with mesenchymal stem cells (MSCs), and cultured under pro-chondrogenic conditions for 42 days, demonstrated hydrogel support for cell mediated functional matrix production. Importantly, the hydrogel maintained MSC viability and promoted proliferation, as evidenced by increasing DNA content with culture duration. MSCs differentiated along a chondrogenic lineage, evidenced by up-regulation of aggrecan and collagen II mRNA, and increased GAG and collagen content, and mechanical properties with increasing culture duration.

CONCLUSION: Collectively, these results establish the therapeutic potential of this novel hydrogel for functional regeneration of the NP. Future work will confirm the ability of this hydrogel to normalize the mechanical stability of cadaveric human motion segments, and advance the material towards human translation using preclinical large animal models.

8:10 – 8:20 CEREBROSPINAL FLUID DRAINAGE AND INDUCED HYPERTENSION IMPROVE SPINAL CORD PERFUSION AFTER ACUTE SPINAL CORD INJURY IN PIGS

Nicholas Theodore, M.D., F.A.A.N.S., F.A.C.S.; *Nikolay L. Martirosyan, M.D.; M. Yashar S. Kalani, M.D., Ph.D., William D. Bichard, Ali A. Baaj, M.D., Robert F. Spetzler, M.D., Mark N. Hadley, M.D., Mark C. Preul, M.D.; Barrow Neurological Institute*

INTRODUCTION: Elevation of the mean arterial blood pressure (MAP) and cerebrospinal fluid drainage (CSFD) has been used as treatment modalities in patients after acute spinal cord injury (SCI). Currently there is no evidence in support of the routine use of either modality. We sought to determine the efficacy of aggressive MAP augmentation combined with lowering of intrathecal pressure (IP) by CSFD to improve spinal cord blood flow (SCBF) after SCI.

METHODS: We induced mild spinal cord injury at the fifth thoracic level in pigs. The animals were divided evenly between five groups: *Control* (laminectomy) (n=3); *SCI* only (n=3); SCI with elevated MAP (*SCI+MAP*) (n=3); SCI with CSFD (*SCI+CSFD*) (n=3); SCI with CSFD and elevated MAP (*SCI+MAP+CSFD*) (n=3). Elevated MAP and CSFD was initiated 1 hour after SCI. CSF diversion was achieved via insertion of a lumbar drain at L5. Elevated MAP was achieved by continuous injection of Phenylephrine. Parameters before SCI, at 1h, 2h, 3h and 4h after SCI were analyzed. All animals underwent continuous monitoring and recording of IP, SCBF at SCI level and MAP.

RESULTS: The SCBF in the SCI group was decreased by 56% after SCI in comparison with baseline. Increase in blood pressure after SCI resulted in a 34% decrease in SCBF, whereas CSFD resulted in a 59% decrease in SCBF. The combination of CSFD and induced hypertension resulted in a 24% increase in SCBF. The SCI group had stable IP throughout experiment.

The *SCI+MAP* group had an average of 5.45 mmHg IP increase after MAP increase 1 hour after SCI and remained at that level throughout experiment.

CONCLUSION: SCI does not result in increase in IP. Increased MAP in the setting of SCI causes increase in IP, which results in decreased spinal cord perfusion pressure (SCPP) (SCPP=MAP-IP). Both elevated MAP and CSFD showed only short-term improvement of SCBF followed by hypoperfusion when implemented independently. The combination of increased MAP and CSFD improves SCBF after SCI. This preliminary data was used to secure DOD funding for a prospective, randomized study of the use of CSFD in acute spinal cord injury in humans set to begin in late 2014.

8:20 – 8:30 THE NUCLEOTIDE IS MIGHTIER THAN THE SCALPEL: NEUROSURGICAL CARE FOR PATIENTS WITH EPENDYMOMA IN THE POST-GENOME ERA

***Michael D. Taylor, M.D.**, The Hospital for Sick Children*

INTRODUCTION: Ependymoma is the third most common childhood brain tumor, and is found throughout the neuraxis. In the recent past, ependymoma was regarded as one disease found in different locations due to its histologically homogeneity. We initially demonstrated that ependymomas from the supratentorial, posterior fossa and spinal compartments are biologically very different from another. More recently we demonstrated that among the posterior fossa ependymomas, there are two very different molecular subgroups with distinct demographics, clinical presentation, transcriptomics, genetics, and clinical outcome. 'PFA' ependymomas are found primarily in very young patients (infants), are often lateral, and have a very poor prognosis. 'PFB' ependymomas in contrast occur in older children, are commonly midline, and have an almost universally good prognosis.

METHODS: Most recently, we undertook next generation sequencing of a large cohort of posterior fossa ependymomas and found that neither PFA nor PFB ependymomas have any recurrent mutations, making PF ependymoma the first lethal human malignancy without any recurrent mutations in coding space. We also demonstrate that PFA ependymomas exhibit a 'CIMP' phenotype in which they have extensive hypermethylation of CpG dinucleotides in gene promoter regions. This CpG hypermethylation converges on genes that normally silenced in undifferentiated cells (i.e., embryonic stem cells) by the Polycomb Related Complex 2 (PRC2). Where-as there currently is no known effective chemotherapy for ependymoma, we demonstrate that FDA approved drugs that drive DNA demethylation (i.e., Vidaza), or drugs that inhibit PRC2 (i.e., GSK343) are highly effective against PFA ependymoma patient explants, but not supratentorial ependymoma patient explants. We conclude that PFA ependymomas are very unique in that they lack mutions, but are driven by a strong epigenetic phenotype. Where-as there are currently

no known effective chemotherapy agents for PF ependymoma, we demonstrate activity of epigenetic drugs, and have started a clinical trial to test these agents in human children. We have now validated our human epigenomics through the creation of the first mouse model of posterior fossa ependymoma, which is driven purely by over-activity of the PRC2 complex in radial glial cells of the posterior fossa.

RESULTS: Currently, the most important prognostic factor for patietns with PF ependymoma is the extent of resection. Currently, most patients with PF ependymoma in North America receive posterior fossa radiation therapy. These data however are all from the 'pre-genomic era'. Based on a set of 450 PF ependymomas from around the world, we now demonstrate that extent of resection has no prognostic value for patients with PFB ependymoma who have an almost 100% survival rate, even in the face of subtotal resection. Furthermore, after GTR of a PFB ependymoma, if radiation is withheld, up to 2/3 of patients will not recur, and those that do recur can be salvaged by delayed radiotherapy for an overall survival approximating 100%. The value of cytoreductive surgery for PFA tumors is still seen after accounting for subgroup, but is much less compared to non-subgrouped cohorts.

CONCLUSION: We suggest that a great deal of the prior literature claiming a benefit for GTR was a reflection of a terrible natural history in a tumor that is difficult to resect (PFA) and a good natural history in a tumor that is relatively easier to resection (PFB). In this case at least, it turns out that natural history trumps therapy, and that the nucleotide is mightier than the scalpel.

8:30 – 8:40 **POST-INJURY ERYTHROPOIETIN TREATMENT MITIGATES GATE AND COGNITIVE DEFICITS FOLLOWING PRENATAL HYPOXIA-ISCHEMIA IN RATS**

Lauren Jantzie, Ph.D.[1], ***Shenandoah Robinson, M.D. F.A.A.P., F.A.C.S.***[2], *University of New Mexico*[1] *and Boston Children's Hospital*[2]

INTRODUCTION: Globally, >15 million infants are born prematurely each year. Preterm birth causes chronic neurological deficits including cerebral palsy and cognitive delay. We hypothesize that preterm birth results in encephalopathy of prematurity through a complex cascade of injury over a sustained perinatal period that disrupts the sequential formation of cerebral circuits. We also propose that interventions to ameliorate this impaired circuit development will require multiple overlapping mechanisms delivered over an extended window to limit excess cell death, inflammation, and calpain degradation. Erythropoietin (EPO) is a neurorestorative agent with multiple mechanisms of action that is being evaluated in clinical trials of extremely preterm infants. Because the mechanisms of injury and recovery for brain injury following preterm birth are poorly understood, EPO dosing regimens currently cannot be tailored to specific indications, injury severity, or individual vulnerability. Here we use a rat model of brain injury from extreme preterm birth to investigate whether post-injury EPO treatment in a clinically relevant paradigm can produce sustained functional improvement in young adult rats.

METHODS: Transient systemic hypoxia ischemia (TSHI) was induced on embryonic day 18. Half of each litter was randomly assigned to intraperitoneal EPO (2000 U/kg/dose) or vehicle on postnatal day 1 (P1)-P5. Gait was analyzed with automated treadmill analysis. Cognition was tested using novel object recognition (NOR). *Ex vivo* brain imaging was performed on a 4.7T MRI, with diffusion (DWI) and fractional anisotropy (FA) quantified. Two-way ANOVA with Bonferonni's correction (gait) or repeated measures split plot analysis (NOR) was used with $p<0.05$ significant.

RESULTS: Following prenatal TSHI, vehicle-treated (TSHI-veh) adolescent (P24) rats (n=14) had a shorter hindlimb stride length ($p<0.001$), more toe-walking ($p=0.009$) and more ataxia ($p<0.001$) than shams (n=18). With EPO treatment (TSHI-EPO, n=12), gait was restored, with all indices similar to shams, and different from TSHI-veh (all $p<0.001$). Subset analyses for gender showed both sexes had deficits with TSHI-veh that improved with EPO treatment (n=5-10, all $p<0.02$), except TSHI-veh males did not have more toe-walking than shams. To avoid the need for intact motor performance, NOR was used to test memory. Young adult (P35) TSHI-veh rats (n=16) were unable to discriminate novel from familiar objects ($p=0.77$), while sham (n=14, $p=0.01$) and TSHI-EPO (n=13, $p=0.008$) did, suggesting that EPO treatment resulted in sustained improvement in memory and attention, the first time that improved cognition has been shown using a clinically relevant model of extreme preterm birth and post-injury treatment. Gender subset analyses showed that male rats (n=5-8) performed similar to the total cohort, while female TSHI-veh rats (n=11) did not show a deficit in object discrimination. At P35 *ex vivo* MRI images revealed higher DWI values in white matter (32% increase) and cortex (47% increase) in TSHI-veh rats (n=2) compared to shams (n=2), and lower FA values in white matter (22% decrease) and cortex (20% decrease) compared to shams, consistent with changes in DWI and FA observed in term-equivalent human infants with brain injury from preterm birth. Additional brains are being imaged.

CONCLUSION: Here we show for the first time gait and cognitive deficits that mimic those observed in children using a preclinical model of encephalopathy of preterm birth, and sustained reversibility of those deficits in adult rats. This model supports testing of mechanisms of injury and recovery in the microenvironment during the critical neurodevelopmental window. Most importantly, these findings emphasize that injury to the developing brain is not permanent and is potentially reversible.

10:25 – 10:35 STRATIFICATION OF RECANALIZATION FOR PATIENTS WITH ENDOVASCULAR TREATMENT OF INTRACRANIAL ANEURYSMS

***Christopher S. Ogilvy, M.D.**, Michelle Chua, Matt Fusco, M.D., Suresh Reddy, M.D., Ajith J. Thomas, M.D., Beth Israel Deaconnes Medical Center*

INTRODUCTION: With increasing utilization of endovascular techniques in the treatment of both ruptured and unruptured aneurysms, the issue of obliteration efficacy has become increasingly important. There are a variety of aneurysm specific factors such as (1) size, (2) end on (terminal) or sidewall lesion, (3) dome to neck ratio, (4) presence of thrombus and (5) whether the aneurysm is ruptured or unruptured which influence recanalization rates. In addition there are treatment related factors including (6) degree of treatment with coils only (Raymond Roy degree of aneurysm obliteration), (7) stent assisted coiling, and (8) utilization of flow diversion devices that have been demonstrated to have impact on aneurysm recanalization rates. The purpose of this study was to systematically develop and evaluate a comprehensive model for predicting clinically significant aneurysm recanalization including both aneurysm specific factors and treatment related factors with the goal of being able to more accurately predict the chance of clinically significant aneurysm recanalization with various types of endovascular treatment.

METHODS: We retrospectively analyzed clinical data that was prospectively collected on 285 patients with aneurysms treated with endovascular techniques at the Beth Israel Deaconess Medical Center (BIDMC) from 2007 to 2014. Our primary outcome of interest was retreatment as this reflects clinically significant aneurysm recanalization. The 8 aneurysm specific factors and treatment related factors were collected and statistical analysis was performed.

RESULTS: Retreatment was performed in 79 patients (27.7%). Using multivariable logistic regression, size (>10 mm) (odds ratio [OR], 5.23; $p < 0.05$), thrombus (OR, 8.87; $p = 0.15$), rupture (OR, 3.67; $p < 0.05$), stent assistance (OR, -2.00; $p = 0.10$), flow diverter placement (OR, -9.49; $p = 0.08$), and post-treatment obliteration (RR2: OR, 2.50; $p < 0.05$; RR3: OR, 4.22; $p < 0.05$) were most predictive of retreatment. This model performed well with a c-statistic of 0.782. Size provides a statistically similar impact as dome to neck ratio and is easier to use. End on versus side wall retreatment rates were not significantly different in this model. Using this analysis, we have generated a grading scale that predicts clinically significant recanalization.

Aneurysm specific factors

Size ≤10 mm (0 point) or >10 mm (2 points)

Unruptured (0 point) or ruptured (2 points)

Thrombus absent (0 point) or present (2 points)

Treatment specific factors

Coils only (0 point)

Stent assisted coiling (-1 point)

Flow diversion (-2 points)

Raymond Roy 1 occlusion (0 point)

Raymond Roy 2 occlusion (1 point)

Raymond Roy 3 occlusion (2 points)

CONCLUSION: Using this scale with a range from -2 to +8, we can predict the chance of clinically significant aneurysm recanalization as follows: -2, 1.17%; -1, 4.04%; 0, 8.81%; 1, 18.8%; 2, 29.8%; 3, 49.8%; 4, 64.8%; 5, 83.3%; 6, 90.3% (no patients in this series grade 7,8). This is very helpful in discussions with patients regarding treatment. While these results are highly encouraging, it is in a limited sample size. We are in the process of testing this system at two other large institutions with well-maintained databases of endovascular treatment for validation.

10:35 – 10:45 MULTIMODALITY TREATMENT STRATEGIES FOR COMPLEX CEREBRAL ARTERIOVENOUS FISTULAS IN THE PEDIATRIC POPULATION: CONTEMPORARY CASE SERIES AT THE BARROW NEUROLOGICAL INSTITUTE

Felipe C. Albuquerque, M.D. *and Hasan A. Zaidi, M.D., Barrow Neurological Institute*

INTRODUCTION: Pediatric Cerebral Arteriovenous Fistulas (AVF) are rare and potentially lethal vascular lesions. Management strategies have undergone considerable evolution in the last decade with the advent of new endovascular, surgical and radiosurgical methods. We sought to review current treatment strategies and long-term clinical outcomes at a high volume cerebrovascular institute.

METHODS: Prospective evaluation of a retrospectively-maintained database was performed on patients with cerebral arteriovenous fistulas from 1999-2012. Patients with carotid-cavernous fistulas, vein of Galen malformations and age >18 years were excluded from analysis. Medical history, surgical and nonsurgical treatment, and clinical outcomes were documented. Pre- and postoperative angiograms were analyzed to assess for obliteration of the fistula.

RESULTS: Seventeen patients with pial AVFs (29.4%), dural AVFs (64.7%), and mixed pial/dural AVF (5.9%) were identified. The majority of lesions were paramedian (70.6%) and supratentorial (76.5%). Patients had a mean age of 6.4 years with a slight male predominance (52.9%), and most common presenting symptoms were seizures (23.5%), headaches (17.6%), congestive heart failure (11.7%) or enlarging head circumference (11.7%). The majority of patients were treated with endovascular therapy alone (52.9%), whereas 35.3% of patients required a multimodal approach, including surgery (41.2%) or radiosurgery (5.9%). Endovascular embolisates included onyx (n=6), n-BCA (n=3), or coil embolization (n=7) with or without balloon assistance (n=2). Among patients who underwent intervention (n=16), complete angiographic

obliteration was achieved in 87.5% at last follow up (average 3.1 years). One infant with incomplete obliteration died of congestive heart failure, and one patient with complete obliteration died of acute sinus thrombosis, with an overall complication rate of 17.6%.

CONCLUSION: Pediatric cerebral AVF are challenging neurosurgical lesions. Although advancements in endovascular therapy in the last decade have greatly changed the natural course of this disease, a multidisciplinary approach is still necessary for a large subset of patients. Surgeon experience with thorough analysis of preoperative imaging is paramount to achieving acceptable clinical outcomes. Pictorial examples of the multimodality therapeutic strategies employed in this case series will be presented.

10:45 – 10:55 RESOLUTION OF OCULOMOTOR NERVE PALSY SECONDARY TO POSTERIOR COMMUNICATING ARTERY ANEURYSMS: COMPARISON BETWEEN CLIPPING AND COILING

D. Jay McCracken, M.D., Brendan P. Lovasik, B.S., Nefize Turan, M.D., Justin M. Caplan, M.D., Courtney E. McCracken, Ph.D., M.S., C. Michael Cawley, M.D., ***Daniel L. Barrow, M.D.****, Jacques E. Dion, M.D., Raphael J. Tamargo, M.D., Gustavo Pradilla, M.D., Emory University*

INTRODUCTION: Posterior communicating artery aneurysm (PCoA) induced oculomotor nerve palsy (ONP) is a well-established entity. Previous studies have attempted to address the effectiveness of clip ligation or coil embolization on the rate and completeness of ONP resolution, but have been limited by small sample sizes.

METHODS: In this multi-centered study 84 patients with ruptured and unruptured PCoA and acute ONP from January 1991 to October 2013 were reviewed. Included patients had angiographically confirmed PCoA and complete or partial ONP on admission. Treatment option was based on physician discretion. Rate of resolution of ONP was determined from treatment date to last known follow-up and was defined as complete vs. partial or no resolution. Aneurysm characteristic and resolution data on 322 similarly treated patients was extracted from the literature and combined to increase sample size. Outcomes and treatment groups were directly compared. Complete primary data from the literature was not available for all patients and thus for certain groups the number of patients reviewed was not equal to the total number of patients available.

RESULTS: Overall, 399 patients were compared (205 clipped and 194 coiled). In both groups there was no difference between the size of the aneurysm (7.7 ± 2.7 mm vs. 7.7 ± 3.4 mm), time from symptom onset to treatment (4.5 days vs. 6.0 days), % of complete ONP at presentation (60% vs. 51.6%), % of partial ONP at presentation (40% vs. 48.5%), and % of ruptured aneurysms (50.5%

vs. 62%) and unruptured aneurysms (49.5% vs. 38%) in the clipped and coiled groups, respectively. Overall, in the 399 patients, 56.1% of those who underwent clipping had full ONP recovery vs. 45.5% in the coiling group (OR 1.54, p=0.032). Of the 223 patients who presented with complete ONP those who underwent clipping had a 45.5% full ONP recovery vs. 29.0% in the coiling group (OR 2.05, p=0.012). Of the 176 patients who presented with partial ONP 75.6% who underwent clipping had a full recovery vs. 58.5% in the coiling group (OR 2.20, p=0.014). In the ruptured aneurysm group (n=130), 70.9% of those who underwent clipping had full recovery vs 49.7% in the coiling group (OR 2.50, p=0.014). In the unruptured aneurysm group (n=100), 59.3% who underwent clipping had full recovery vs. 45.7% in the coiling group (OR 1.73, p=0.174).

CONCLUSION: In our series of treated aneurysm patients who presented with either partial or complete ONP secondary to PCoA aneurysms, those who underwent clip ligation were much more likely to achieve full recovery compared to those undergoing coil embolization. There was no difference in resolution of ONP between the two treatments in the elective, unruptured aneurysm group though this is likely due to smaller sample size. There was no difference between the size of the aneurysms, time from symptom onset to treatment, % of partial or complete ONP at presentation, or % of ruptured or unruptured aneurysms in either group.

10:55 – 11:05 MICROSURGICAL RESECTION OF INTRACRANIAL ARTERIOVENOUS MALFORMATIONS FOLLOWING STEREOTACTIC RADIOSURGERY TREATMENT

Gary K. Steinberg, M.D., Ph.D.[1], *Omar Choudhri, M.D.*[1], *Mihir Gupta, B.A.*[1], *Steven D. Chang, M.D.*[1], *Richard P. Levy, M.D., Ph.D.*[2], *Huy Do, M.D.*[1], *and Michael P. Marks, M.D.*[1], *Stanford University School of Medicine*[1], *and Loma Linda University Medical Center*[2]

INTRODUCTION: Large and complex intracranial AVMs can be challenging to treat and may require a multimodality strategy. Endovascular embolization, stereotactic radiosurgery and microsurgical resection represent three approaches for this treatment paradigm. The success rates of stereotactic radiosurgery alone for large and deep intracranial AVMs is only 25-50%. Many of these previously irradiated AVMs, with or without embolization may require additional treatment. This study hypothesizes that prior remote radiation therapy can aid microsurgical resection of lesions to achieve cure.

METHODS: This retrospective study utilized the Stanford AVM database, to identify 92 patients treated with microsurgery after prior radiation between 1990-2014. A total of 84 patients with complete data were used for this study.

RESULTS: Patients were 7 to 64 years old (mean 33), and underwent microsurgical resection 6 mos-11 yrs. after radiosurgery. Sixty-nine patients (82%) underwent endovascular embolization prior to surgery. Initial AVM volumes were 0.6-117 cm^3 (mean 21). Radiation doses were 4.6-45 GyE (mean 21.5). Seventy-three AVMs (87%) were located in eloquent or critical areas. Venous drainage was deep in 28, superficial in 32 or both in 20 lesions. Spetzler-Martin grades were I (4%), II (12%), III (31%), IV (39%) and V (14%). Prior to surgery, twenty-one patients (25%) experienced hemorrhage in a delayed fashion following radiation or embolization, while 14 (17%) developed radiation necrosis. At surgery AVMs were partially thrombosed, markedly less vascular, and more easily resected than if the patient had not received radiosurgery. Blood loss was minimal and the radiosurgery transformed

difficult AVMs into easily resectable ones. Despite persistent angiographic AVM filling, much of the small-vessel component was obliterated by the radiosurgery. Complete AVM resection was achieved in 71 (85%) of cases. Five patients (6%) died of delayed re-bleeding from residual AVM following deliberate subtotal surgical resection. Over a mean follow-up of 24 months, clinical outcome was excellent in 33%, good in 48% and poor in 11%. Histopathological analysis showed endothelial proliferation, vessel thrombosis and hyalinization of AVM vessels. Many cases also demonstrated calcification of vessel walls and necrosis of vessels or surrounding brain tissue.

CONCLUSION: Stereotactic radiosurgery several years prior to microsurgical resection is a useful adjunct for treating large and complex intracranial AVMs. Excellent or good clinical outcome can be achieved in most patients using this multimodal therapy.

11:05 – 11:15 SELECTIVE INTRA-ARTERIAL VERAPAMIL AS AN ADJUNCT TO THROMBECTOMY IS HIGHLY NEUROPROTECTIVE IN ANIMALS AND FEASIBLE IN HUMANS

***Justin F. Fraser, M.D.**, Michael Maniskas, Jill Roberts, Ph.D., and Gregory J. Bix, M.D., Ph.D.; University of Kentucky*

INTRODUCTION: Large vessel occlusive ischemic stroke results in high rates of morbidity and mortality. While intravenous t-PA and intra-arterial (IA) thrombectomy are mainstays in acute stroke therapy, clinical outcomes lag significantly behind improving rates of revascularization. In this setting, there is a vital need for novel adjunctive therapy to reduce stroke volume and improve outcome. Previous neuroprotective drug studies failed due to long intervals between symptom onset and drug administration, lack of concordant thrombolytic revascularization, and lack of targeted administration to the affected vessel. We aimed to develop a retro-engineered mouse model of large vessel stroke that was clinically relevant. Using this model, we evaluated the neuroprotective properties of verapamil, a calcium channel blocker (CCB) that is already safely injected intra-arterially (IA) for vasospasm, and which has never been rigorously investigated as a stroke therapy. Finally, based on the results of our animal studies, we aimed to perform a single-institution Phase I feasibility study of verapamil as an intra-arterial neuroprotective adjunct to mechanical thrombectomy.

METHODS: We developed a novel method to mimic the clinical condition of superselective IA pharmacotherapy administration after vessel recanalization in mouse models after experimental ischemic stroke (transient middle cerebral artery occlusion, MCAO). We performed intra-arterial infusion studies with carbon black to optimize flow rates of study substance to the ipsilateral affected hemisphere, while limiting exposure to the systemic circulation. After 1 hour MCAO in three-month old male C57/Bl6 mice, we examined the potential neuroprotective effects of IA verapamil (10mg/kg) to the ipsilateral internal carotid artery (N=10 in each group). We evaluated post stroke day 3 (PSD3)

stroke volume using tetrazolium chloride (TTC), as well as protein levels of GFAP (a marker of activated astrocytes) and NeuN (a marker of mature neurons). In a separate set of experiments, we evaluated post-stroke behavioral-motor effects using standardized pre-conditioned clinical tests (Rotarod). Animal experiments were blinded. Finally, based on these experiments, we conducted a single-institution Phase I study to evaluate the feasibility and safety of superselective IA verapamil (10mg) administration immediately following mechanical thrombectomy.

RESULTS: Using our model and control normal saline injections, we were able to obtain reproducible infarcts compared to sham animals. IA carbon black infusion at varying flow rates (1.0, 2.5, 5.0, 7.5 μL/Min) yielded optimization at 2.5 μL/Min with infusion to the ipsilateral hemisphere and minimization of exposure to the contralateral hemisphere and systemic circulation. On PSD3, TTC staining demonstrated significant reduction in stroke volume compared to controls ($p=0.03$). Quantitative western blot analysis demonstrated significant increase in GFAP and significant reduction in NeuN in control animals compared to treated, which were more similar to sham (non-stroked) animals. Behavioral testing demonstrated that verapamil treated animals improved after initial post-stroke testing significantly more than controls ($p=0.047$). The Phase I study yielded successful administration of IA verapamil to the affected vessel immediately following thrombectomy in all subjects with no significant hemodynamic side effects. The primary safety outcome variable was significant intracranial hemorrhage (ICH) as defined by the Interventional Management Stroke (IMS) III Trial; none of the enrolled patients suffered significant ICH.

CONCLUSION: Large vessel occlusive stroke can be clinically devastating. Given the lack of relevant translational research in this field, we retro-engineered a mouse model to reproducibly study IA pharmacotherapy. IA verapamil administration resulted in significant improvements in stroke volume, protein markers of injury, and behavioral outcomes. Furthermore, initial evaluation in human subjects demonstrated feasibility of this technique, and preliminary safety at a recognized dose.

11:15 – 11:25 INTERLEUKIN-17 BLOCKADE INHIBITS CEREBRAL ANEURYSM FORMATION AND PREVENTS CEREBRAL ANEURYSM RUPTURE

Brian L. Hoh, M.D., F.A.A.N.S., F.A.C.S., F.A.H.A.*, Kelley Rojas, B.S., Lin Lin, B.S., Kamil Nowicki, Ph.D., and Koji Hosaka, Ph.D.; University of Florida*

INTRODUCTION: The mechanisms for cerebral aneurysm (CA) formation and rupture are not clearly understood. There is growing evidence that inflammation has a key role. IL-17 is a potent proinflammatory cytokine that recruits monocytes and neutrophils to sites of inflammation, and is implicated as a key mediator in the inflammatory axis within the vessel wall in vasculitis. Our hypothesis is that IL-17 has a role in CA formation, the rupture of already developed CAs, and blockade of IL-17 inhibits CA formation and prevents CA rupture.

METHODS: Cytokine array was performed for analysis of differential expression with Circle of Willis (COW) from C57BL6 mice that developed CAs vs. mice that did not develop CAs, using a murine CA model we have previously described. In this model, approximately 80-90% of mice develop CAs. Immunohistochemistry (IHC) was performed on human aneurysm tissue and superficial temporal artery (control) for human validation of findings from the murine cytokine array studies. C57BL6 mice were administered rat anti-mouse IL17 antibody or rat IgG2A (control) prior to CA induction to study blockade of CA formation; or one week after CA induction to study prevention of rupture of already developed CAs, and IHC was performed on the COW.

RESULTS: IL-17 was significantly elevated in the COW of mice that developed CAs compared to mice that did not develop CAs (P=0.03). IL-17 was robustly expressed in human aneurysms and not in control superficial temporal artery. IL-17 blockade in mice prior to CA induction inhibited CA formation: CAs developed in 36% of mice given rat anti-mouse IL17 antibody compared to 86% of mice given rat IgG2A (P=0.02). IL-17 blockade in mice one week after CA induction inhibited rupture of already developed CAs: CA rupture

occurred in 21% of mice given rat anti-mouse IL17 antibody compared to 62% of mice given rat IgG2A ($P<0.05$). The COW of mice given rat IgG2A had abundant monocytes and neutrophils whereas the COW of mice given rat anti-mouse IL17 antibody did not, implicating the mechanism of IL-17 in CA formation is the proinflammatory recruitment of monocytes and neutrophils.

CONCLUSION: IL-17 seems to have a role in the formation of CAs and the rupture of already developed CAs via a proinflammatory monocyte and neutrophil-mediated mechanism. IL-17 is found in human CAs validating murine findings. This could have clinical translation with IL-17 blockade being a potential therapeutic target for preventing the ruptured of incidentally found unruptured CAs in patients.

11:35 – 11:45 TARGETING THE IMMUNE CHECKPOINT NETWORK WITH MIR-138 EXERTS THERAPEUTIC EFFICACY IN MURINE MODELS OF GLIOMA

Edjah Nduom, M.D., Jun Wei, Ph.D., Ling-Yuan Kong, Ph.D., Cristina Ivan, Ph.D., M.S., Gregory N. Fuller, M.D., Ph.D., Mark Gilbert, M.D., Charles A. Conrad, M.D., George A. Calin, M.D., Ph.D., and ***Amy Heimberger, M.D.****; The University of Texas MD Anderson Cancer Center*

INTRODUCTION: Antibody therapeutic targeting of the immune checkpoints CTLA-4 and PD-1 has demonstrated marked tumor regression in clinical trials; however, this requires multimodality treatment and has known toxicity. Furthermore, the targeting of one checkpoint often results in the up-regulation of another. MicroRNAs (miRNAs) can modulate gene transcripts, including those of tumor-mediated immune suppressive pathways and networks. Additionally, miRNAs can be delivered to the systemic immune compartment, which can initiate anti-tumor immune response, including within the central nervous system, thereby overcoming the confounding issue of miRNA delivery to the tumor.

METHODS: To identify potential immune modulatory miRNA therapeutics, we exploited human glioblastoma miRNA expression assays followed by a screening process of predicted binding sites in the 3' UTR of immune suppressive pathways and immune checkpoints. MiR-138 emerged as a leading candidate with three predicted binding sites in the 3' UTR of CTLA-4 and one within PD-1, which was functionally confirmed with luciferase expression assays. The miR-138 targeting of CTLA-4 and PD-1 was further validated by expression analysis of transfected human $CD4^+$ T cells.

RESULTS: Using human glioma tumor microarrays and *in situ* hybridization, heterogeneous expression of miR-138 was found amongst all glioma grades and pathological subtypes. The PD-1 ligand, PD-L1, was frequently expressed in glioblastomas based on immunohistochemistry and *ex vivo* flow cytometry from fresh human glioblastoma. Analysis of TCGA database revealed that co-

expression of PD-1 and PD-L1 impacts glioblastoma survival. Given the previously documented role of CTLA-4 as an operational mechanism of glioblastoma-mediated immune suppression, this cumulative data suggests that dual targeting of CTLA-4 and PD-1 with miR-138 in glioblastoma patients may have anti-tumor activity. *In vivo* treatment with miR-138 in immune-competent mice with GL261 gliomas demonstrated marked tumor regression, a 43% increase in median survival (P=0.011), and an associated decrease in intratumoral FoxP3+ Tregs, CTLA-4, and PD-1 expression.

CONCLUSION: Conversely, in an immune-incompetent animal background, miR-138 failed to exert any therapeutic effect, indicating that miR-138 mediates *in vivo* activity via the immune system. Cumulatively, our data indicate that miR-138 may be an active and novel immunotherapeutic agent for human glioblastoma patients.

11:45 – 11:55 MAGNETIC RESONANCE FINGERPRINTING OF BRAIN TUMORS: INITIAL CLINICAL RESULTS

Andrew E. Sloan, M.D., F.A.A.N.S., F.A.C.S.[1,2], *Badve Chaitra, M.D.*[1,2], *Vikas Gulani, M.D., Ph.D.*[1,2], *Mark Griswold, Ph.D.*[1], *and Jeffrey Sunshine, M.D.*[1,2]; *Case Western Reserve University of Medicine*[1], *and University Hospitals of Cleveland*[2]

INTRODUCTION: Magnetic Resonance Fingerprinting (MRF) uses pseudo-randomized variation in acquisition parameters to generate a multi-parametric signal. Moreover, unlike conventional MRI sequences which yield qualitative comparisons, MRF can rapidly quantify T1, T2, M0 and off-resonance signals to aid in non-invasive tissue identification and delineation of various tissues. Here we present our initial clinical results from a series of 20 patients.

METHODS: 20 patients with the various newly diagnosed b rain neoplasms were scanned: glioblastoma multiforme (GBM; N = 10), Anapastic oligodendrogliomas (AO; N = 5) and brain metastases (METS; N = 5) were scanned using an MRF protocol[1]. Imaging was acquired through representative areas of brain and quantitative T1 and T2 maps were generated. T1 and T2 quantification of solid tumor component, immediate perilesional white matter (PWM) within 1 cm from enhancing margin, and contralateral white matter (CWM) was performed using ROI analysis. Student's t-test was used for statistical analysis.

RESULTS: All solid tumor measurements were in agreement with published literature[2-3]. Solid tumor T1, T2 were different than T1, T2 of CWM ($n=20$, $p < 0.001$). There was difference between T1, T2 of PWM of GBMs and METS from their CWM ($n=15$, $p<0.001$, $p<0.001$). There was difference between the T1, T2 of solid regions of GBMs and METS ($p < 0.01$). Also, there was T1, T2 difference between the PWM of GBMs and METS ($p < 0.05$). T2 relaxometry revealed difference between GBMs and AOs ($p < 0.02$).

CONCLUSION: MRF is able to simultaneously measure T1 and T2 values of various brain tumors and surrounding tissues. It can distinguish with high

statistical significance between tumor types and PWM changes from CWM. Preliminary data supports using MRF to identify regions of infiltrative edema in GBM, and differentiation of different tumor types and grades. The preliminary data on MRF of brain tumors suggest application of this technique to identify, diagnose, and offer prognosis of intracranial masses, delineation of tumor margins, and characterization of therapeutic response.

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11:55 – 12:05 CIRCULATING TUMOR CELLS IN PATIENTS WITH GLIOBLASTOMA

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INTRODUCTION: Glioblastoma (GBM) is characterized by necrosis, angiogenesis, and inevitable recurrence. Despite its aggressiveness, GBM rarely form extra-cranial metastases suggesting impediments in vascular invasion, survival in circulation or implantation. Advances in microfluidics have successfully identified circulating tumor cells (CTCs) in lung, prostate, and breast cancer patients. Using a novel CTC microfluidic device, we hypothesize that GBM patients have CTCs, which can be captured, quantified, and analyzed for molecular and genetic markers.

METHODS: We developed a microfluidic device (CTC-iChip) capable of capturing CTCs from whole blood via immunomagnetic depletion of hematopoietic blood cells. Using GBM-specific antibodies, we validated our CTC-iChip using GBM cell lines spiked into healthy donor blood. After successfully establishing our device, we evaluated venous blood samples (10ml) from 6 healthy donors and 33 GBM patients preoperatively and postoperatively including chemotherapy and radiation therapy. CTCs were stained with a cocktail of GBM-specific antibodies and scanned by automated fluorescence microscopy. CTCs and their matched pathological specimens from surgery were further analyzed by Fluorescence in-Sutu Hybridization (FISH).

RESULTS: CTCs were detectable in at least one blood sample in 14/33 (42%) GBM patients. Patients with progressive disease harbored a median 11.8 CTCs per ml (mean 13.6 $\pm$ 10.7) compared to 2.1 CTCs per ml (mean: 4.0 $\pm$ 2.7) in patients with stable disease. CTC detection was significantly associated with disease progression (p-value: 0.03), but not with other clinical variables such as

disease location, extent of resection, or genotype. FISH analysis of CTCs from EGFR-amplified and Chr7-polysomy GBM patients revealed 30/36 (83.3%) CTCs harbored concordant molecular aberrations. Of the 14 patients with detectable CTCs, one had autopsy confirmed metastatic GBM lesions in the lung. CTCs were identified at high numbers (48.2 cells per ml) in this patient. In addition, EGFR amplification was identified in the patient's CTCs and the metastatic lesions (lymph nodes, and pulmonary nodules).

CONCLUSION: We identify the first evidence of CTCs in the peripheral blood of GBM patients. CTC frequency often varies during the course of therapy and is correlated with disease progression. Further studies are needed to define this novel discovery and its potential role in the care of GBM patients.

12:05 – 12:15 USE OF VOLUMETRIC MR SPECTROSCOPIC IMAGING AND 5-ALA FLUORESCENCE-GUIDED SURGERY FOR RESECTION OF GLIOBLASTOMA

Costas G. Hadjipanayis, M.D., Ph.D.*, J. Scott Cordova, B.S., Chad A. Holder, M.D., Daniel Brat, M.D., Ph.D., Hui-Kuo Shu, M.D., Ph.D., and Hyunsuk Shim, Ph.D.; Emory University*

INTRODUCTION: Glioblastoma (GBM) resection based on neuronavigation with contrast-enhanced MRI (CE-MRI) results in a high rate of local recurrence as infiltrating tumor cells extend beyond areas of contrast enhancement. Integrating metabolic maps from magnetic resonance spectroscopic imaging (MRSI) into neuronavigation may identify high-risk tumor infiltration zones outside of CE-MRI for surgery. Coupling MRSI with fluorescence-guided surgery (FGS) using 5-aminolevulinic acid (5-ALA) may provide a means to further enhance the degree of tumor resection.

METHODS: In a new Phase II trial for new and recurrent GBM patients, 3D-echo planar spectroscopic imaging was performed and processed to give full-brain metabolite volumes for import into a neuronavigation station. Patients were administered 5-ALA orally 3-5 h before surgery. To minimize error due to shift, needle biopsies were collected from tumor regions with elevated choline/NAA values within T1CE and/or T2/FLAIR hyperintense regions before tumor resection. Fluorescence intensity of fresh tissue was quantified ex vivo using a hand-held spectroscopic device. Samples were then fixed/stained with H&E and analyzed for tumor cell density and tissue infiltration using automated image analysis techniques. Quantitative tumor segmentation was used to evaluate extent of tumor resection.

RESULTS: Choline/NAA values show a positive linear trend with the number of tumor nuclei per high power field and the degree of tumor infiltration. Real-time intraoperative tumor fluorescence was also confirmed ex vivo and shows a similar positive linear trend with choline/NAA ratios.

CONCLUSION: The linear trend that Cho/NAA values exhibit with histopathology and quantitative intraoperative fluorescence of tumor tissue outside of CE-MRI regions supports its use for identifying regions of tumor infiltration. This is the first time that 5-ALA induced tumor fluorescence has been shown to correlate with MRSI-derived metabolic markers in GBM tumors. We believe the continued combination of MRSI-neuronavigation with 5-ALA FGS in this trial will result in more complete GBM resections.

12:15 – 12:25 ALKYLPHOSPHOCHOLINE ANALOGS FOR BROAD SPECTRUM CANCER IMAGING AND THERAPY

***John S. Kuo, M.D., Ph.D., F.A.A.N.S., F.A.C.S.**, and Jamey P. Weichert, Ph.D.; University of Wisconsin-Madison*

INTRODUCTION: Many solid tumors contain an over-abundance of phospholipid ethers relative to normal cells. Capitalizing on this difference, we created cancer-targeted alkylphosphocholine (APC) analogs through structure activity analyses.

METHODS: CLR1404 [18-(*p*-iodophenyl) octadecylphosphocholine] was identified among 9 APC analogs as the best tumor-imaging agent in rodent models, and exhibited low toxicity and low liver, kidney, bladder, and abdominal exposure in toxicology studies. Unlike classical DNA-targeted cytotoxic agents, APC analogs target cellular and intracellular membranes, and enter via lipid rafts, which are more abundant in cancer cells relative to normal cells. Depending on the iodine isotope added, radioiodinated APC analog CLR1404 is used as either a PET imaging (^{124}I) or molecular radiotherapeutic (^{131}I) agent. The fluorescent analogs CLR1501 (green fluorescence) and CLR1502 (near infrared) were created for real-time tumor cell visualization.

RESULTS: We report results of in vitro and in vivo testing with radioisotope-labeled CLR1404 for diagnostic imaging (^{124}I-CLR1404) and for cancer therapy (^{131}I-CLR1404), and imaging data with the fluorescent APC analogs in a wide variety of tumor models. Tumor-specific APC analogs were evaluated in vitro and in vivo as imaging and therapy agents, showing preferential tumor-selective uptake and retention in 55 different spontaneous and transgenic models of rodent and human cancers ranging from GBM, breast, lung, colorectal, pancreatic, melanoma, prostate, renal, ovarian cancer. APC analogs also displayed prolonged tumor-selective retention in patient-derived GBM cancer stem cells and xenografts, and low retention in normal stem cells and tissues. Testing of ^{131}I-CLR1404 also showed therapeutic efficacy (tumor growth suppression, survival extension) in a wide range of human tumor xenograft

models. Clinical trials in advanced cancer patients using human PET/CT and SPECT/CT imaging with ^{124}I- or ^{131}I-CLR1404, respectively, demonstrated selective uptake and prolonged retention in both primary and metastatic malignant tumors. Fluorescent APC analogs have distinct practical advantages when directly compared with 5-ALA for intraoperative applications.

CONCLUSION: We present first-in-human imaging results that show CLR1404 analogs have tumor targeting and retention properties in cancer patients. CLR1404 represents a new class of synthetic APC analogs useful as broad spectrum, tumor-selective molecular imaging and therapy agents in human cancers, with fluorescent analogs showing potential for intraoperative visualization of cancer cells. Combined application of these chemically identical APC-based radioisosteres will enable personalized dual modality cancer therapy by using molecular ^{124}I-CLR1404 and fluorescent APC for tumor imaging, and for planning follow-up ^{131}I-CLR1404 therapy.

12:25 – 12:35 SURVIVIN TRANSCRIPT VARIANT 2 DRIVES ANGIOGENESIS AND MALIGNANT PROGRESSION IN PRONEURAL GLIOMAS

***Ganesh Rao, M.D.**, and Khatri Latha, Ph.D.; University of Texas MD Anderson Cancer Center*

INTRODUCTION: The influence of Survivin isoforms on outcome in glioblastoma is poorly understood. We analyzed the dominant anti-apoptotic transcript variants of Survivin using expression data and modeled them in vivo to determine their impact on glioma formation and progression.

METHODS: Using data from low- and high-grade glioma knowledge bases, we expressed the anti-apoptotic isoforms of Survivin (transcript variants 1 and 2) in vivo using the RCAS/Ntv-a model of murine glioma.

RESULTS: In low-grade gliomas, Survivin RNA expression was increased in 22/167 (13.2%) of cases and was associated with shortened survival ($p=0.005$). Survivin RNA was preferentially expressed in proneural (PN) relative to mesenchymal high-grade gliomas ($p<0.0001$). In proneural gliomas, Survivin was expressed in 94/141 (67%) of cases and was associated with shorter disease-free survival ($p=0.04$). In a PDGFB-dependent murine model of PN glioma, ectopic expression of variant 1 yielded tumors in 28/30 (93%) of mice, of which 25% were high-grade tumors, whereas ectopic expression of variant 2 yielded tumors in 27/28 (96%), of which 81% were high-grade tumors ($p<0.0001$). Microvascular proliferation was significantly more prominent ($p<0.0001$) and tumor-free survival was shorter in mice with variant 2 than variant 1-derived tumors ($p=0.01$).

CONCLUSION: Survivin expression in low-grade gliomas is associated with poor survival and is preferentially expressed in PN gliomas. Compared with variant 1, variant 2 was associated with poorer survival and, in the PN murine model, promoted malignant progression, angiogenesis, and shorter tumor-free survival. Inhibiting *Survivin* transcript variant 2, rather than variant 1 (the common isoform), may be an effective treatment strategy for glioma.

12:35 – 12:45 A COMPARISON OF THE SUBLABIAL MICROSCOPIC AND ENDOSCOPIC ENDONASAL RESECTION OF PITUITARY ADENOMAS: A VOLUMETRIC ANALYSIS ON 272 CASES

Peter Amenta, M.D., Ashish Shah, M.D., Charif Sidani, M.D., and ***Jacques Morcos, M.D.****; University of Miami*

INTRODUCTION: The resection of pituitary adenomas has evolved over the past decade, as the sublabial (SL) microscopic approach has been largely abandoned in favor of the endoscopic endonasal (EE) approach. At our institution, the senior author (JJM) adopted the EE approach in 2007. We reviewed pituitary adenoma resections from 2003 to 2012 performed by the senior author to compare extent of resection, surgical outcomes and the incidence of complications in both the SL and EE groups. Our primary goal is to volumetrically examine the extent of tumor resection achieved by the SL and EE approaches. We present our preliminary results, which define multiple characteristics of the patient population and reflect clinical outcomes.

METHODS: Data pertaining to the resection of pituitary adenomas by the senior author from 2003 to 2012 was retrospectively analyzed. The patient population was divided based on surgical approach (SL, EE, or hybrid). Demographic information, including, age, sex, and type of pituitary tumor (non-functional or functional) were recorded. The incidences of cerebrospinal fluid (CSF) leak, gross total resection (GTR) versus subtotal resection (STR), and re-resection were calculated. Using a **DICOM volume measuring program,** the preoperative volume of the tumor was measured on T1-weighted MRI. Postoperative MRI was performed within two days of surgery and the volume of residual tumor was measured. The analysis was restricted to 2 epochs: 2003-2006 (SL group) and 2009-2012 (EE group), and follow-up periods were arbitrarily limited to a maximum of 3 years in both groups to maintain follow-up equality in both.

RESULTS: A total of 272 patients (114 males/ 158 females) underwent resection of a pituitary adenoma and were eligible for the study. Ages ranged from 17 to 85 (median 49) years old. 181 (64.3%) tumors were non-functional adenomas and 96 (34.8%) were functional. 132 (46.9%) patients were treated via the SL approach, while the EE approach was used in 139 (49.4%) patients. Tumors in 10 (3.5%) patients were resected with a hybrid approach comprised of the SL microscopic approach in which the endoscope was used to complete the resection. An intraoperative CSF leak was noted in 29.5% of SL cases and 41.4% of EE cases. Postoperative leaks were encountered in 1.5% of SL cases and 3.6% of EE cases. GTR, as judged by the operating surgeon, was reported in 81.8% of SL approaches and 72.9% of EE approaches. 22.3% of patients underwent a re-resection during the time period of the study. The volumetric analysis had not been completed on all patients at the time of this abstract submission and will be presented in detail. Comparison between "operative impression" and actual postoperative MRI findings will be presented, and extent of resection will be correlated with incidence of regrowth.

CONCLUSION: The SL approach resulted in a lower incidence of CSF leak. The use of volumetric analysis of preoperative and postoperative MRIs is a useful tool in quantifying degree of resection. Further conclusions will be drawn at the completion of the volumetric analysis.

12:45 – 12:55 TRANSCORTICAL TRANSVENTRICULAR AND ENDOSCOPIC REMOVAL OF COLLOID CYSTS: SINGLE INSTITUTION COMPARISON OF RESULTS AND CLASSIFICATION OF OPERATIVE ZONES

Joseph Osorio, M.D., Ph.D., and ***Michael W. McDermott, M.D., F.A.A.N.S.****; University of California, San Francisco*

INTRODUCTION: To describe the transcortical transventricular and endoscopic removal of colloid cysts and compare results. Develop a classification of surgical operative corridirs as it relates to microsurgical approaches.

METHODS: 33 patients included in the study, 20 had an endoscopic operation, 5 had transcortical-transventricular, and 8 underwent an interhemispheric approach for resection. Based on common cyst location in the roof of the third ventricle we propose a simple classification of surgical operative zones (Zones 1-3) based on relationships defined by the anterior column of the fornix, the septal vein and the lateral atrial vein.

RESULTS: Complete capsule removal was achieved in 35% of endoscopic operations, 100% of transcortical transventricular operations, and 63% of the interhemispheric operations. Operative time was 176 minutes for endoscopic operations, whereas the operative time for cases that converted from endoscopic to the transcortical transventricular approach was 190 minutes ($p=0.39$).

CONCLUSION: A surgical based classification of zones within the roof of the third ventricle that can be accessed with microsurgical techniques is proposed. Both endoscopic and microsurgical cyst aspiration and excision remain options. We believe that for younger patients, patients with large cysts that fill the third ventricle or for those with recurrence after prior treatment would benefit from open transcortical excision as a safe and effective operative approach using modern image guided systems.

12:55 – 1:05 LONG-TERM QUALITY OF LIFE AFTER ENDOSCOPIC ENDONASAL RESECTION OF CRANIOPHARYNGIOMAS

Kunal S.Patel, B.S., Shaan M. Raza, M.D., Edward D. McCoul, M.D., M.P.H., Jeffery Greenfield, M.D., Ph.D., Mark M. Souweidane, M.D., Vijay K. Anand, M.D., and ***Theodore H. Schwartz, M.D.****; Weill Cornell Medical College*

INTRODUCTION: Craniopharyngiomas are benign parasellar tumors whose surgical removal often leads to morbidity with resulting decreases in quality of life. The endonasal endoscopic approach is a minimal access method for removing these tumors which may reduce post-operative morbidity. Quality of life following this procedure for craniopharyngiomas has not been documented.

METHODS: We reviewed a database of consecutive endonasal endoscopic surgeries done at Weill Cornell Medical College. Patients with histologically-proven craniopharyngiomas who filled out either only post-operative or both pre- and post-operative (>9 month) quality of life forms (ASBQ and SNOT-22). Rates of resection, complications, visual and endocrine function were determined. Retrospective independence (Wen Score) was also assigned. A contemporaneous larger group of patients undergoing endonasal endoscopic pituitary adenoma resection was used as a control.

RESULTS: There were 38 procedures done in 36 patients. The average long-term post-operative ASBQ score was 3.34 and SNOT-22 score was 22.0, obtained in 27 of 36 patients. Better QOL was associated with GTR and post-operative radiation. Worse QOL was associated with childhood onset, persistent visual defects, hypopituitarism, tumor recurrence and an increase in BMI. In a subset of 12 patients, both pre-and post-operative (> 9 months) QOL scores were obtained. Both ASBQ and SNOT scores showed stability and a trend to improvement from 3.0 $\pm$ .07 to 3.3 $\pm$ 1.56 (ASBQ) and 23.4 $\pm$ 17.68 to 22.0 $\pm$ 27.58 (SNOT). Compared with 62 patients undergoing pituitary

adenoma resection, craniopharyngiomas had worse post-operative QOL on the ASBQ (3.34 versus 3.80; $p<0.02$) and SNOT-22 (22.0 versus 13.4; $p<0.02$).

CONCLUSION: Endonasal endoscopic surgery results in an overall maintenance of post-operative QOL compared with pre-operative QOL in spite of worsening Wen scores. Improvements can be seen in patients with GTR and radiation therapy and deterioration in patients with visual or endocrine deficits. Nevertheless, these patients still have worse QOL than patients with non-hormone producing pituitary macroadenomas, confirming the more nefarious nature of craniopharyngiomas even when removed through a minimally invasive approach. These measures should serve as benchmarks for comparison with open transcranial approaches to similar tumors.

7:35 – 7:45 **THE ROLE OF LASER INTERSTITIAL THERMAL THERAPY IN ENHANCING PROGRESSION-FREE SURVIVAL OF DIFFICULT-TO-ACCESS HIGH-GRADE GLIOMAS: A MULTICENTER STUDY**

Alireza M. Mohammadi[1], Ammar H. Hawasli[2], Analiz Rodriguez[3], Jason L. Schroeder[1], Adrian W. Laxton[3], Paul Elson[1], Stephen B. Tatter[3], Gene H. Barnett[1], and ***Eric C. Leuthardt[2]****; Cleveland Clinic[1], Washington University School of Medicine[2], Wake Forest School of Medicine[3]*

INTRODUCTION: Surgical extent-of-resection has been shown to have an impact on high-grade glioma (HGG) outcomes; however, complete resection is rarely achievable in difficult-to-access (DTA) tumors. Controlled thermal damage to the tumor may have the same impact in DTA-HGGs.

METHODS: We report our multicenter results of laser interstitial thermal therapy (LITT) in DTA-HGGs. We retrospectively reviewed 34 consecutive DTA-HGG patients (24 glioblastoma, 10 anaplastic) who underwent LITT at Cleveland Clinic, Washington University, and Wake Forest University (May 2011–December 2012) using the NeuroBlate System. The extent of thermal damage was determined using thermal damage threshold (TDT) lines: yellow TDT line (43°C for 2 min) and blue TDT line (43°C for 10 min). Volumetric analysis was performed to determine the extent-of-coverage of tumor volume by TDT lines. Patient outcomes were evaluated statistically.

RESULTS: LITT was delivered as upfront in 19 and delivered as salvage in 16 cases. After 7.2 months of follow-up, 71% of cases demonstrated progression and 34% died. The median overall survival (OS) for the cohort was not reached; however, the 1-year estimate of OS was 68 9%. Median progression-free survival (PFS) was 5.1 months. Thirteen cases who met the following two criteria—(1) <0.05 cm3 tumor volume not covered by the yellow TDT line and (2) <1.5 cm3 additional tumor volume not covered by the blue TDT line—had better PFS than the other 21 cases (9.7 vs. 4.6 months; P = 0.02). LITT can be

used effectively for treatment of DTA-HGGs. More complete coverage of tumor by TDT lines improves PFS which can be translated as the extent of resection concept for surgery.

CONCLUSION: LITT can provide a viable therapeutic option for patients with difficult to access high glade glial neoplasms.

7:45 – 7:55 LASTER INTERSTITIAL THERMAL THERAPY: LESSONS LEARNED

***Michael Schulder, M.D.**, and Ashesh D. Mehta, M.D., Ph.D.;*

INTRODUCTION: Complications of laser interstitial thermal therapy (LITT) tend to be underreported. This paper will discuss how we have modified our technique for LITT in the context of technical and treatment-related complications.

METHODS: Laser probes were inserted in the operating room using low-field intraoperative MRI (iMRI) guidance (5 patients), frameless stereotaxy (FS, in 2), or frame-based placement in 17. LITT itself was done in a 1.5 Tesla diagnostic MRI (dMRI). 28 patients were treated, including 10 with brain tumors, 1 with a filum terminale ependymoma (in whom the lasers were inserted in the dMRI itself), 15 with mesial temporal lobe epilepsy (MTLE), and 3 with hypothalamic hamartomas (HH).

RESULTS: Laser misplacement occurred in two patients, in whom the laser probe was found to be misplaced upon imaging in the diagnostic MRI; in one patient FS was used for tumor targeting, and in the other, a patient with MTLE, the laser was suboptimally placed when an alignment rod was not inserted before the styletted laser probe carrier. No other patients in whom a stereotactic frame was used sustained laser fiber misplacement.

Three complications resulted from the LITT itself. Two patients treated for recurrent brain tumors had new neurological deficits after treatment, because of laser hyperthermia affecting the brainstem in one patient, and the primary motor cortex in the other. The patient with the filum terminale ependymoma developed a paraparesis the day after treatment; MRI showed expansion of the intraspinal mass with resolution of enhancement, consistent with tumor ablation.

CONCLUSION: Complications of LITT can result from laser misplacement, hemorrhage from laser insertion, and from the laser treatment itself. Our lessons learned include:

1) Use of a stereotactic frame will provide optimal laser fiber placement.

2) In patients in whom a long laser placement is needed (as in many undergoing ablation for epilepsy), an alignment rod should be inserted before the laser fiber itself.

3) Critical structures should not be treated with the full LITT hyperthermia dose in order to minimize the risk of neurological complications from the treatment itself.

4) Intraspinal LITT should be used with great caution.

7:55 – 8:05 **OUTCOMES OF OPERATIVE AND NONOPERATIVE TREATMENT FOR ADULT SPINAL DEFORMITY: A PROSPECTIVE, MULTI-CENTER MATCHED AND UNMATCHED COHORT ASSESSMENT WITH MINIMUM 2-YEAR FOLLOW-UP**

*Justin S. Smith, M.D., Ph.D., F.A.A.N.S.[1], **Christopher I. Shaffrey, M.D., F.A.A.N.S.[1]**, Virginie Lafage, Ph.D.[2], Frank J. Schwab, M.D.[2], Shay Bess, M.D.[3], and Christopher P. Ames, M.D., F.A.A.N.S.[4]; University of Virginia[1], New York University Hospital for Joint Diseases[2], Rocky Mountain Hospital for Children[3], University of California, San Francisco[4]*

INTRODUCTION: The prevalence of adult spinal deformity has been reported to range from 2% to 32% and has been reported to be as high as 68% among the elderly. The finding of spinal deformity in many adults is simply incidental and requires only education and follow-up, but for others it can result in significant pain and disability. As the population continues to age due to longer life expectancy and the desire for maintained active lifestyles continues to increase, there are growing numbers of patients seeking medical and surgical evaluation for spinal deformity. Recent reports have suggested that operative treatment for symptomatic adult spinal deformity can offer improvement of pain and disability, but the impact of surgical versus nonsurgical treatments warrants further study. Our objective was to compare outcomes for operative (op) and nonoperative (nonop) treatment for adult spinal deformity based on a prospective, multi-center patient population with min 2-yr follow-up.

METHODS: This is a multicenter, prospective analysis of consecutive adult spinal deformity patients electing for op or nonop care at enrollment. Inclusion criteria included age>18 yrs and adult spinal deformity as defined by at least one of the following: coronal Cobb angle >20°, C7 sagittal vertical axis (C7 SVA) >5cm, pelvic tilt (PT) >25°, or thoracic kyphosis >60°. Standardized measures of health-related quality of life (HRQOL) were collected at baseline and follow-up, including Oswestry Disability Index (ODI), Scoliosis Research

Society-22 (SRS-22), Short Form-36 (SF-36), and numeric rating scale (NRS) scores for back and leg pain. Standing full-length postero-anterior and lateral spine x-rays were used for measurement of radiographic parameters. Radiographic measurements included: coronal Cobb angle, C7 SVA, thoracic kyphosis, lumbar lordosis (LL), pelvic incidence (PI), and PT. Propensity scores were used to match op and nonop patients based on baseline ODI, SRS-22, maximum thoracolumbar/lumbar coronal Cobb angle, mismatch between PI and LL (PI-LL), and leg pain NRS.

RESULTS: 689 patients met criteria, including 286 op and 403 nonop, with mean ages of 53 and 55 years, min 2-yr follow-up rates of 86% and 55%, and mean follow-up of 24.7 and 24.8 months, respectively. At baseline, compared with the nonop group, op patients had significantly worse HRQOL based on ODI, SRS-22, SF-36, and leg and back pain NRS scores ($p<0.001$) and had worse deformity based on PT, PI-LL, and C7 SVA ($p\leq0.002$). Before reaching min 2-yr follow-up 38 nonop patients converted to op treatment and were analyzed in the op group. At min 2-yr follow-up, all HRQOL measures assessed significantly improved for op patients ($p<0.001$), but none of these measures improved significantly for nonop patients ($p\geq0.11$). 97 matched op-nonop pairs were identified based on propensity scores. At last follow-up, the 97 matched op patients had significant improvement in all HRQOL measures assessed ($p<0.001$), but the 97 matched nonop patients lacked significant improvement in any of the HRQOL measures ($p\geq0.20$). Paired op-nonop analysis demonstrated the op patients to have significantly better HRQOL scores at follow-up for all measures assessed ($p<0.001$), except SF-36 mental component score ($p=0.058$). Minor and major complication rates for op patients were 53% and 40%, respectively.

CONCLUSION: The present study is a large prospective, multicenter analysis of operative and nonoperative treatment for adult spinal deformity. At min 2-yr follow-up, both unmatched and matched analyses demonstrated significant improvement in multiple measures of HRQOL for op patients. In contrast, nonop treatment at best maintains presenting levels of pain and disability.

8:05 – 8:15 CLINICAL AND RADIOGRAPHIC ANALYSIS OF AN ARTIFICIAL CERVICAL DISC: SEVEN-YEAR FOLLOW-UP FROM THE PRESTIGE® PROSPECTIVE RANDOMIZED CONTROLLED CLINICAL TRIAL

***Praveen V. Mummaneni, M.D.**; University of California, San Francisco*

INTRODUCTION: To assess the long-term safety and efficacy of cervical disc replacement with the PRESTIGE® disc in a prospective, randomized, multicenter trial at 7 years of follow up.

METHODS: At 31 investigational sites, 541 patients with single-level cervical disc disease with radiculopathy were randomized to 1 of 2 treatment groups: 276 investigational group patients underwent anterior cervical discectomy and arthroplasty with the PRESTIGE® disc, and 265 control group patients underwent anterior cervical discectomy and fusion. Clinical outcomes included Neck Disability Index (NDI), 36 Short-Form Health Survey (SF-36), neck and arm pain scores. Radiographs were assessed for angle of motion and fusion. Clinical and radiographic outcomes were evaluated preoperatively, intraoperatively, and at 1.5, 3, 6, 12, 24, 36, 60, and 84 months.

RESULTS: Of the 541 patients treated, 395 (73%) patients (212 investigational and 183 control patients) completed 7 years of clinical follow-up. Significant improvements achieved by 1.5 months in both groups were sustained at 7 years. In the investigational group, mean Neck Disability Index improvements from preoperative scores were 38.2 and 37.5 at 60 and 84 months, respectively. In the control group, the corresponding means were 33.8 and 31.9. The differences between the investigational and control groups at 60-month and 84-month periods were significant ($p = 0.014$ and 0.002, respectively). The overall rates of maintenance or improvement in neurological status in the investigational group were significantly higher: 92.2% and 88.2% at 60 months and 84 months as compared with 85.7% and 79.7% in the control group ($p = 0.017$ and 0.011, respectively). At 84 months, the percentage of working patients in the investigational group was 73.9%, and in the control

group, 73.1%. Postoperatively, the implant effectively maintained average angular motion of 6.67° at 60 months and 6.75° at 84 months. Cumulative rates for surgery at the index level were lower ($p < 0.001$) in the investigational group (11/276; 4.8%) when compared to the control group (29/265; 13.7%) (based on life table method), and there were statistical differences between the investigational and control groups with specific regard to the rate of subsequent revision and supplemental fixation surgical procedures. Rates for additional surgical procedures that involved adjacent levels were lower in the investigational group than in the control group (11/276 [4.6%] versus 24/265 [11.9%], respectively).

CONCLUSION: The PRESTIGE® Disc maintains improved clinical outcomes and segmental motion after implantation at 7-year follow-up and may result in a reduction in adjacent segment degeneration.

8:15 – 8:25 CERVICAL DISC ARTHROPLASTY VS. ACDF: SEVEN-YEAR OUTCOMES

***Mark E. Shaffrey, M.D.**; University of Virginia*

INTRODUCTION: For properly selected patients, cervical disc arthroplasty (CDA) is an FDA-approved alternative to standard-of-care anterior cervical discectomy and fusion (ACDF). This study compared the safety and efficacy of treatment with a low-profile, titanium ceramic composite ball-in-trough cervical disc to treatment using control ACDF (plated fusion with allograft).

METHODS: Prospectively-collected data from 20 investigational sites were compared, per FDA-approved protocol, to that of the 265 historical control ACDF patients in a prior cervical disc investigational device exemption study. The 280 investigational patients with single-level cervical disc disease with radiculopathy and/or myelopathy underwent anterior cervical decompression and arthroplasty with a low-profile artificial disc. Key safety and efficacy outcomes included Neck Disability Index (NDI), Neck and Arm Pain Numerical Rating Scales, SF-36 Health Survey, work status, disc height, range of motion, adverse events (AE), additional surgeries, and neurological status. Clinical and radiographic follow-ups were completed preoperatively, intraoperatively, and at 1.5, 3, 6, 12, 24, 36, 60 and 84 months.

RESULTS: The investigational and historical control groups were mostly similar demographically. Patient follow up at 84 months was 75.0% for CDA and 68.7% for ACDF. There was no significant difference in blood loss (51.0 ml CDA vs. 57.1 ml ACDF) or hospital stay (0.98 days CDA vs. 0.95 days ACDF). The investigational group had statistically longer operative time (1h22m vs. 1h29m). Statistically significant improvements ($P < 0.001$) vs. pre-op in NDI, neck and arm pain and SF-36 were achieved by 1.5 months in both groups and maintained up to 84 months. At 84 months, mean improvements in NDI were 40.1±23.3 points for CDA and 31.9±21.8 for ACDF patients. SF-36 PCS/MCS mean improvements at 84 months were 13.1±11.9/8.2±12.3 points for CDA and 10.7±11.8/8.3±13.6 points for ACDF. Neurological

success was 92.8% for CDA and 79.7% for ACDF patients. Cumulatively up to 84 months, the percentages of CDA and ACDF patients who had an AE classified as possibly implant or implant/surgical procedure related were similar. Eighteen (6.4%) CDA and 29 (10.9%) ACDF patients had any second surgery at the index level. Following implantation of the CDA device, mean angular motion at the target level was maintained at 24 (7.5°) and 84 (6.9°) months. Bridging bone, evaluated by three independent radiologists, was reported in 5.9% of CDA patients at 24 months, 9.5% at 36 months, 9.8% at 60 months, and 10.3% at 84 months. Change in mean angulation (°) vs. pre-op of the adjacent segment above/below the index level was 1.16±4.31/1.27±4.11 for CDA and (-0.23)±5.37/1.25±5.07 for ACDF patients. At 84 months, 90.9% of CDA and 85.6% of ACDF patients were satisfied with the results of their treatment. Median return to work time for CDA patients was 40 days, vs. 60 for ACDF. At 84 months, 68.3% of CDA and 73.1% of ACDF patients were working.

CONCLUSION: This anterior low-profile CDA device maintains mean postoperative segmental motion while providing the potential for biomechanical stability. CDA patients reported significantly improved clinical outcomes vs. baseline, at least equivalent to standard-of-care ACDF, up to 84 months after surgery.

9:30 – 9:40 TRANSPLANTATION OF AUTOLOGOUS SCHWANN CELLS AFTER SUB-ACUTE THORACIC SPINAL CORD INJURY

Allan D. Levi, M.D., Ph.D., F.A.C.S.*; University of Miami Miller School of Medicine*

INTRODUCTION: The current clinical trial is designed to test the safety and tolerability of autologous Schwann cells (SCs) after sub-acute thoracic human SCI. Autologous SCs offer important safety advantages that include the absence of a requirement of immune suppression, minimal risk of disease transfer, and an exceedingly low risk of tumorigenicity. The rationale for implantation of autologous SC in humans with acute SCI is based on 25 years of research demonstrating that SCs reparative including 1. neuroprotection 2. capable of myelinating injured axons after SCI.

METHODS: This FDA approved dose-escalation, phase I study is registered with clinicaltrials.gov (NCT01739023). After appropriate psychological assessment and consent; sural (9-18 cm) nerve was harvested within 7 days of injury and SCs were purified and expanded in a cGMP facility and transplanted via laminectomy and a table mounted syringe device into the epicenter of the SCI 4 weeks post-injury.

RESULTS: We have recruited 3 of the anticipated 8 subjects. The ages of the patients were 40,25 and 24 y.o. with T3, T7 and T2 AIS A injuries respectively. Two cases resulted from MCC and one was a roll-over MVA. Cell dosage delivered at the time of surgery was 5×10^6 (n=2) and 10×10^6 SCs (n=1). SC purity varied from 92 – 98 %. There were no intra or post-operative complications. Patients regained some sensory function but no motor recovery after average follow-up of 1.5 years. Electrophysiologic testing suggested the recovery of some autonomic function.

CONCLUSION: The studies presented suggest that autologous SCs can be safely transplanted into patients with sub-acute severe thoracic SCI. We continue to recruit patients for the sub-acute protocol and are investigating the potential of SC transplantation after chronic injuries.

9:40 – 9:50 DIFFERENTIAL ABILITIES OF ACUTELY AND CHRONICALLY DENERVATED NERVE DERIVED AND SKIN DERIVED SCHWANN CELLS TO SUPPORT AXONAL REGENERATION AND REMYELINATION

Ranjan Kumar, B.Sc., Jo Anne Stratton, Ph.D., Jeff Biernaskie, Ph.D., and ***Rajiv Midha, M.D.****; University of Calgary*

INTRODUCTION: Schwann cells (SCs) play a key role in supporting axonal regeneration and remyelination following a peripheral nerve injury. It is well known that outcomes following delayed nerve repair are poorer. It has been postulated that, in the chronically denervated nerve, SCs progressively lose their capacity to support axonal regeneration and may be less robust for remyelination.

HYPOTHESIS: We hypothesized that recapitulating the early denervation phenotype of SCs in chronic denervation may restore remyelination and regeneration support capacity.

METHODS: In this study, we compared SCs from adult rodent sciatic nerve with acute and chronic denervation, adult rodent skin derived precursor SCs (SKP-SCs), and nerve derived SCs from E16 embryonic nerve. Cells were expanded in identical culture conditions. They were tested *in vitro* and *in vivo* for a number of phenotypic characteristics and assays. Specifically, we tested and compared the various SCs for myelination both *in vitro* and *in vivo* and neurite outgrowth assay (DRG-SCs co-culture) *in vitro*. Additionally we compared SKP-SCs and SCs for cellular proliferation, cytokine releasing capacity and immune modulation by macrophage (M2 type) activation.

RESULTS: SCs re-express key pro-myelinating transcription factors (Oct-6 and Krox-20) following acute (day 5) nerve injury, but lose this phenotype with chronic denervation (day 56) both *in vivo* and in cultured nerve SCs *in vitro*. We found that SKP-SCs express Oct-6 and Krox-20, *in vitro*, to similar levels as the ones from acutely denervated nerve and significantly greatly than ones from

chronically denervated nerve. Adult SKP-SCs were comparable to acutely denervated nerve SCs or embryonic nerve SCs in terms of proliferation, survival in injured nerve, *in vitro* and *in vivo* myelination, *in vitro* neurite outgrowth and immune modulation in injured nerve. Chronically denervated SCs were significantly poorer in all these capabilities.

CONCLUSION: From this study we conclude that: 1) temporal delay following injury results in important phenotypic changes in distal Schwann cells within the nerve and 2) adult SKP-SCs can be used as an alternate therapy to modulate immune response, restore myelination and promote axonal regeneration, in injured peripheral nerve, making these cells a favorable source of autologous cell transplantation.

9:50 – 10:00 NON-IMMUNOGENIC AND ANTI-INFLAMMATORY PROPERTIES OF DISCOGENIC CELLS, A NOVEL CELL POPULATION USED FOR THE TREATMENT OF DEGENERATIVE DISC DISEASE

***Lara I. Silverman, Ph.D.*[1]**, *Terry Tandeski, Ph.D.*[1], *Kavita M. Gupta, Ph.D.*[1], *Kevin T. Foley, M.D.*[2]; *DiscGenics, Inc.*[1], *University of Tennessee Health Science Center*[2]

INTRODUCTION: Degenerative disc disease (DDD) is a primary cause of back pain, which affects over 65 million people in the US and costs over $100B annually to the US economy. Current treatments for DDD are limited and do not result in repair/regeneration of the disc. We have developed a method to isolate progenitor cells directly from human disc tissue and form a therapeutic cell population known as 'discogenic cells' for use in treating DDD. Previously, we have shown that discogenic cells regenerated injured discs in rabbit and pig models of DDD (AAcNS 2013 Meeting Presentation). Despite xenogenic transplantation of these cells in these studies, no signs of sub-acute, acute or chronic inflammation was observed, suggesting that the cells lack immunogenic potential. Now, we seek to better understand the immunogenic properties of these cells to help rule out allograft rejection upon human testing and to determine whether the cells possess anti-inflammatory properties, which could contribute to efficacy in treating human DDD. First, we performed a set of mixed leukocyte reactions (1-way and 2-way MLRs), which are used for matching donor tissues and connote a lack of immune response. Then, we assessed expression of surface markers associated with immunogenicity using flow cytometry and also evaluated the cytokine response of cells when exposed to endotoxin. These studies demonstrate that discogenic cells have a unique immunomodulatory profile that is highly favorable for a cellular therapy.

HYPOTHESIS: Discogenic cells are not immunogenic and possess anti-inflammatory properties.

METHODS: First, 1-way MLRs were performed by exposing mytomycin-c modified discogenic cells to peripheral mononuclear blood cells (PMBC) from 3 unique blood lines (A, B and C, one blood line per experiment) for 5 days. Proliferation of T-cells within PCMBs was measured by quantifying BrdU incorporation within 24 hours in proliferating cells using ELISA. Similarly, 2-way MLRs were performed by exposing discogenic cells to mixed PBMCs from two bloodlines (A+B, B+C, A+C) for 5 days to quantify suppression of T-cell proliferation. Next, a FACSCanto flow cytometer was used to assess expression of HLA-DR/DQ/DP, CD40, CD80 and CD86 compared to unlabelled control. Finally, cells were exposed to lipopolysaccharide (LPS; endotoxin) for 24 hours and assayed by Ray Biotech for cytokines IL-1, IL-6, IL-10, TGF-β and TNF-α.

RESULTS: Discogenic cells did not stimulate proliferation of T-cells in 1-way MLRs, demonstrating that the cells are not immunogenic (stimulation index 0.3, 0.04, 0.1; measurement above 1.5 considered immunogenic). In the 2-way MLRs, the addition of discogenic cells significantly suppressed T-cell proliferation (93%, 62% and 81% reduction from positive control), suggesting the cells have anti-inflammatory properties. Discogenic cells did not express the surface markers tested, additionally supporting the hypothesis that the cells are not immunogenic. Finally, after 24-hour exposure to endotoxin, none of the cytokines tested were upregulated, with IL-6 and IL-10 expression noted with and without endotoxin, suggesting that the cells do not follow classic pathways of inflammatory control described in the literature for DDD.

CONCLUSION: *In vitro* studies are useful to understand the immunogenic potential of a cell therapy prior to administration in humans in order to anticipate safety concerns. These studies support that allogeneic human application of discogenic cells will be safe, and that the therapy will likely reduce inflammation in degenerated discs.

10:50 – 11:00 INTRAOPERATIVE MAPPING DURING REPEAT AWAKE CRANIOTOMIES REVEALS FUNCTIONAL PLASTICITY OF THE ADULT CEREBRAL CORTEX

Shawn L. Hervey-Jumper, M.D., Derek Southwell, M.D., Ph.D., and ***Mitchel S. Berger, M.D.****; University of California, San Francisco*

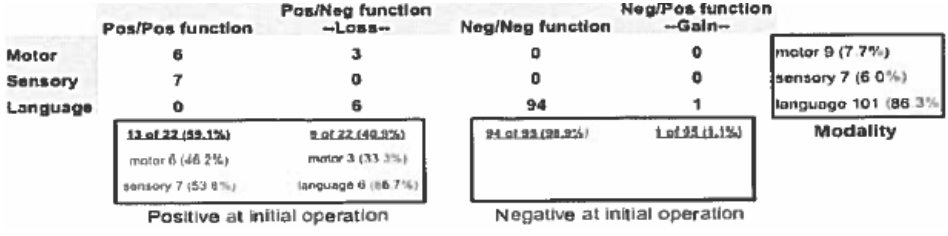
INTRODUCTION: Central nervous system plasticity is a dynamic and continuous process for the maintenance of neuronal networks in both children and adults. During awake craniotomy, direct cortical stimulation is used to map language, motor and sensory function. In patients who undergo repeat awake craniotomies, mapping provides a unique opportunity to examine reorganization of functional cortex in the setting of local disease.

METHODS: We examined 561 consecutive patients with glioma who underwent intraoperative language and sensorimotor mapping during awake craniotomies at our institution. Of these, 40 patients underwent more than 1 stimulation mapping craniotomy for treatment of glioma. Of these 18 patients had complete records including photograph brain maps, hand drawn interatoperative maps, and operative reports. Each procedure was performed by a single surgeon using the same intraoperative mapping protocol. Inclusion criteria included age >18, baseline intact language and sensorimotor function, and complete intraoperative and perioperative records. Overlapping stimulation points were considered positive if there was overlap of stimulation testing (testing every 5 mm of exposed cortex) between maps in the same area of cortex.

RESULTS: The study population included 18 patients who were mapped more than once. This included 583 total stimulation points and 117 overlapping stimulation points (20.1%). Mapping occurred predominately for insular (50%), frontal (27.8%), temporal (16.7%), and parietal (5.6%) gliomas. Tumor pathology included WHO II (45%), WHO III (50%), and WHO IV (5%). Mean age initial mapping was 33.8 +/- 8.9 years and remapping was 37.9 +/- 9.8 years. Mean time interval between mapping was 4.0 +/- 1.9 years. Sites that

were positive in the initial map and positive at remapping (Pos/Pos function) were observed in 11.1% (n=13, 46.2% motor, 53.8% sensory, 0% language). Neg/neg function occurred in 80.3% of sites (n=94, all language). Pos/neg function (cortical loss of function) was observed in 7.7% of sites (n=9, 33.3% motor, 66.7% language). Neg/Pos function (cortical gain of function) was observed in 0.9% of sites (n=1, 100% language). Seven of the 18 study subjects experienced either loss or gain of function between mapping intervals (38.9%). There were no significant differences in mean age, time interval between maps, tumor grade (Low vs. High grade pathology), malignant transformation, chemotherapy or brain radiation therapy, or tumor location between subjects who experienced organization and those who did not. We did not observe any case in which function shifted from one modality to another (eg, from language to motor or sensory).

CONCLUSION: The adult central nervous system functionally is able to reorganize motor and language areas in patients with gliomas. This functional plasticity may allow for the preservation of function in disease states. In order to avoid causing functional deficits during re-operation, surgeons should not rely solely on previously obtained mapping data when considering a surgical plan at recurrence.



11:00 – 11:10 CIRCUIT MODULATION: DISSECTING STRUCTURE-FUNCTION OF DEEP BRAIN STIMULATION (DBS) USING DIFFUSION TENSOR IMAGING (DTI)

Nandan Lad, M.D., Ph.D.*; Duke University Medical Center*

INTRODUCTION: Deep brain stimulation (DBS) is now the primary neuromodulation technique for treating movement disorders, yet its precise effects on brain regions surrounding the site of stimulation and efficiency in modulating neural networks is still under investigation. Accurate targeting and selective stimulation are essential in optimizing symptom alleviation and minimizing potential side effects. The size and position of the neural targets is variable, and it is sometimes difficult to localize these structures anatomically. Historically, various imaging techniques and targeting methods have been used to achieve successful clinical outcomes, including MR imaging, CT scanning and ventriculography. Recent advances in imaging have refined the visualization of surgical targets and landmarks. Multi-modal and advanced techniques such as diffusion tensor imaging (DTI) show great promise for providing insight to these underlying structure–function relationships. Here, we examine the role of these techniques for DBS lead targeting, intraoperative testing, postoperative programming and potential for novel patient-specific algorithms and treatment strategies.

METHODS: Postoperative lead visualization and overlapping of contacts with their underlying DTI target has been done in a limited fashion to date. To assess the impact of lead location on structure-function relationships, a standardized protocol was developed to model the placement of DBS leads and contacts with overlapping DTI fiber tracts. Deterministic fiber tracking was performed using iPlan stereotaxy software (Brainlab, Feldkirchen, Germany). After loading individual datasets into Brainlab iPlan and ensuring accurate and overlapping fusion of all dataset image pairs (Stereotactic CT, 3T MRI- DTI, FLAIR and T2 sequences) in the Image Fusion function. Regions of interest (ROI) were mapped using the FLAIR MRI image set for clear structural contrast. We examined ten patients with Essential Tremor (ET) with thalamic

Vim DBS and five patients treated for Parkinson's disease with STN DBS. An ultra-high resolution (7T) human cadaveric model was also used to further validate mechanistic structure-function relationships.

RESULTS: We examined the two currently commercially available DBS leads (3387 and 3389, Medtronic, Inc., Minneapolis, MN) to examine the underlying fiber connectivity and putative circuits being modulated by neurostimulation. The function of these circuits has been extensively studied in preclinical models, however visualization in humans has been limited due to inability to reliably visualize the lead and its contacts and their relation to associated fiber tractography in stereotactic space. Furthermore, the ability to visualize the underlying circuit being modulated and regional neuroanatomy is critical for optimal clinical results. In the case of ET patients, the putative mechanisms of DBS of the VIM thalamus is the underlying white matter fiber tract termed the dentatorubrothalamic (DRT) tract. The DRT tract is the primary fiber bundle forming the superior cerebellar peduncle, which is one of the largest efferent connections of the cerebellum and consists of axon fibers arising from cells located in the dentate, emboliform, and globose nuclei. These fibers then project to the thalamus and terminate in the ventral lateral and ventral posterolateral thalamic nuclei, which go on to project to the primary motor cortex. Specifically, it was found that the DRT tract was reproducibly visualized passing through the active DBS contacts of ET patients undergoing Vim stimulation. In the case of PD patients, the motor subthalamic nucleus (STN) and associated hyperdirect pathway (HDP) connecting it to the ipsilateral premotor and motor area were visualized. For the first time, the HDP could be visualized passing through the DBS active contacts in PD patients undergoing STN stimulation.

CONCLUSION: Here, we present a protocol for modeling implanted DBS electrode leads and evaluating electrode contact positions relative to white matter fiber tracts thought to play a key role in therapeutic efficacy. This has utility and implications not only for understanding circuit modulation of current grey matter DBS targets (Vim, STN, GPi) in movement disorder surgery, but will also be critical for future white matter targets (fornix, ALIC, cingulate). The purpose of developing this protocol was to standardize the

imaging of these patients and to better visualize and understand the correlation between DBS electrode contact positioning, structure-function of circuit modulation and efficacy of treatment outcomes.

11:10 – 11:20 THE PREDICTIVE ABILITY AND CLINICAL UTILITY OF SERUM MEASUREMENT OF GFAP-BDP BIOMARKER FOR THE DETECTION OF TRAUMATIC BRAIN INJURY

***David Okonkwo, M.D., Ph.D.*[1]*, and Geoffrey T. Manley, M.D., Ph.D.*[2]*; University of Pittsburgh Medical Center*[1]*, University of California, San Francisco*[2]

INTRODUCTION: Glial Fibrillary Acidic Protein and its breakdown products (GFAP-BDP) are brain specific proteins released into serum as part of the pathophysiologic response following traumatic brain injury (TBI). As part of a multicenter trial, we validated and characterized the use of GFAP-BDP levels in the diagnosis of intracranial injury in a broad population of patients with a positive clinical screen for head injury.

OBJECTIVE: To determine the utility of GFAP-BDP as a biomarker for identifying intracranial injury as seen on CT and MRI and its correlation with injury severity following TBI.

METHODS: This multicenter, prospective cohort study included patients 16 to 93 years of age presenting to 3 Level I trauma centers with a clinical history of TBI (loss of consciousness, post-trauma amnesia, etc.). Serum GFAP-BDP levels were drawn within 24 hours and analyzed in a blinded fashion using a sandwich enzyme-linked immunosorbent assay. The ability of GFAP-BDP to predict intracranial injury on admission CT was analyzed by multiple regression was assessed by the area under the receiver operating characteristic curve (AUC). Secondary end-points included the correlation of GFAP-BDP with the Rotterdam score as well as injury identified by MRI screening. Clinical utility of GFAP-BDP to predict injury and reduce unnecessary CT scans was assessed utilizing decision curve analysis.

RESULTS: A sample of 215 patients was available for analysis, of which 83% suffered mild TBI, 4% moderate, and 12% severe; the mean age was 42.1± 18 years. There was evidence of intracranial injury in 51% of the sample (median

Rotterdam Score 2 (IQR 2)). GFAP-BDP demonstrated high-value predictive ability for intracranial injury (AUC= 0.87), and demonstrated significant discrimination of injury severity (OR 1.45, 95%CI 1.29-1.64). Use of GFAP-BDP was determined to yield a net benefit above clinical screening alone and a net reduction in unnecessary scans by 12 to 30%.

CONCLUSION: Used in conjunction with other clinical information, rapid measurement of GFAP-BDP is useful in establishing or excluding the diagnosis of radiographically apparent intracranial injury following TBI. As an adjunct to current screening practices, GFAP-BDP may help avoid unnecessary CT scans without sacrificing sensitivity.

11:20 – 11:30 HIGH-RESOLUTION, VESSEL WALL MRI IN THE EVALUATION OF RUPTURED/SYMPTOMATIC INTRACRANIAL ANEURYSMS AND AVMS

Charles C. Matouk, M.D., F.R.C.S.(C)*, Ryan M. Hebert, M.D., Brandon Cord, M.D., Ph.D., Murat Gunel, M.D., and Michele H. Johnson, M.D.; Yale University School of Medicine*

INTRODUCTION: High-resolution magnetic resonance vessel wall imaging (MR-VWI) is a newer imaging paradigm that has been used to characterize steno-occlusive diseases, for example, intracranial atherosclerosis and cerebral vasculitis. More recently, we reported for the first time thick vessel wall enhancement in 5 patients with ruptured intracranial aneurysms, and demonstrated its utility in determining the site-of-rupture in 3 patients harboring multiple aneurysms. MR-VWI has not yet been reported in a large series of ruptured or symptomatic aneurysms, and ruptured brain arteriovenous malformations (AVMs). We hypothesized that vascular wall enhancement is a new imaging property of ruptured or symptomatic aneurysms, and could also help establish the site-of-rupture in ruptured brain AVMs.

METHODS: Medical records of patients admitted with ruptured intracranial aneurysms and brain AVMs between January 2012 and April 2014 were reviewed. High-resolution MR-VWI was routinely performed for patients treated in the IMRIS Neurovascular Suite (a combined neurovascular operating room, biplane angiography suite, and MR imaging facility) immediately before definitive treatment of the ruptured intracranial aneurysm, or diagnostic angiography ± partial targeted embolization of the brain AVM. The admission CT head, CT angiogram, and diagnostic cerebral angiogram were independently reviewed by an endovascular neurosurgeon (CCM) and interventional neuroradiologist (MHJ). Differences in interpretation were resolved by consensus.

High-resolution MR-VWI was performed on a Verio 3.0T scanner with a 32-channel head coil in the IMRIS Neurovascular Suite. The following sequences were acquired: time-of-flight MRA and T1-weighted black blood vessel wall sequence (turbo spin echo acquisition) before and after IV administration of gadolinium. Each vessel wall sequence was performed in axial and coronal planes.

RESULTS: In 20 patients presenting with aneurysmal SAH, all demonstrated thick vessel wall enhancement of the ruptured aneurysm. Two patients with symptomatic, but unruptured, intracranial aneurysms (1 patient with a very severe, typical headache syndrome and 1 patient with an acute third nerve palsy) also demonstrated thick vessel wall enhancement. Among 13 patients with ruptured brain AVMs, 3 micro-AVMs could not be adequately resolved on MR-VWI. Of the remaining 10 AVMs, a site-of-rupture could be established in 9 patients based on the following two imaging criteria: (1) contiguity of blood product with specific, angioarchitectural vascular structure; and (2) thick vessel wall enhancement.

CONCLUSION: High-resolution MR-VWI demonstrated thick vessel wall enhancement in all ruptured intracranial aneurysms in our series and may represent a new imaging property of rupture. Similarly, a site-of-rupture could be established in 9 of 10 ruptured brain AVMs (that could be resolved on MR-VWI) and can facilitate target selection for partial targeted embolization.

11:30 – 11:40 PRELIMINARY EXPERIENCE WITH LONGITUDINAL EVALUATION OF CORTICOSPINAL TRACT IN PATIENTS WITH SURGICALLY RESECTED BRAINSTEM CAVERNOUS MALFORMATIONS USING HIGH DEFINITION FIBER TRACTOGRAPHY AND DIFFUSION CONNECTOMETRY ANALYSIS

Amir H. Faraji, M.D., Ph.D.[1], Kumar Abhinav, M.D.[1], Kevin Jarbo, B.S.[1], Samuel S. Shin, M.D., Ph.D.[1], Sudhir Pathak, M.S.[1], Barry E. Hirsch, M.D.[1], Walter Schneider, Ph.D.[1], Fang-Cheng Yeh, M.D., Ph.D.[2], Juan C. Fernandez-Miranda, M.D.[1], and ***Robert M. Friedlander, M.D., M.A.[1]****; University of Pittsburgh Medical Center[1], Carnegie Mellon University[2]*

INTRODUCTION: The management of brainstem cavernous malformations (CMs) is challenging due to a higher symptomatic hemorrhage rate compared to the supratentorial CMs and due to potential morbidity associated with surgical resection of these lesions, surrounded by eloquent white matter (WM) tracts. High definition fiber tractography (HDFT), based on diffusion spectrum imaging (DSI) provides superior qualitative data compared to diffusion tensor imaging (DTI).

OBJECTIVES: We aimed to preoperatively define the relationship of the brainstem CMs to the perilesional corticospinal tracts (CST) by using HDFT to obtain both qualitative and quantitative data, thereby assessing its utility for surgical planning. We further examined this data postoperatively using longitudinal scans and in relation to patients' clinical symptomatology. We finally also aimed to ascertain the extent of rostrocaudal involvement of CST longitudinally using the automated 'diffusion connectometry' analysis, which addresses the limitations of a conventional tractography approach and DTI.

METHODS: Fiber tractography was performed with DSI-studio, using a Quantitative anisotropy (QA)-based generalized deterministic tracking algorithm. Contralateral CST was used for comparison. Qualitatively CST was classified as either being 'disrupted' or 'displaced'. Quantitative analysis involved obtaining mean QA for the perilesional CST segments (defined anatomically according to the CMs' location on T1-weighted MR) and

comparing to contralateral homologous segment to obtain a percentage difference. Diffusion connectometry analysis included comparison of the DSI data of the patients with a template, derived from the imaging data of 90 neurologically normal subjects.

RESULTS: Three patients (Male =1; Female=2) with symptomatic pontomesencephalic hemorrhagic CMs were identified and scanned longitudinally. The number of scans and follow-up period were as follows: Case 1 [(preoperative = 1; postoperative = 2 (at 3 weeks and 6 months follow-up)]; Case 2 (preoperative = 1; immediate postoperative =1; 3 months overall follow-up); Case 3 [(preoperative = 3; postoperative = 2 (immediate and at 4 months follow-up)]. All patients had varying degrees of preoperative hemiparesis. Qualitatively CST was partially disrupted and displaced in all. Direction of displacement of CST, crucial to the planning of surgical (apical petrosectomy and intradural subtemporal approach) entry point into the brainstem included posterior; anteromedial and lateral. The observed displacement of the fibers progressively improved in all. Perilesional mean QA percentage decreases preoperatively supported disruption of CST in all three and dropped further over the follow-up period (Case 1: 26% to 49%; Case 2: 35% to 66%; Case 3: 63% to 78%). Diffusion connectometry demonstrated appropriate *overall* rostrocaudal involvement of the CST with larger segments affected in the preoperative and immediate postoperative phase followed by improvement over the follow-up. The qualitative and connectometry data correlated with significant clinical improvement in all.

CONCLUSION: Hemorrhagic brainstem CMs can disrupt and displace perilesional WM tracts with the latter occurring in unpredictable directions, necessitating the use of HDFT to accurately delineate their location to optimize surgical entry point and minimize potential surgical morbidity. Observed further anisotropy drops in the disrupted perilesional segments is consistent with neural degeneration following hemorrhagic insults. Connectometry allows an *overall* assessment of the CST beyond just the perilesional segment and in addition to qualitative data can be potentially used for correlation with clinical symptomatology. Future studies with greater number of patients are needed to further elucidate the implications of these findings for prognostication and neurological recovery.

11:40 – 11:50 IDENTIFYING THE THALAMIC NUCLEI USING 3-T MRI TRACK DENSITY IMAGING

Timothy Shepherd, M.D., Ph.D., Sohae Chung, Christopher Glielmi, Alon Mogilner, M.D., Fernando Boada, Ph.D., and ***Douglas Kondziolka, M.D.****; New York University Medical Center*

INTRODUCTION: Thalamic surgery is based on the identification of target structures using indirect techniques such as measurement of intercommissural distances and third ventricular width. Routine MRI fails to detect thalamic nuclei so targeting is based on anatomic atlas-based coordinates. Diffusion MRI-based track density imaging (TDI) can better depict internal thalamic structure, but previously has required high-field MRI or long acquisitions that are not clinically practical. We applied multiband diffusion MRI to enable 3-T RI TDI in patients with essential tremor.

METHODS: Six patients with essential tremor underwent standard preoperative MRI with an additional multiband diffusion sequence that used slice-acceleration factor of 3, 3-mm isotropic image resolution, whole-brain coverage (45 slices) and 256 diffusion gradient directions (b = 2500 s/mm^2) acquired in 11 min. TDI data post-processing generated track density and direction-encoded color maps at 500-micron isotropic super-resolution.

RESULTS: Combining TDI and multiband diffusion acquisitions resulted in high-quality images of the human thalamus in typical elderly essential tremor patients using 3-T MRI. TDI-derived 500-micron isotropic resolution fiber-orientation maps overlaid on conventional T2 demonstrate most of the internal nuclei of the thalamus can be identified using different fiber orientations, including massa intermedia, VA, dorsomedial thalamus, VLa, VLp or VIM, centromedial thalamus, VPL and pulvinar. Results also were consistent for repeat imaging in the 3 healthy volunteers.

CONCLUSION: Multiband diffusion acquisitions makes TDI-based parcellation of the thalamus feasible in patients with essential tremor using 3-T MRI. This approach provides at least equivalent data to previous diffusion tractography or TDI approaches for thalamus parcellation, but without long scan times or a 7-T MRI system [4-6]. While planning for gamma knife radiosurgery of VIM for these initial 6 patients still relied on conventional methods, future efforts will focus on validation and careful introduction of TDI-derived thalamic maps to actual surgical planning. Similar techniques have now been used in obsessive-compulsive disorder patients.

11:50 – 12:00 VOLUMETRIC BRAIN ANALYSIS FOR HYDROCEPHALUS AND EPILEPSY IN THE DEVELOPING WORLD

***Steven J. Schiff, M.D., Ph.D., F.A.C.S.**; Penn State University*

INTRODUCTION: Brain image analysis in the developing world is largely limited to CT, as the expense of MRI scanning renders it largely inaccessible to the vast majority of people living in developing countries. We wished to develop a flexible, automated strategy for improving brain diagnostics and treatment in developing countries for both hydrocephalus and epilepsy.

METHODS: We invented a novel technology that employed a particle filter to follow the boundary of the brain in the manner often used in autonomous robotic air and ground vehicle navigation. Our goal was to create a versatile tool to segment brain and fluid in MRI and CT images of the developing brain, lay the foundation for an intelligent automated edge tracker that is modality independent, and segment normative data from MRI that can be applied to both MRI and CT. Segmentation with varied levels of noise (0-9%) and spatial inhomogeneity (0-40%) resulted in percent error ranging from 0.06% to 5.38% for brain volume and 2.45% to 22.3% for fluid volume. We applied this method to the NIH Pediatric MRI database to develop the first human growth curves for brain and cerebrospinal fluid (Mandel et al J Neurosurg Peds 2014a, in press).

In all countries in the world, the evaluation of hydrocephalus remains focused on ventricular size, which is directly related to CSF volume, yet the goal of treatment is to allow for healthy brain development, which is dependent on brain volume. Brain and CSF volumes were measured in 33 infants with myelomenigocele treated at the CURE Children's Hospital of Uganda (CCHU), 26 of whom required surgical treatment for hydrocephalus. Linear discrimination analysis (LDA) was used to test if age-normalized brain and fluid volumes can discriminate neurocognitive outcome. Brain volume alone, unlike fluid volume, could discriminate high from low cognitive outcome. It was

further shown that a combination of age normalized brain and fluid volumes can discriminate neurocognitive outcome by 2-way LDA ($p < 0.01$) and 3-way LDA ($p < 0.01$). The multivariate LDA demonstrated the secondary contribution of large fluid volume to a decrement in cognition. This strategy offers a way to predictively manage such patients by tracking brain growth rates to optimize neurocognitive development (Mandel et al J Neurosurg Peds 2014b, in press).

RESULTS: Lastly, the incidence of temporal lobe epilepsy (TLE) due to mesial temporal sclerosis (MTS) can be high in developing countries. Current diagnosis of MTS relies on structural MRI, which is generally unavailable in developing world settings. Given widespread effects on temporal lobe structure beyond hippocampal atrophy in TLE, we proposed that CT volumetric analysis can be used in patient selection to help predict outcomes following resection. Temporal lobe and whole-brain volumes in 10 epilepsy surgical patients treated at CCHU were measured from CT and contrasted with from normative temporal lobe growth curves. A multivariate measure of the volume of each temporal lobe separated patients that were seizure-free (Engel IA) from those with incomplete seizure control (Engel IB/IIB) with LDA ($p < 0.01$). Additionally, we demonstrated that age-normalized whole brain volume, in combination with temporal lobe volumes, may further improve outcome prediction ($p < 0.01$). This provides strong evidence that temporal lobe and brain volume can be predictive of seizure outcome following temporal lobe resection, and that volumetric CT analysis of the temporal lobe may be feasible in lieu of structural MRI when the latter is unavailable (Mandel et al J Neurosurg Peds 2014c, in press).

CONCLUSION: Our volumetric methodology has the capability to allow CT to be a more effective diagnostic tool for neurological disorders, a task of substantial importance in developing countries where CT is often the only available method of brain imaging. Nevertheless, all of this methodology is readily ported to MRI imagery, and can be of benefit to clinical practice in the US and other industrialized countries.

12:00 – 12:10 CREATING VISUAL PERCEPTS WITH ELECTRICAL STIMULATION OF HUMAN VISUAL CORTEX

Xiaomei Pei, Ph.D., Ping Sun, M.S., William H. Bosking, Ph.D., Michael S. Beauchamp, Ph.D., ***Daniel Yoshor, M.D., F.A.A.N.S.****; Baylor College of Medicine*

INTRODUCTION: A cortical visual prosthetic has the potential to restore useful visual perception to the blind by directly activating the visual cortex. Electrical stimulation of a single site in early visual cortex produces perception of a spatially restricted spot of light, known as a phosphene. We hypothesized that the location and shape of the phosphene percept produced with electrical stimulation of a single site should correspond to the location and shape of the receptive field (RF) of the stimulated population of neurons, and that concurrent stimulation of multiple electrode sites should result in the creation of a complex percept useful for guiding behavior.

METHODS: We studied 13 patients implanted with cortical surface electrodes positioned on early visual cortex. First, we mapped the spatial RF for each electrode site (Yoshor et al., Cerebral Cortex, 2007). Then, we stimulated each of the electrodes and selected those that produced phosphene percepts. The average location and spatial extent of the phosphene for each electrode was then determined by having the patient draw the phosphene on a touchscreen over multiple stimulation trials. Electrodes that produced spatially distinct phosphenes were then selected for multi-electrode stimulation. Combinations of electrodes were then stimulated and subjects were required to discriminate the resulting phosphenes using match-to-sample and two-alternative forced choice behavioral tasks.

RESULTS: To compare the RF and the phosphene locations for individual electrodes, we calculated the distance between the RF center and the phosphene center across electrodes using polar co-ordinates and obtained mean r = 0.3° ± 2.3° SD (not significantly different from zero, p = 0.54) and mean theta = -0.04° ± 1.1° SD (not significantly different from zero, p = 0.85). In behavioral testing, the shape predicted by the RF map of an individual

electrode was highly predictive of the subject's behavioral performance, and was selected as the target at a frequency far better than chance level for all 4 electrodes tested with this task. Discrimination of multi-electrode stimulation (3 electrode combinations) was tested in 5 subjects, and these subjects were able to discriminate between percepts produced by stimulation of different electrode combinations at a rate of 94%.

CONCLUSION: These results show that it is possible to use the spatial RF of an electrode site to predict the spatial form of a percept produced by electrical stimulation of that site. Furthermore, stimulation of multiple electrodes sites reliably produced percepts of more complex forms that subjects can use to guide behavior, illustrating the potential of cortical visual prosthetics in the treatment of blindness. Simultaneous stimulation of a small number of electrode sites produces only a limited number of possible forms - to create artificial percepts with greater verisimilitude, a higher density of implanted electrodes will be required.

7:05 – 7:15 HOLDING POLICY MAKERS ACCOUNTBLE: WHAT PATIENT SAFETY GAINES HAVE DUTY HOURS REGULATIONS PRODUCED?

Kiersten Norby, M.D., Farhan Siddiq, M.D., Malik Adil, M.D., and ***Stephen Haines, M.D.****; University of Minnesota*

INTRODUCTION: It has been estimated that the national imposition of duty hours regulations in 2003 cost $1.6 billion. While this has resulted in undeniable benefits for resident lifestyle, such a major investment has been justified primarily in terms of improvement in patient safety.

OBJECTIVES: In order to determine the patient safety benefit of this large investment and the attendant changes in resident training we asked the question: "has increased regulation of resident duty hours resulted in measurable changes in neurosurgical patient outcomes?"

METHODS: Using the Nationwide Inpatient Sample (NIS), patients undergoing neurosurgical procedures at hospitals with neurosurgery training programs were identified and screened for in-hospital complications, in-hospital procedures, discharge destination and in-hospital mortality. Comparisons in the above outcomes were made between New York (NY) hospitals and non-New York hospitals before and after the Accreditation Council for Graduate Medical Education (ACGME) regulations were put into effect in 2003.

RESULTS: There was no difference in in hospital mortality or discharge to a location other-than-to-home between NY and non-NY neurosurgical teaching hospitals before the 2003 implementation of duty hours regulations. After the regulations were in place, there continued to be no difference in in-hospital mortality but NY patients were significantly more likely to be discharged to a location other than home than were non-NY patients.

Discharge Destination	NY			Non-NY	
2000 2001 2002	Home	81.9%		84.1%	Home
	Long tem	14.8%		12.7%	Long tem
	Other	0.4%		0.2%	Other
	Death	2.9%		3.0%	Death
2003					
2004 2005 2006	Home	78.0%		81.5%	Home
	Long tem	18.3%		15.1%	Long tem
	Other	0.4%		0.3%	Other
	Death	3.4%		3.1%	Death

CONCLUSION: Regulation of resident duty hours has not resulted in significant improvement in outcomes among neurosurgical patients. In the future, Investments and structural changes in education of this magnitude should be supported by careful, well-informed cost-benefit analysis.

7:15 – 7:25 DIVIDE AND CONQUER – A HISTORY OF ORGANIZED NEUROSURGERY AND A BLUEPRINT FOR THE FUTURE

Daniel K. Resnick, M.D.; *University of Wisconsin School of Medicine and Public Health*

INTRODUCTION: Neurosurgery is a relatively young field practiced by relatively few. Despite the relatively small number of neurosurgeons, there are a plethora of organizations made up of various combinations of neurosurgeons and affiliated professionals. This high "organization to practice" ratio is confusing to many. Furthermore, one may question the appropriateness of so many organizations for so few neurosurgeons in an era of restricted resources.

METHODS: The history of organized neurosurgery will be presented in order to describe the impetus for, organization of, and stated purpose of each of the major neurosurgical organizations (AANS, CNS, CNS, NSA, AAcNS, SUNS). The evolution of these societies and their current activities of will be reviewed and put into the larger context of organized medicine.

RESULTS: The relationships between neurosurgical organizations are not completely straightforward. Due to a variety of factors however, the major neurosurgical organizations have evolved into mutually supportive and complementary entities. Neurosurgeons, particularly those at the beginning of their careers, benefit substantially from the continued constructive competition and cooperation between the societies.

CONCLUSION: The existence of multiple societies acts a force multiplier for the educations and financial benefit of all neurosurgeons.

8:15 – 8:25 TRANSCRIPTIONAL PROFILING OF GBM INVASION GENES IDENTIFIES EFFECTIVE INHIBITORS OF THE LIM KINASE-COFILIN PATHWAY

James T. Rutka, M.D., Ph.D., *Christian Smith, Ph.D., Jun Bum Park, M.D., Sameer Agnihotri, Ph.D., Michael Berens, Ph.D., Amanda Luck, B.Sc., and Brian Golbourn, M.Sc.; Arthur and Sonia Labatt Brain Tumour Research Centre, University of Toronto*

INTRODUCTION: Malignant gliomas are highly proliferative and invasive neoplasms that infiltrates diffusely into regions of normal brain rendering total surgical resection impossible and effective local radiation therapy difficult. To advance the treatment of patients with malignant gliomas, the need to develop a greater understanding of the molecular machinery driving invasion and to identify novel treatment targets is essential.

METHODS: Using microarray analysis comparing normal brain samples and mesenchymal glioblastoma multiforme (GBM), which are highly invasive and of poor prognosis, we identified over 140 significant genes involved in cell migration and invasion. Of interest was that the cofilin (CFL) pathway (including LIMK1, LIMK2, CFL, CAP1), which disassembles actin filaments was highly up-regulated compared to normal brain. Furthermore up-regulation of LIM domain kinase 1 and 2 (LIMK1/2) that phosphorylates and inactivates cofilin was confirmed in an additional independent data set comparing normal brain to GBM. Spatially, we identified that LIMK1 and phospho-CFL (pCFL), were enriched in the periphery of the GBM compared to the tumor core. We next identified and utilized two small molecule inhibitors BMS-5 and Cucurbitacin I directed against the cofilin regulating kinases, LIMK1 and LIMK2, to target this pathway.

RESULTS: Significant decreases in cell viability in U87 and T98G cells using doses of 10-20 μM BMS-5 and 100nM-10μM Cucurbitacin I were observed in cell viability assays, while no cytotoxic effects were seen in normal human astrocytes that lack LIMK expression. BMS-5 and Cucurbitacin I promoted increased adhesion in GBM cells, accompanied with decreased migration and invasion. Finally, preliminary results from flank and intracranial tumor modeling suggest that these two LIMK inhibitors decrease the growth of GBM in vivo.

CONCLUSION: Collectively, these data suggest that the use of LIMK inhibitors may provide a novel way to target the invasive machinery in GBM.

8:25 – 8:35 TRANSCRIPTIONAL SIGNATURE OF IRRADIATED MICROGLIA – IMPLICATIONS FOR COGNITION AND TUMOR INFILTRATION

***Terry C. Burns, M.D., Ph.D.**, Matthew D. Li, B.S., Alexander A. Morgan, Ph.D., and Theo D. Palmer, Ph.D.; Stanford University*

INTRODUCTION: Brain irradiation remains important in the management of brain tumors, though is associated with cognitive impairment in long-term survivors. A chronic inflammatory state characterized by microglial activation has been implicated in the pathophysiology of radiation-induced cognitive decline and alters the microenvironment for residual tumor cells. However, no molecular characterization of irradiated microglia has previously been undertaken.

METHODS: CD11b+ microglia were FACS-isolated from the hippocampi of 10 week old C57Bl/6 and Balb/C mice 1 month after 10Gy or sham cranial irradiation and comprehensive transcriptome analysis was performed using Affymetrix gene arrays. Linear modeling and rank product analyses were used to determine the conserved signature of irradiation across strains. Bioinformatics techniques were then use to functionally analyze the irradiated microglia signature, and assess correlations with public data sets.

RESULTS: One month after irradiation 448 and 85 genes were differentially up- and down-regulated, respectively, revealing a signature distinct from previously described microglial states. Gene set enrichment analysis demonstrated enrichment for inflammation-related gene sets including a subset of genes characteristic of M1 macrophage polarization, but further revealed an unexpected enrichment for extracellular matrix and coagulation-related gene sets. Weighted gene co-expression network analysis revealed 3 distinct modules that accounted for 95% of the upregulated genes and further implicated mitochondrial dysregulation after irradiation. Remarkably, one of these modules was consistently enriched in public data sets of brain aging, while all 3 were significantly enriched in a meta-analysis of human neurodegeneration

suggesting shared mechanisms underlying neurodegeneration- aging- and irradiation-induced cognitive decline. Analysis of human glioma datasets revealed that patients with the lowest enrichment for the irradiated microglia signature survived over twice as long as those with the highest enrichment. Consistent with this, implanted stem cells from parallel work showed dramatically enhanced infiltration in mouse brains pre-irradiated with 15Gy. Ingenuity pathway analysis identified CEBPA and the aryl hydrocarbon receptor as key upstream regulators of the microglial irradiation.

CONCLUSION: Our findings define a unique signature for irradiated microglia characterized by inflammatory signaling and extracellular matrix changes. These data suggest that insights from the irradiated microglia transcriptome could inform strategies to improve cognitive outcomes and slow recurrence following brain irradiation.

8:35 – 8:45 RNA INTERFERENCE TARGETING HIF-1A VIA A NOVEL MULTIFUNCTIONAL SURFACTANT ATTENUATES GLIOMA GROWTH IN AN INTRACRANIAL MOUSE MODEL

Randy Jensen, M.D., Ph.D.; *University of Utah*

INTRODUCTION: High-grade gliomas are the most common form of adult brain cancer, and patients have a dismal survival rate dispite aggressive therapeutic measures. Intratumoral hypoxia is thought to be a main contributor to tumorigenesis and angiogenesis of these tumors. Since Hif-1 the major mediator of hypoxia-regulated cellular control, inhibition of this transcription factor could reduce glioblastoma growth.

METHODS: Using an orthotopic mouse model with U87-LucNeo cells, we utilized RNA interference to knock down HIF-1α in vivo. The siRNA was packaged using a novel multifunctional surfactant, EHCO, a nucleic acid carrier that facilitates cellular uptake and intracellular release of siRNA. Stereotactic injection was used to deliver siRNA locally through a guide set screw system and delivery/uptake was verified by imaging of fluorescently labeled siRNA. Osmotic pumps were used for extended siRNA delivery to model the commonly used human intracranial drug delivery technique convection-enhanced delivery (CED).

RESULTS: Mice receiving daily siRNA injections targeting HIF-1α had a 79% lower tumor volume after 50 days of treatment when compared with controls. The HIF-1 transcriptional targets VEGF, GLUT-1, c-MET, and CA-IX and markers for cell growth (MIB-1 and MVD) were also significantly lower. Altering the carrier EHCO by adding polyethylene glycol significantly increased the efficacy of drug delivery and subsequent survival of the treated mice.

CONCLUSION: Treating glioblastoma with siRNA targeting HIF-1α in vivo can significantly reduce tumor growth and increase survival in an intracranial mouse model that has direct clinical implications.

8:45 – 8:55 ACTIVATED CD4+ T CELL-INDUCED CCL3 IMPROVES DENDRITIC CELL VACCINE IN MICE AND CANCER PATIENTS

Kristen A. Batich[1], Duane A. Mitchell[2], Michael D. Gunn[1], Min-Nung Huang[1], Luis Sanchez-Perez[1], Smita K. Nair[1], Kendra L. Congdon[1], Elizabeth A. Reap[1], Gary E. Archer[1], Annick Desjardins[1], Allan H. Friedman[1], Henry S. Friedman[1], James E. Herndon, II[1], April Coan[1], Roger E. McLendon[1], David A. Reardon[3], James J. Vredenburgh[4], Darell D. Bigner[1], and ***John H. Sampson[1]****; Duke University Medical Center[1], University of Florida[2], Dana-Farber Cancer Institute[3], St. Francis Medical Group[4]*

INTRODUCTION: In immunotherapy, dendritic cell (DC) vaccine efficacy has been limited by suboptimal migration to targeted lymph nodes. Vaccine site pre-conditioning with inflammatory cytokines or mature DCs increases lymph node homing and the induction of antigen-specific T cells in mice.

METHODS: To assess the impact of vaccine site pre-conditioning in humans, we randomized patients with glioblastoma to mature DCs or tetanus/diphtheria toxoid (Td) unilaterally before bilateral vaccination with tumor antigen-pulsed DCs. Various mouse models were used to determine the mechanistic underpinnings of our findings.

RESULTS: Patients given Td had enhanced DC migration to lymph nodes bilaterally and significantly improved progression-free and overall survival. In mice, Td pre-conditioning also enhanced DC migration in a recall response-dependent manner. Td-activated $CD4^+$ T cells were responsible for the increased systemic migration by induction of the chemokine (C-C motif) ligand 3 (CCL3) which in turn induced the CCL21 at the lymph nodes bilaterally. Both CCL3 induction and Td pre-conditioning were required for the effect. Interference with any component of this axis markedly reduced Td-mediated DC migration and antitumor responses.

CONCLUSION: Our clinical studies and corroborating investigations in mice demonstrate a key relationship between DC migration and antitumor efficacy and highlight CCL3 as a novel and critical mediator of this effect.

8:55 – 9:05 NOVEL SELECTIVE MITOCHONDRIAL BASED CHEMOTHERAPY FOR GLIOBLASTOMA – IN VITRO AND IN VIVO STUDIES

David S. Baskin, M.D., F.A.A.N.S., F.A.C.S., and Martyn Sharpe, Ph.D.; Methodist Neurological Institute, Houston

INTRODUCTION: In humans, high levels of monoamine oxidase B (MAOB) are typically only found in the outer mitochondrial membranes of astrocytes. Although glioma cells typically have lower mitochondrial concentrations than astrocytes, the cellular levels of MAOB are 5-fold higher. It has long been known that MAOB can catalytically convert neutral tetrahydropyridin substrates into cationic pyridinium products. We designed and synthesized a pro-Drug, MP-MUS, that consists of a nitrogen mustard moiety attached to a MAOB sensitive tetrahydropyridin. We postulated that elevated glioma MAOB should rapidly convert MP-MUS into the lipophilic, pyridinium-cation, P^+-MUS. The glioma mitochondrial membrane potential will produce a 1000-fold accumulation of cytosolic P^+-MUS into the mitochondrial matrix. High intra-mitochondrial levels of reactive nitrogen mustard will then result in mitochondrial dysfunction, at the mtDNA level, and cause cell death.

METHODS: The ability of human MAOB, but not MAOA, to convert the Pro-Drug, MP-MUS into P^+-MUS was demonstrated using an AmplexRed/HRP assay. *In vitro* experiments using cultured primary human glioma cells were carried out in the presence and absence of the MAOB inhibitor, selegiline. Cell viability and mitochondrial function were assayed using conventional labeling techniques. In an intracranial model of human primary glioma 22 nude mice received brain injections of primary human GBM cells that had been previously grown in cell culture. 11 animals received tail vain injections of 3x8mg/kg doses of MP-MUS five days apart and the 11 controls received saline. The onset of terminal neurological symptom was monitored, and at this point, or at the 10-month study endpoint, the brains removed, fixed and histologically analyzed. Human cells in the sliced mouse brain sections were identified using the anti-(human)-vimentin antibody, V9.

RESULTS: MAOB, but not MAOA, is capable of oxidizing MP-MUS, exhibiting a K_m of 3.3mM and a V_{max} similar to that of benzylamine, a classical MAOB substrate. *In vitro* studies indicated that MP-MUS is highly toxic to primary human glioma. MP-MUS induced gliomal mitochondrial damage and cellular toxicity is completely arrested by co-incubation with the MOAB inhibitor, selegiline. Mechanistically, *in vitro* experiments indicated that MAOB-generated P^+-MUS targeted mitochondria. P^+-MUS increased the generation of mitochondrial peroxides, superoxide and hydroxyl radical and collapsed membrane potential. Additionally, mtDNA was a particular target of P^+-MUS, inducing large increases in number of mtDNA breaks, nicks and adducts.

MP-MUS therapy greatly reduced morbidity in mouse xenograft models. There were 10 survivors in the MP-MUS treatment group at the 10 month end-point, but only 4 saline controls. All the saline control animals had high levels of infiltrating gliomal cells throughout their brains. Of 11 MP-MUS treated animals gliomal cells to be completely absent in the brains of 5 mice. The remaining 6 MP-MUS treated mice had <50% less gliomal cells in their brains than that present in the saline controls.

CONCLUSION: Our first MAOB specific pro-Drug, MP-MUS, is able to kill human primary glioma *in vitro* and in an *in vivo* mouse intracranial primary human xenograft model.

9:05 – 9:15 DESTABILIZATION AND RESTABILIZATION OF THE OCCIPITOCERVICAL JUNCTION AFTER A FAR LATERAL TRANSCONDYLAR RESECTION: A BIOMECHANICAL ANALYSIS

***Marcus D. Mazur, M.D.**, William T. Couldwell, M.D., Ph.D., and Andrew T. Dailey, M.D.; University of Utah*

INTRODUCTION: During transcondylar surgical approaches to tumors at the anterior foramen magnum occipitocervical instability may result from resection of the occipital condyle. Initially, patients may be able to maintain a neutral alignment in the immediate postoperative period but over time severe occipitoatlantal subluxation may occur with cranial settling, kinking of the spinal cord, and neurological injury. This clinical scenario has received very little attention in the literature. We conducted a biomechanical analysis to determine whether occipitocervical instability could be predicted based on the extent of condylar resection. We also tested potential fixation constructs to stabilize the occipitocervical junction in patients who developed a severe deformity after a condylar resection.

METHODS: Ten human cadaveric specimens (Oc-C2) underwent biomechanical testing in two phases. During the destabilization phase, a far lateral transcondylar resection was performed extending into the hypoglossal canal. Range of motion and stiffness testing was performed in the intact and resected states. The extent of condylar resection was quantified using a volumetric comparison between pre- and post-resection CT scans. ROC analysis was performed to determine the extent of resection that produced instability. During the restabilization phase, unilateral and bilateral Oc-C1 and Oc-C2 fixation techniques were compared. Biomechanical testing was performed to compare range of motion and stiffness between constructs under physiological loads (1.5 N-m).

RESULTS: Bone removal during condylar resection ranged from 15-66%; average = 33%. Resected specimens had less stiffness and increased motion in flexion-extension (-5% stiffness, p=0.052; +5% motion, p=0.024), lateral bending (-14%, p=0.021 +9%, p=0.063), and axial rotation (-17%, p=0.012; 19%, p=0.007) relative to their intact states. ROC analysis demonstrated that 33% resection was the optimal threshold for predicting a significant change in stability. After restabilization, bilateral fixation constructs (Oc-C1 and Oc-C2) provided more stability than unilateral constructs [up to 51% decrease in motion (p=0.001) and 122% increase in stiffness (p=0.003) for Oc-C1 fixation and up to 46% decrease in motion (p=0.004) and 149% increase in stiffness (p=0.005) for Oc-C2 fixation]. A bilateral Oc-C2 construct provided no biomechanical advantage over a bilateral Oc-C1 construct in lateral bending (1.80 vs. 1.37 N-m/deg, p=0.38). A unilateral Oc-C1 construct increased stiffness greater than 400% compared to the intact state, but was the least stiff of all constructs tested.

CONCLUSION: Patients who undergo condylar resections extending beyond the hypoglossal canal require close surveillance for occipitocervical instability. Changes in occipitocervical stability may be observed after as little as 33% of the occipital condyle is resected. If stabilization is required after a transcondylar operation, a bilateral Oc-C1 construct provides suitable biomechanical strength and will enable preservation of atlantoaxial motion.

9:15 – 9:25 DURABILITY OF A SINGLE HIGH DOSE OF INTRA-ARTERIAL BEVACIZUMAB WITH BLOOD-BRAIN BARRIER DISRUPTION FOR THE TREATMENT OF RECURRENT GLIOBLASTOMA

Imithri Bodhinayake, M.D.[1], Kartik Kesavabhotla, M.D.[2], Ashley Ray, M.S.[1], Aposolos J. Tsiouris, M.D.[2], and ***John A. Boockvar, M.D.[1]****; Hofstra North Shore-Long Island Jewish School of Medicine[1], Weill Cornell Medical College[2]*

INTRODUCTION: In patients with recurrent Glioblastoma (GBM), bevacizumab has been administered intra-arterially (IA) with blood-brain barrier disruption (BBBD) to increase local drug concentration. A single dose of IA bevacizumab after BBBD has been safe and well tolerated in clinical trials, and has been shown to improve PFS. However, these patients subsequently received biweekly IV bevacizumab after a single dose of IA bevacizumab with BBBD. Here we present the durability of a single dose of IA bevacizumab after BBBD.

METHODS: This prospective study enrolled patients with recurrent GBM with tumors less than 3.5cm and no prior exposure to bevacizumab. At the time of initial diagnosis, all patients had undergone resection, temozolomide chemotherapy and radiation treatment. Patients were treated with superselective intra-arterial cerebral infusion (SIACI) of bevacizumab after BBBD with mannitol. MR brain imaging was obtained at baseline, 30 days post-treatment and monthly thereafter. The Risk Assessment in Neuro-Oncology (RANO) criteria were used to evaluate treatment response.

RESULTS: After a single SIACI of bevacizumab after BBBD, patients had a median PFS of 106 days (3.53 months). The shortest time to progression (TTP) was 25 days while the patient with the most favorable response was progression-free for 1030 days. There were no adverse events related to a single administration of IA bevacizumab.

CONCLUSION: PFS was 106 days (3.53 months) after a single dose of IA bevacizumab with BBBD, which is comparable to PFS after IV bevacizumab alone. These first results on the durability of a single IA bevacizumab dose after BBBD will help guide the design of future Phase II IA bevacizumab alone trials.

9:25 – 9:35 PERINEURAL SPREAD IN PELVIC MALIGNANCIES

Stepan Capek, M.D., B. Matthew Howe, M.D., Kimberly K. Amrami, M.D., and ***Robert J. Spinner, M.D.****; Mayo Clinic*

INTRODUCTION: Perineural tumor spread in pelvic malignancies has emerged as an anatomic explanation for selected cases of neoplastic lumbosacral plexopathy. Previously, it has been assumed to be due to hematogenous spread and frequently misdiagnosed and mistreated as spine disease. We present a case series and provide summarized clinical and imaging characteristics. To our knowledge a similar series has not been presented yet.

METHODS: We retrospectively reviewed cases of perineural tumor spread and excluded cases without histological confirmation and cases with widespread pelvic disease infiltrating the plexus. We reviewed clinical data and imaging studies.

RESULTS: Ten patients (8 men, 2 women) were included in the study (prostate cancer n=5; rectal cancer n=2, bladder cancer n=2, cervical cancer n=1). Mean age was 69 years (range 48-85 years). Pain was the initial symptom in 6 patients, pain and weakness in 1 patient, weakness in 1 patient; 2 patients were asymptomatic. In 1 patient the diagnosis of lumbosacral plexopathy preceded the tumor by 3 months, in other patients the mean time from the tumor diagnosis to the initial symptom was 67 months. On presentation, 6 symptomatic patients had pain, sensory loss and weakness corresponding to the affected nerves. On MRI (n=10) the affected nerves were enlarged and demonstrated thick perifascicular enhancement. MRI finding correlated with increased uptake on FDG PET/CT (n=4) and ^{11}C-Choline PET/CT (n=3) scans. EMG (n=9) demonstrated lumbosacral plexopathy in 8 patients; in 1 patient it was normal. Eight patients had no signs of distant metastatic disease at the time of the lumbosacral plexopathy diagnosis; 1 patient had metastases in the pelvis and lung, and 1 patient, in the pelvis. Seven patients were alive at the time of the last follow-up. Mean time from the initial symptom to the last follow-up was 51 months.

DISCUSSION: Our proposed route of the tumor spread is from the pelvic organ to the lumbosacral plexus and beyond using the splanchnic nerve as a conduit. We believe this theory can explain selected cases of neoplastic lumbosacral plexopathy. The route of spread can be visualized as a unilaterally thickened and enhancing perirectal fascia containing the pelvic and sacral splanchnic nerves.

CONCLUSION: We present a series of 10 cases of perineural tumor spread in pelvic malignancies. We believe that this mechanism is an otherwise under recognized cause of morbidity in pelvic cancer patients.

10:10 – 10:20 QUALITY OF LIFE AND REFERRAL PATTERNS IN HEMIFACIAL SPASM PATIENTS UNDERGOING MICROVASCULAR DECOMPRESSION

Raymond F. Sekula, Jr., M.D., F.A.C.S.*, and Andrew M. Frederickson, M.D.; University of Pittsburgh Medical Center*

INTRODUCTION: Hemifacial spasm (HFS) is a syndrome of unilateral facial nerve hyperactivity. Microvascular decompression (MVD) is a safe and effective therapy for HFS. This study was conducted in order to determine the impact of MVD on quality of life (QOL) in patients with HFS and to examine the referral patterns that led patients to seek an operation.

METHODS: We identified 331 consecutive patients who had undergone MVD for HFS with a single surgeon between 2007 and 2013. We attempted to contact all patients by telephone in order to administer a retrospective questionnaire containing 11 HFS-specific QOL metrics. Patients were asked to rate each QOL metric on a 0-4 scale, with 4 indicating "extremely debilitating." Additionally, we obtained information about the referral patterns to our practice.

RESULTS: Long term follow-up with the QOL questionnaire was available for 242 (73.1%) patients. The mean preoperative QOL score across all metrics was 2.3 and the mean postoperative score was 0.31. With a mean preoperative score of 3.1 (median = 4), "feeling embarrassed about having the condition" was the most debilitating problem associated with HFS. Following MVD, this improved to a mean score of 0.32 (median = 0). Of these 242 patients, 151 (62.4%) reported that they were self-referred, 64 (26.4%) were referred by a neurologist, 18 (7.4%) were referred by an ophthalmologist, 6 (2.5%) were referred by a primary care physician, 2 (0.8%) were referred by an otolaryngologist, and 1 (0.4%) was referred by a plastic surgeon.

CONCLUSION: HFS can severely reduce the QOL of patients. Despite an improvement in all QOL metrics following MVD for HFS, a majority of patients presenting to our practice were not referred for MVD by a physician.

10:20 – 10:30 LONG-TERM DIZZINESS HANDICAP ANALYSIS IN VESTIBULAR SCHWANNOMA PATIENTS. AN INTERNATIONAL MULTICENTER CROSS-SECTIONAL STUDY COMPARING MICROSURGERY, STEREOTACTIC RADIOSURGERY, OBSERVATION AND NON-TUMOR CONTROLS

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INTRODUCTION: Many previous studies have shown that ongoing dizziness is a powerful predictor of reduced quality of life (QoL) and disability in vestibular schwannoma (VS) patients. We recently showed that VS patients have a relatively similar long-term QoL regardless of treatment strategy but have a very significant decreased QoL compared to a group of non-tumor control subjects surveyed. The purpose of the current study is: 1) to characterize long-term dizziness in patients harboring small to medium-sized VS and 2) to identify clinical variables associated with long-term dizziness handicap.

METHODS: All patients with sporadic small to medium-sized VS who underwent primary stereotactic radiosurgery, observation or microsurgery between 1998 and 2008 at two academic tertiary referral centers; one in the U.S. and one in Norway, were surveyed using the Mayo Clinic Vestibular Schwannoma Symptom Questionnaire (MCVSSQ), the Penn Acoustic Neuroma Quality of Life Questionnaire (PANQOL) and the Dizziness Handicap Inventory (DHI).

RESULTS: A total of 538 respondents (79% of all VS patients contacted) returned completed questionnaires (mean age 64 years; 56% women) at a mean follow-up of 7.7 years after diagnosis. Patients who reported dizziness at presentation were more likely to have either SRS or MS compared to observation. Overall, 61% of patients reported some degree of dizziness at time of survey with 9% being dizzy most or all of the time. Increasing age, having

dizziness at presentation, the type of dizziness experienced and severity of ongoing headache after treatment correlated with a DHI score suggestive of severe dizziness (DHI > 26) at last follow-up. On multivariate analysis treatment modality (SRS vs. Obs vs. MS) did not influence long-term dizziness handicap.

CONCLUSION: More than 50% of VS patients will have ongoing dizziness at long-term follow-up. We have identified several features that might help predict risk for persistent dizziness. Treatment modality does not seem to influence long-term DHI score. We found a strong relationship between post-treatment headache and ongoing dizziness handicap. Further study is necessary to better define this relationship and a potential role in the etiology and treatment of persistent dizziness.

10:30 – 10:40 QUALITY OF LIFE METRICS FROM AN INITIAL 4 YEAR EXPERIENCE IN A TRANSITIONAL SPINAL DYSRAPHISM CLINIC

***Jeffrey P. Blount, M.D., F.A.A.N.S.**, University, Bergen, Norway*[2]

INTRODUCTION: The majority of pediatric patients with all forms of spinal dysraphism can now be expected to survive into adult years. This creates challenges for patients, families, providers and health care systems. Transition is often a difficult process as families are reluctant to depart a supportive experienced environment of the pediatric Spina Bifida clinic. Simultaneously adult neurosurgeons are often reluctant to inherit a population of patients that may harbor brittle hydrocephalus, symptomatic tethered cord and other problems unique to dysraphism. Many academic centers are currently struggling with this challenge.

METHODS: In response to the challenge of transition we initiated a Spinal Dysraphism Transition Clinic four years ago. We have enrolled 136 patients and have utilized a validated standardized instrument (HUI-3) to query Quality of Life data for a cohort of 47 of these patients and have surveyed all of them with questionnaires. These data were retrospectively reviewed, compiled and compared with a larger data set from the Pediatric Clinic.

RESULTS: One hundred and thirty six patients were enrolled in the clinic. HUI 3 scores were in the lowest quartile but reflected overall functional capacity and depression more than any factor related to transition per se. HRQOL appears bi-modal in adults with a small group of independent highly functional adults while a larger group appears marginal and poorly adapted to independent living or self-sufficiency. Transition clinic was uniformly considered of great benefit in facilitating transition to adult care.

CONCLUSION: QOL indices for SB adults demonstrate a wide range but are generally low. A validated instrument for Spinal Dysraphism is needed. Transition can be greatly facilitated by an experienced provider participating in a dedicated Transition clinic.

10:40 – 10:50 THREE-YEAR EXPERIENCE AS A SPINE SURGEON AT SHRINERS HOSPITAL – NEUROSURGICAL PERSPECTIVE

Anthony H. Sin, M.D., F.A.A.N.S.*, and Anil Nanda, M.D., M.P.H., F.A.A.N.S.; LSU Health Science Center - Shreveport*

INTRODUCTION: Pediatric deformity experience is limited for neurosurgeons in most of the training programs in United States. An early experience as the spine surgeon for pediatric deformity practice at Shriners Hospital in Shreveport was reviewed with emphasis on complications.

METHODS: Retrospective review of prospectively collected case logs from January 2012 to June 2014 was done. Basic demographic information including age, sex, type of surgery, number of segmental levels, diagnosis, and perioperative complications was collected and analyzed.

RESULTS: One hundred twelve patients were treated during first 30 months of practice at Shriners Hospital in Shreveport. There were 72 females and 40 males with average age of 15.3 years (6 – 18 years-old). A total of 121 operations were performed for following diagnosis: 70 adolescent idiopathic scoliosis (AIS), 6 juvenile idiopathic scoliosis (JIS), 6 hemivertebrate malformations, 11 Scheurmann's kyphosis, 18 neuromuscular (NM) scoliosis, 1 spondylolisthesis. An average of 11 segments was fused per case (2 – 16 levels). Four (3.6%) patients had neurological deterioration following the operation with three patients regaining the function within six months. One NM scoliosis patient had an epidural hematoma in the cervical spine even though her upper most instrumented level was at T3, and she was the only patient who had residual neurological decline compared to her baseline. Two patients had removal of pedicle screws due to malfunction. There was one superficial wound infection in a NM scoliosis case (0.9%). Three patients needed extension of fusion to the previous fused segments due to progression of non-fused segments.

CONCLUSION: Although it is early in experience of treating pediatric deformity as a neuro-spine surgeon, the complexity of cases and complications rate is comparable to existing experience from the pediatric orthopedic community.

10:50 – 11:00 QUANTITATIVE IMAGING EVALUATION OF TUMOR RESPONSE IN MALIGNANT GLIOMA PATIENTS TREATED WITH DENDRITIC CELL VACCINATION

Linda Liau, M.D.; *University of California, Los Angeles*

INTRODUCTION: To ascertain the radiologic response and serial volumetric changes in patients with malignant gliomas treated with dendritic cell (DC) vaccine using contrast enhanced (CE) T1-weighted subtraction maps.

METHODS: All patients participating in this study signed institutional review board-approved informed consent. At the time of writing, 20 patients with either newly diagnosed or recurrent WHO Grade III or VI gliomas enrolled as part of HIPPA-compliant single institution clinical trial (NCT01204684). Of the 20 patients, 14 had consistent serial MR imaging data. Genetic analyses and intratumoral histopathology were done on thirteen of the fourteen patients. Changes in contrast-enhancing tumor volumes as a response to the therapy were assessed with CE T1-weighted subtraction maps generated by voxel-wise subtraction of Gaussian-normalized signal intensities from non-enhanced T1-weighted images and CE T1-weighted images. Response criterion was determined as 25% reduction in the T1 subtraction map-defined contrast-enhancing tumor volume with respect to baseline measurements. Patient response stratification was then tested as a predictor of PFS using log-rank univariate analysis.

RESULTS: Four patients responded to the DC vaccine treatment within approximately the first three months of treatment. Ten patients did not have an imaging response within the same period of time following vaccination. One patient exhibited a growth pattern consistent with pseudo-progression between 100 and 300 days after vaccination. A significant difference in tumor growth rate ($P=0.0064$) between responders and non-responders was found within the first three months via linear regression. A preference for an unfavorable response in MGMT unmethylated, EGFR amplified, and EGFR VIII mutated tumors, and a favorable response in IDH1 mutant tumors were observed. Based

upon the stratification criterion, a significantly longer PFS was found both from the date of surgery just prior to enrollment into the trial for each patient (*Log-rank, P=0.0149*) and from the date of first vaccination (*Log-rank, P=0.0440*) for responders compared with non-responders.

CONCLUSION: This study supports the use of T1 subtraction maps in the context of tumor visualization and tumor burden evaluation following immunotherapy. Response outcomes to DC vaccine therapy should become apparent within the first three months of following treatment. The incidence of exacerbated pseudo-progression in the context of immune-based therapy for malignant glioma may not be as much of a concern as originally hypothesized. Genetic analyses and histopathological considerations may be important components in assessing treatment response to immunotherapy in malignant gliomas.