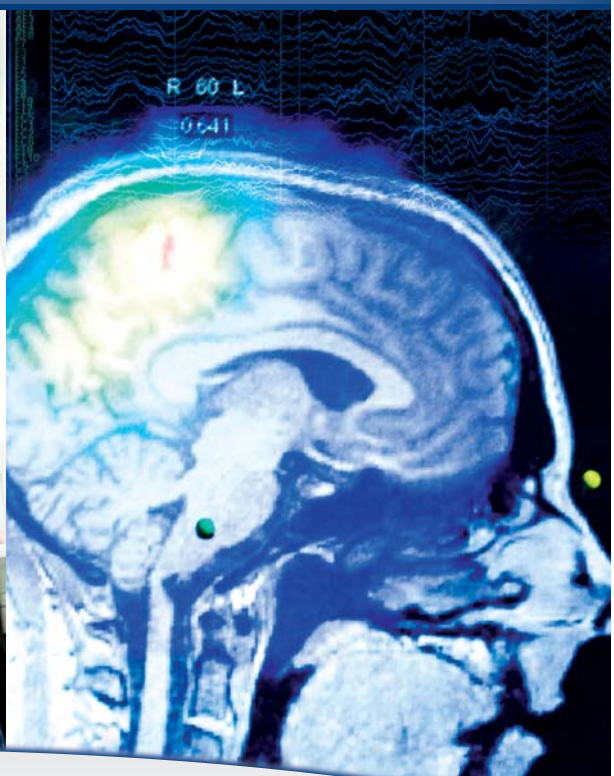
5th Annual ACMEG Conference | New Orleans, LA | February 3

ACMEGS
CONFERENCE 2011



ACMEGS

AMERICAN CLINICAL MEG SOCIETY

Welcome to New Orleans!

On the behalf of the Organizing Committee and the ACMEGS Board, I hope that you enjoy your visit to New Orleans, its architecture, music, culture, food and people.

This is our 5th annual conference of the ACMEGS and the second joint meeting with the American Clinical Neurophysiology Society (ACNS). The goal of this format is to save ACMEGS members who are also associated with ACNS one trip to a conference, as well as to spark some interest with members of ACNS who are not so familiar with MEG technology and its clinical applications. After all, MEG is a neurophysiological method.

Therefore, we moved the business meeting and the MEG-Economics part into the first half of the day to encourage interested ACNS members to join us in the afternoon for the scientific presentations.

During this year's business meeting two ACMEGS Committees will deliver their reports. The PR Committee, chaired by Susan Bowyer, will give an overview of the ongoing and planned activities for 2011. Anto Bagic, chair of the Clinical Practice Guidelines Committee, will conclude t that significant project with a final report.

Never before was our scientific program that extensive as it will be this year with eight presentations delivered by experts in the field of clinical MEG. During the scientific afternoon sessions we will focus on a variety of clinical topics, ranging from language mapping over high frequency oscillations to traumatic brain injury.

Our conference aims to provide an informal and friendly atmosphere for discussing and exchanging recent clinically relevant studies that might lead to new clinical MEG indications. In addition we want to enable our member to promote the appropriate use of the technology. And we want to empower them to work closely with national and local health insurance carriers and governmental regulatory bodies to ensure accurate and successful reimbursement.

The highlight of the 2011 conference will be the 4th John Gates Memorial Lecture. We are very delighted that the *Pioneer of Clinical MEG,* **William Sutherling**, accepted our invitation to come to New Orleans, and are looking forward to his lecture with anticipation.

Welcome to New Orleans and I hope you will enjoy the conference and our traditional society dinner at the end of a day filled with lectures and discussions.

Sincerely,

Michael E Funke, M.D., Ph.D.
President, American Clinical Magnetoencephalography Society

Organizing Committee:
Jeffrey Lewine, MIND Research Network, Albuquerque NM
Bruce Fish, University of New Mexico, Albuquerque NM
Michael Funke, University of Utah, Salt Lake City UT

PROGRAM

Thursday, February 3, 2011

8:00 am **Arrival / Breakfast Reception**

8:30 am **ACMEGS Presidential Address**
Welcome and Introduction (Michael Funke, Salt Lake City, UT)

9:00 am **Business Meeting (for ACMEGS members only)**
a) Financial Report (Anto Bagic, Pittsburgh PA)
b) Public Relations Committee (Susan Bowyer, Detroit MI)
c) Clinical Practice Guidelines (Anto Bagic, Pittsburgh PA)
d) New Business

10:00 am **Reimbursement / Economics** (Michael Longacre, Crofton MD)

10:30 am **Workshop on Language Mapping (chair: Jeffrey Lewine)**
- **Why use MEG for language mapping?** (Jeffrey Lewine, Albuquerque NM)
- **Language mapping using MEG: Practical considerations.** (Eduardo Castillo, Houston TX)
- **What to look for in a language study?** (Susan Bowyer, Detroit MI)

12:00 pm **ACMEGS Photo shooting / Lunch / Posters (chair: Michael Funke)**

1:45 pm **From the Clinic: Ramping up an MEG center from scratch: The Cleveland Clinics experience.** (Richard Burgess, Cleveland OH)

2:30 pm **Workshop on Epilepsy: Beyond Spikes – High Frequency Oscillations and Coherence (chair: Anto Bagic)**
- **Identification of pathological high frequency oscillations in epilepsy using MEG.** (Julia Stephen, Albuquerque NM)
- **MEG coherence imaging for lateralizing temporal lobe epilepsy** (Susan Bowyer, Detroit MI)

3:30 pm **Coffee Break / Poster Session**

4:00 pm **Emerging Applications – Traumatic Brain Injury (chair: Roland Lee)**
- **Making the invisible wounds of war visible: multimodal imaging in TBI, PTSD, and Depression**. (Jeffrey Lewine, Albuquerque NM)
- **Diagnostic Value of an Automated MEG Slow-wave Imaging Approach for Mild TBI (mTBI) Patients.** (Roland Lee, San Diego CA)

4:45 pm **John-Gates-Lecture 2011**
Use of MEG/MSI interictal spikes in presurgical ICEEG planning
(William Sutherling, Pasadena CA)

5:30 pm **Meeting Adjourn**

5:45 pm **ACMEGS Dinner at the - *Le Foret* - 129 Camp Street**

Michael Funke

ACMEGS Presidential Address

Michael Funke, M.D., Ph.D.
Department of Neurology, University of Utah, Salt Lake City, UT

ACMEGS

AMERICAN CLINICAL MEG SOCIETY

5th Annual Society Meeting

New Orleans

February 3, 2011

AMERICAN CLINICAL MEG SOCIETY

2010 in retrospect . . .

2010 in retrospect . . .

2010 Jan 12

A 7.0 Magnitude Earthquake Strikes Haiti, Causing Severe Damage The 2010 Haiti earthquake was a magnitude 7.0 Mw earthquake that occurred approximately 10 miles (16 km) from Port-au-Prince, Haiti.

2010 Feb 12

XXI Olympic Winter Games Held in Vancouver, British Columbia

2010 March 30

The ***Patient Protection and Affordable Care Act (PPACA)*** was signed into United States law by President Barack Obama on March 23, 2010. This Act and the ***Health Care and Education Reconciliation Act*** of 2010 (signed into law on) made up the health care reform of 2010.

2010 Apr 20

Offshore Oil Rig 'Deepwater Horizon' Explodes Off the Gulf of Mexico, 11 workers missing after an explosion and fire sunk an offshore drilling platform.

AMERICAN CLINICAL MEG SOCIETY

4th Clinical and Economic Workshop

February 4, 2010

Westin Gaslamp Quarter, San Diego

An unforgettable BIOMAG . . .

17th BIOMAG

March 28 – April 1

Dubrovnik, Croatia

Accomplishments in 2010

- Clinical Practice Guidelines (CPG) finalized!
  (chair: Anto Bagic)
  - Culmination point of two years of sustained effort
  - Committee of 11 society members involved
  - World Premier: First Clinical Practice Guidelines for MEG

Accomplishments in 2010

- United Healthcare and CIGNA cover MEG!
  (Bagic, Funke, Longacre)
  - Sustained team effort with AAN since 2009
  - Critical analysis of negative policies
  - Tele-Conference with United/CIGNA leadership
  - Follow-up

UnitedHealthcare

Date: July 9, 2010

ACMEGS team:
- Anto Bagic
- Michael Funke
- Michael Longacre


UnitedHealthcare

MEDICAL POLICY

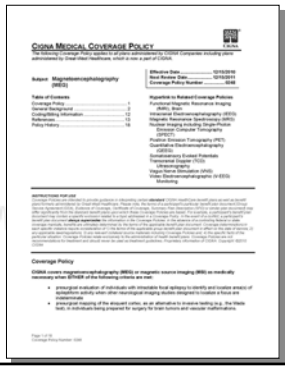
MAGNETOENCEPHALOGRAPHY AND MAGNETIC SOURCE IMAGING FOR SPECIFIC NEUROLOGICAL APPLICATIONS

CIGNA

Date: September 21, 2010

ACMEGS team:
- Anto Bagic
- Michael Funke
- Michael Longacre

Letter: November 16, 2010


CIGNA MEDICAL COVERAGE POLICY

Subject: Magnetoencephalography (MEG)

Coverage Policy

Accomplishments in 2010

- United Healthcare (August 2010)
- CIGNA (December 2010)
- Coverage for 42.6 million members
- Additional 14% of US population

2009
- AETNA, WellPoint, BCBS MI, BCBS NE
- 57.4 Mio members
- 16% of US population

Accomplishments in 2010

- This has a significant and tangible effect on all clinical MEG centers:
  - Improved access for patients
  - Improved revenue stream
  - Decreased number of denials
  - Decreased need for expansive appeals

Accomplishments in 2010

- PR committee established and working (Bowyer, Longacre, Singh)
- Markedly improved fiscal situation (Bagic, Funke)
- MEG revenue code went into effect
- Presentation to APC panel (Funke, Longacre)

Today ACMEGS represents . . .

- Professional organization with high level of competence in practice of clinical MEG and clinical credibility
- Professional organization with most comprehensive knowledge and competence in MEG reimbursement & coverage in the US
- Professional organization that collaborates successful with other national professional organizations, including AAN and ACNS

Challenges and Goals in 2011

- Clinical MEG course and CME credits
- Publish Clinical Practice Guidelines (CPG)
- National commercial payers (BCBS Association)
- Present ACMEGS at relevant meetings
- MEG line in CMS cost report
- Outreach to patient advocacy groups
- Outreach to MEG/EEG techs

Challenges and Goals in 2011

- Utilize ACMEGS resources more effectively
  - Membership recruitment & retention
  - Meeting event planning and management
  - Financial management
  - CME compliance
- Increase membership
- Fundraising
- Present ACMEGS at national meetings

Mark your calendar . . .

3rd ISACM

Fall 2011

Las Vegas, Nevada

What happens in Vegas, will be published by ISACM!

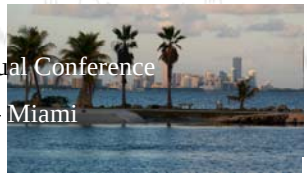
Mark your calendar . . .

6th ACMEGS Annual Conference

February 9, 2012 – San Antonio

7th ACMEGS Annual Conference

February 7, 2013 – Miami



Acknowledgments

- Active participation of ACMEGS members
- **Jackie Coleman & Michael Deegan!**

- Unrestricted educational grant from

ELEKTA

Words of Caution

- Please do not share with each your institutional reimbursement rates and your billing rates.
- Sharing such information could be considered collusion and could have legal ramifications for you and the society.

Enjoy the Meeting!

ACMEGS BUSINESS MEETING

1. Financial Report — Anto Bagic

2. Public Relations Committee — Susan Bowyer

3. ACMEGS Clinical Practice Guidelines — Anto Bagic

3. New Business
   - Election of one new Board Member
   - Annual Meeting 2012
   - Other

NOTES

ACMEGS _ Financial Report FY 2010

Anto Bagic, M.D.
Department of Neurology, University of Pittsburgh Medical Center, Pittsburgh, PA

Anto Bagic

NOTES

Susan Bowyer

ACMEGS Public Relations Committee – Report FY 2010

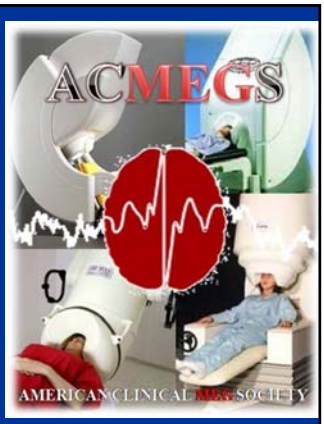
Susan Bowyer, Ph.D.
Henry Ford Hospital, Detroit, MI

Public Relations Committee

Susan M. Bowyer
Michael Longacre
Sanjay P. Singh

Website can be accessed by either:

ACMEGS.org
ACMEGS.com

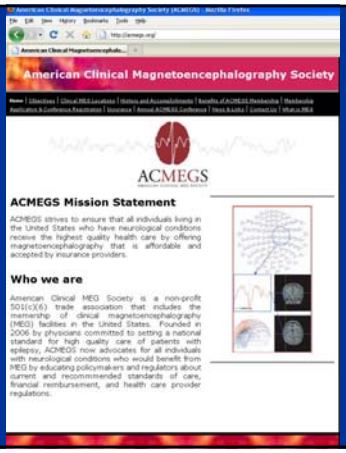


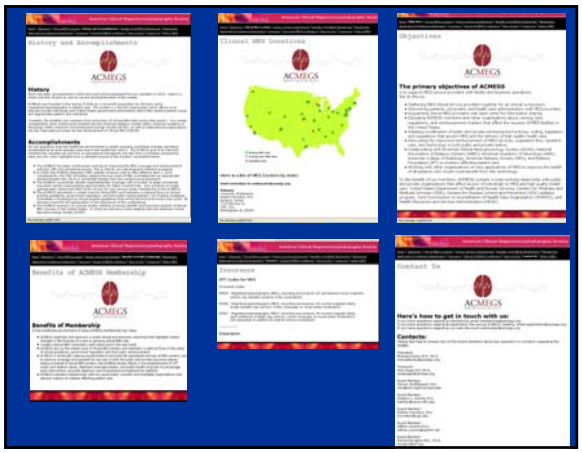
Purpose

Potential Fields of Activities to promote the ACMEG Society Include:

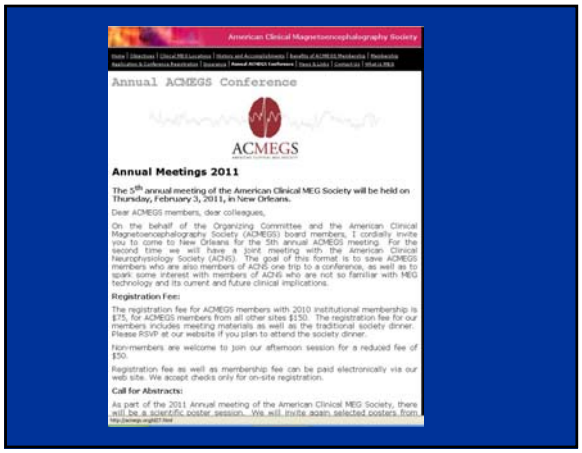
- Website
- ACMEGS presence at national meetings (AES, AAN etc.)
- Outreach (patient advocacy groups)
- Sponsoring (for meetings, exhibitions)
- Speaker Bureau

Website






American Clinical Magnetoencephalography Society
What is MEG
Why is MEG beneficial?
A guide for patients and their families.


American Clinical Magnetoencephalography Society
Annual ACMEGS Conference
Annual Meetings 2011

Presence at Meetings

- ACMEGS will be able to reach out to many clinicians at conferences especially if we have a booth.
- Promoting ACMEGS by sponsoring activities, providing lunches and exhibits at conferences.
- As we are a nonprofit society we are able to have a booth at American Academy of Neurology at no cost (we signed up early enough)
- American Epilepsy Society (AES)
- NeuroSurgical conferences

Presence at Meetings

- Brochures
  - Clinicians
  - Patients
- Banners Free standing and Table
- Chocolates with our Logo imprinted
- Pins for the members of our society
  - When they pay their membership dues

Enlightening Clinicians

- Educating Neurologists and Neurosurgeons about MEG. This is still new technology for many
- Focus on Residents and Fellows.
- They are the future of our field
- They love to learn more about MEG.
- Educating them in a way that they would find interesting is critical.

Speakers Bureau (under construction)

- A list of Topics and Speakers that could be called upon to give presentations at institutions that are thinking about getting MEG or promoting the use of MEG for patients
- Library of topics and speakers available on ACMEGS.org
- A Speakers Bureau is a coordinated effort to distribute the organization's information, goals and needs
- It is an ongoing public relations effort that includes research, strategic market planning, writing, coaching, promotion, monitoring, and evaluation

Key Elements

- Selecting the Speakers
- Selecting the Target Audiences
- Selecting The Message

Patient Advocacy

- Contacting patient advocacy groups to promote awareness of our ACMEG society

- **Epilepsy Foundation**
  - **International**
  - **National**
  - **Local**

Thank you for your attention!

Please provide feed back and comments to these ideas.

We welcome more ideas

Enjoy the Chocolates!

ACMEGS.org

Anto Bagic

ACMEGS Clinical Practice Guidelines (CPG) Committee – Final Report

Anto Bagic, M.D.
Department of Neurology, University of Pittsburgh Medical Center, Pittsburgh, PA

5th Annual Meeting

ACMEGS

February 3, 2011
New Orleans, LA

American Clinical MEG Society (ACMEGS)
ACMEGS Clinical Practice Guidelines (CPG) Committee

FINAL REPORT

Anto Bagić, M.D., M.Sc.
Associate Professor, Neurology
Chief, UPMC Epilepsy Division
Director, UPMC **MEG Epilepsy Program**
Director, University Of Pittsburgh Comprehensive Epilepsy Center (**UPCEC**)

UPMC LIFECHANGINGMEDICINE

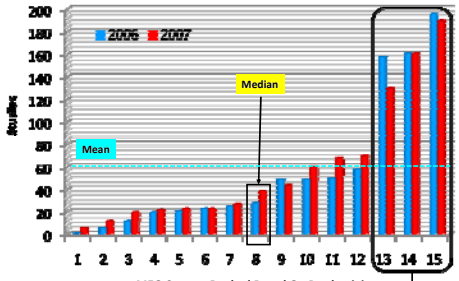
The (Less Traveled) Road

1. A **survey** of the current practice.
   - USA: 2008/2009.
2. An **appointment and subsequent selection.**
   - Boston, MA: November 6 & 7, 2008.
3. The **first report.**
   - Salt Lake City, UT: May 15 & 16,2009.
4. A **progress update.**
   - San Diego, CA: February 4, 2010.
5. The **final report.**
   - New Orleans, LA: February 3, 2011.

Bagić A, 2011

USA:
Clinical Epilepsy MEG Studies In 2006 And 2007

Poster



2006: 3 leading centers performed 512 (**61%**) studies
2007: 3 leading centers performed 478 (**54%**) studies

Bagic A, unpublished data.

Cumulative Answers To Some MEG Center Director's Survey Questions

Poster

1. Duration of center's operation (years)**

N	Total*	Mean	Minimum	Maximum
15	106	7	2	21

6. Annual number of clinically indicated and billed epilepsy localization studies in

2006	15	842	53	0^	195
2007	15	880	59	5	189

8. Annual number of research MEG studies in

2006	15	1222	76	0	340
2007	15	1384	87	0	340

12. Within how many days do you usually report clinical studies?

Epilepsy	15	150	9.3	1	30
Mapping	15	66	4.1	0.5	30

* Rounded to the nearest whole number where appropriate. **Only centers that were in operation for at least 2 years are included.

Baeic A, unpublished data.

Bagić A, 2011

Cumulative Answers To Some MEG Center Director's Survey Questions

Poster

16. How many accepted average responses do you usually require for each modality being mapped?#

	N	Total*	Mean	Minimum	Maximum
AEF	13	2080	160	100	400
LRF	12	2560	213	50	930
MRF	13	2340	180	80	740
SEF	15	2316	154	100	768
VEF	13	2350	181	100	512

Auditory Evoked Magnetic Fields (**AEFs**), Language-Related Brain Magnetic Fields (**LRFs**), Movement-Related Magnetic Fields (**MRFs**), Somatosensory Evoked Magnetic Fields (**SEFs**) , Visual Evoked Magnetic Fields (**VEFs**)],

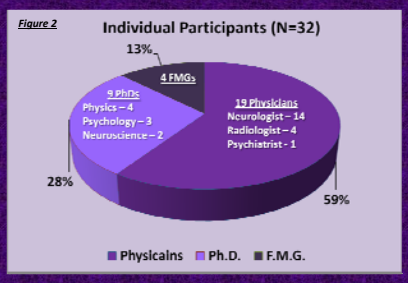
Bagic A, unpublished data.

Bagić A, 2011

Doctoral Level Participants Of The Survey

In Review

Figure 2



Bagic A, unpublished data.

Bagić A, 2011

Are We Concerned That…?

- 1. MEG is labeled a "new" or "investigational" technology even 40 years after the 1st SQUID recording?
- 2. Some professionals may have been exposed to more direct exposure to clinical MEG in an average month in an active institution that performs almost 4 epilepsy studies per week, than in another less active institution in 5 years?
- 3. Some colleagues seem to have a tendency to declare themselves "an expert" on the basis of being an assertive and interested participant of the meetings and have fragmental exposures to various MEG environments even if they barely interpreted a study by themselves?
- 4. A MEG study is reported on the same day in rare centers and within 30 days in other laboratories?

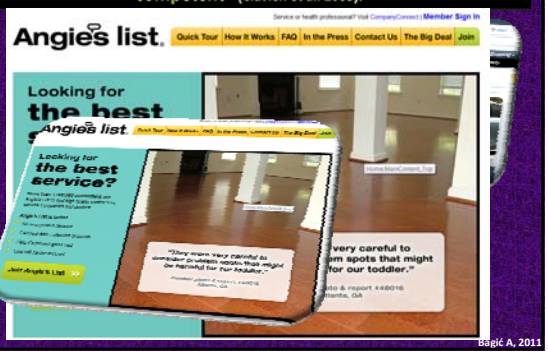
Bagić A, 2011

Are We Concerned That…?

- 5. Some centers use an EEG only as a pointer to the corresponding parts of MEG for dipole modeling while others engage also in EEG source localization?
- 6. The number of averaged responses used for mapping a particular modality may vary between the centers up to 19 times?
- 7. Disrespect for the boundaries of clinical practice seems to be an enduring temptation of some devoted researchers even when they are physicians?
- 8. A considerable number of the USA MEGers care more about standards of their mechanics and hairdressers then those who interpret MEG studies?

Bagić A, 2011

"Our society is pervaded by a fixation on quality. … Accordingly, the public has expectations that providers of services, including mechanics, hairdressers, lawyers, and physicians, will be competent" (Clavien et al. 2005).



Bagić A, 2011

Are We Ready To…?

- Accept **a new phase of the clinical MEG field** that grew on 4 decades-long experience with MEG technology, marking **the inevitable point** when a significant change in clinical practice is necessary for fulfilling our **professional role** in delivering optimal patient care by **accountable clinical MEG practice** commensurate with our undeniable achievements and **necessary responsibility to the profession and public**?

Bagić A, 2011

The Premises / Motivations

- 1. Disturbing variability in **clinical p ice**.
- 2. A hurdle for acceptance as a **outine**.
- 3. An obstacle in **appeal p**
- 4. An obstacle for **bett ent**.
- 5. **Insurers**' direct
- 6. **Users clini** and requests.
- 7. Improv **ealth care**.
- 8. Imp **comes**.
- 9. Optim **ce utilizations**.
- 10. Identify **earch priorities**.

A STAGNATION OF THE FIELD!

Bagić A, 2011

American Clinical MEG Society (ACMEGS)

ACMEGS Clinical Practice Guidelines (CPG) Committee

Chair: Anto Bagić, MD, MSc

1,3,4 Anto Bagić, MD, MSc — UPMC, Pittsburgh, PA
4 Gregory Barkley, MD — HFMS, Detroit, MI
2/L Susan Bowyer, PhD — HFHS, Detroit, MI
2/D Richard Burgess, MD, PhD — CCF, Cleveland, OH
2/L Eduardo Castillo, PhD — UT, Houston, TX
1,3,4 John Ebersole, MD — UC, Chicago, IL
2/D Michael Funke, MD, PhD — UU, Salt Lake City, UT
2/D Heidi Kirsch, MD, MS — UCSF, San Francisco, CA
1,3,4 Robert Knowlton, MD, MSPH — UAB, Birmingham, AL
2/L Jeffrey Lewine, PhD — MIND, Albuquerque, NM
1,3,4 Douglas Rose, MD — CCHMC, Cincinnati, OH

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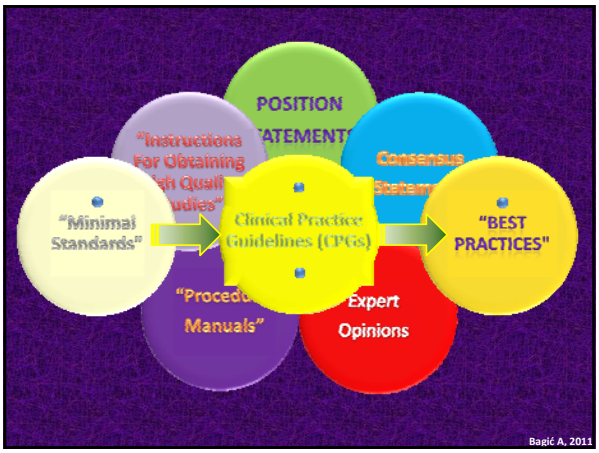

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American Medical Association (AMA): Policy Compendium, H-35.971/ Res. 904, I-06

- ***"Diagnosis of disease and diagnostic interpretation of tests constitutes practice of medicine to be performed by or under the supervision of licensed physicians."***
- **It is AMA policy that:**
- (1) the diagnosis of disease and diagnostic interpretation of a study or studies for a specific patient constitutes ***the practice of medicine***;
- (2) a ***PhD clinical lab scientist*** or ***other non-physician laboratory personnel*** work ***under the supervision of a physician*** under their applicable scopes of work to perform a study or studies that will be the basis of a diagnostic interpretation for a specific patient; and
- (3) the ***Medicare physician fee schedule*** compensate ***only authorized persons*** for the diagnostic interpretation of a specific patient and should not provide payments directly to non-physician lab personnel working under the supervision of a physician to perform a laboratory study or studies. (**Res. 904, I-06**)

Bagić A, 2011

What are Clinical Practice Guidelines (CPGs)?

Definition

"Clinical practice guidelines are **systematically developed statements** to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances"
(Institute of Medicine, 1990).

- ✓ They define **the role** of specific diagnostic and treatment modalities in the diagnosis and management of patients.
- ✓ The statements contain **recommendations** that are **based on evidence** from a **rigorous systematic review and synthesis** of the **published medical literature**.

http://www.nhlbi.nih.gov/guidelines/about.htm, accessed on 11/03/08

Bagić A, 2011

What Is The Purpose Of Clinical Practice Guidelines?

Purpose

*The purpose of the guidelines is to **help clinicians and patients make appropriate decisions about health care**.*

Guidelines attempt to do this by:

1. Describing **a range of generally accepted approaches** for the diagnosis, management, or prevention of specific diseases or conditions.

2. Defining practices that meet the needs of **most patients in most circumstances.**

3. The recommendations are not fixed protocols that must be followed. **Responsible clinician's judgment** on the management of patients remains paramount.

4. Clinicians and patients need to develop **individual treatment plans** that are tailored to the specific needs and circumstances of the patient.

http://www.nhlbi.nih.gov/guidelines/about.htm, accessed on 11/03/08

Bagić A, 2011

Who Are Intended Users Of Clinical Practice Guidelines (CPGs)?

Intended Users

1. These guidelines are primarily for use by **clinicians**-physicians, nurses, and other health professionals in clinical practice.

2. They are also useful to **managed care organizations** and other groups that define benefit plans for patients or handle health care resources.

http://www.nhlbi.nih.gov/guidelines/about.htm, accessed on 11/03/08

Bagić A, 2011

The AAN Definition Of Clinical Practice Guidelines (CPGs)

"***Practice guidelines*** have been developed to improve the process of health care and health outcomes, decrease practice variation, and optimize resource utilizations. They attempt to distill a large body of medical expertise into a convenient, readily usable format."

AMERICAN ACADEMY OF NEUROLOGY

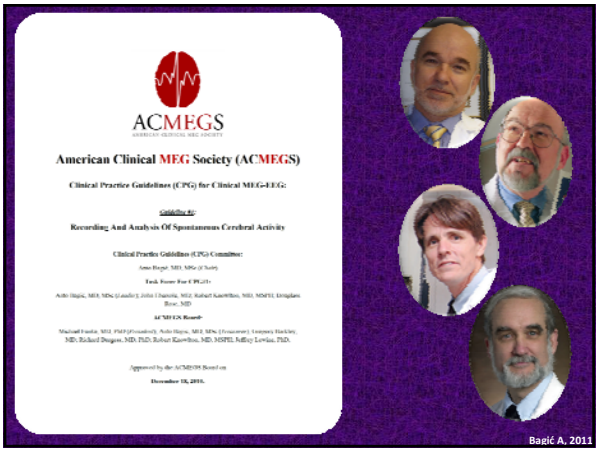
Bagić A, 2011

The AAN Guidelines Are Used To:

- 1. **Improve health outcomes of patients.**
- 2. Stay abreast of the latest in clinical research.
- 3. Appeal payment denials.
- 4. Provide medico-legal protection.
- 5. Advocate for fair reimbursement.
- 6. Determine whether your practice follows current, best evidence
- 7. Affirm the role of neurologists in the diagnosis and treatment of neurological disorders.
- 8. Influence public or hospital policy.
- 9. Promote efficient use of resources.
- 10. Identify research priorities based on gaps in current literature.

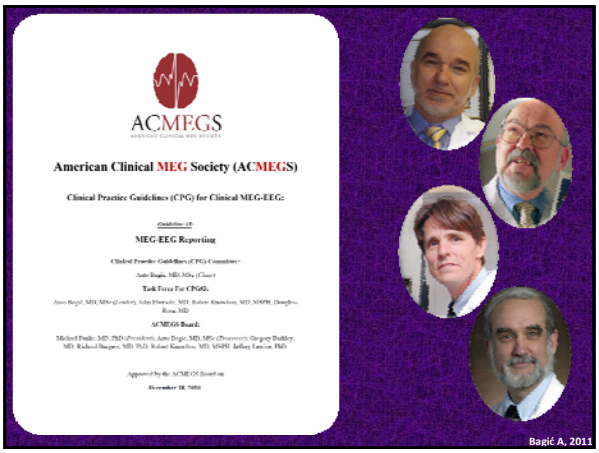
http://www.aan.com/go/practice/guidelines accessed on 11/03/2008

Bagić A, 2011



Bagić A, 2011

Bagić A, 2011



What Have We Done Since 2008 And Where Do We Go In 2011 And Beyond? 1/4

- 1. Defined a set of 4 practical guidelines that capture the best available evidence and clinical expertise in the context of the current transitional phase of the clinical MEG field – a practice of medicine - while recognizing where we should be now and direction for the future.
- 2. Accept the new phase of clinical MEG field that grew on the 4 decades-long experience with MEG technology, crossing the inevitable point when a significant change in clinical practice is necessary for fulfilling our professional role in delivering optimal patient care and responsibility to the profession and public.
- 3. These CPGs indicate a level of professionalism and maturity that signifies an implicit clinical credibility.

Bagić A, 2011

What Have We Done Since 2008 And Where Do We Go In 2011 And Beyond? 2/4

- 4. The CPGs provide a set of practical recommendations that should help laboratories and clinicians practice more uniformly and consistently with all direct and fringe benefits of such a new reality.
- 5. They are intended for all of us in the field and those who intend to come into it. They clearly raise the bar for all of us and represent a benevolent purposeful challenge for each and every member of the community.
- 6. These CPGs also recognize critical but medico-legally different roles of non-physician MEG scientists and MEG technologists.
-

Bagić A, 2011

What Have We Done Since 2008 And Where Do We Go In 2011 And Beyond? 3/4

- 7. None of these documents is aimed at excluding anybody but rather forcing all of us to advance to the next level. They are defined to be a constructive challenge - the way the Committee believed things should be - in the field of practicing modern medicine with all provisions and consequences.

  8. Judicious implementation of the CPGs should be supplemented with and facilitated by the structured comprehensive educational activity covering from the science of MEG to implementing "best practices" and MEG economics and marketing in a modern society strapped with competing priorities that are more likely to affect more expensive studies first and more.
- 9. ACMEGS should appoint Education Committee ("Training Committee") that would carry these efforts into an educational domain leading to the creation of standardized training for all professionals in the field.

Bagić A, 2011

What Have We Done Since 2008 And Where Do We Go In 2011 And Beyond? 4/4

- 10. In the future, a serious consideration should be given to certification and/or accreditation of magnetoencephalographers practicing in the USA.
- 11. At that time, an appropriate degree of sensitivity should be demonstrated towards experienced practitioners and their diverse routes to clinical practice according to well-established approaches in other medical specialties.
- 12. The CPGs per definition have a limited shelf life and their timely evidence- and practice-based revisions are one of the continued responsibilities of the Society.

Bagić A, 2011

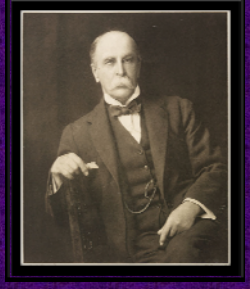
A Social Marketing Theory-based MEG-education Program For The Clinical MEG Community

- **Social marketing** is the systematic application of marketing tools combined with **behavioral** and **communication** science, along with other concepts and techniques, to attain **specific behavioral changes** for a common good.
- While **clinician-based interventions** are more effective than organizational or financial interventions, **local educational activities** involving secondary care specialists show the highest impact on implementation of some CPGs.
- **Social marketing** may be the answer to the failure of **CPGs** and other means of translating **evidence** into **effective practice**.

Bagić A, 2011

*Sir William Osler (1849-1919)

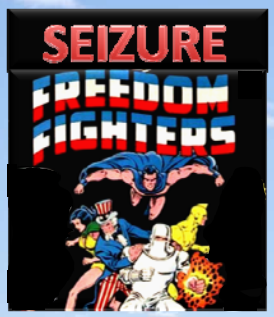
[the "most influential physician in history"]

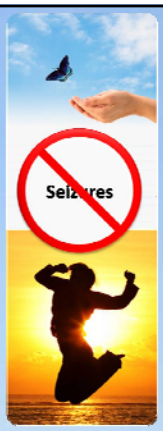


"Medicine is a science of uncertainty and an art of probability."*

Bagić A, 2011

PLEASE, JOIN





Thank You For Your Attention!

ACMEG Society Clinical Practice Guidelines: Introducing them to the Community

Why establish Guidelines?

Who are the Guidelines for?

What the Guidelines are and are not

What purpose do the guidelines serve for the medical community?

- Consistent quality of recordings
- Consistency of practice
- Uniformity of expectations from referring physicians
- Understandable and relevant reports
- Reasonable lab setups, tuning, accuracy, etc.
- Assurance of patient safety
- Better integration into quality patient care
- Natural extension of the AAN and ACMEGS position statements

What are the Guidelines?

- Outline of essential elements
- Important definitions
- Guidelines, not standards
  - I.e. helpful, not dictatorial
  - Consensus starting point
  - “How-tos” and common practices
  - Eventually moves towards “Best practices”
- Vision for where we think we should be
  - Bringing “tricks of the trade” into one place
  - Platform for developing appropriate training

Who is the target audience for the Guidelines?

- Current practitioners of he MEG art?
- Trainees and those who educate them?
- Administrators and dept chairman at hospitals considering establishing a MEG lab?
- Payors?

Who are the Guidelines for?

- Newly established labs
- Labs who don't know exactly what to do when starting up a new test or service
- Already operating labs who wonder what the majority of the other labs are striving towards
- Practioners not satisfied with their results who hope to improve their process

Balance

- Guidelines that are too broad or loose are not helpful guidelines at all.
- Suggestions which are overly strict make it impossible (and discouraging) for labs where the Guidelines cannot be achieved and staunch clinical innovation.
- Must not dictate which services should be provided.
- Not meant to define the "standard of care."

How to Practice?

- Not a compplete “how-to” manual for magnetoencephalography.
- Aimed at those already trained in MEG who are responsible for insuring that their laboratory is conducting high-quality studies.
- Shall we include only CMS-approved clinical studies, or provide more general guidance that can be extrapolated to the conduct of research studies?

What if I don’t want to follow the Guidelines?”

JUSTIFICATIONS:

- 1) Our laboratory controls were obtained with a different methodology and we need to be consistent with that for comparison.
- 2) Our laboratory does things differently, we have vetted our method in N cases, and we get better results using our methodology.
- 3) There are published (either by us or by others) reports that we follow showing that this method is better than the guidelines.
- 4) Our equipment does not permit x, y, or z, so we have employed the next best setting (e.g. placing the VEF viewing screen further away than ideal).
- 5) Clinical judgement dictated an alteration of the procedure in a particular patient's case to accomodate u, v, or w.

JUSTIFICATIONS THAT WON’T FLY:

- “That's the way we've always done it,"

Reimbursement Round Up – Successes, Opportunities, Challenges

Michael Longacre
Executive Director, ACMEGS

Michael Longacre

ACMEGS
AMERICAN CLINICAL MEG SOCIETY

5th Annual Society Meeting

New Orleans

February 3, 2011

Michael Longacre
Executive Director

ACMEGS
AMERICAN CLINICAL MEG SOCIETY

Reimbursement Roundup
Successes
Opportunities
Challenges

Successes

UnitedHealth Group

MAGNETOENCEPHALOGRAPHY AND MAGNETIC SOURCE IMAGING FOR SPECIFIC NEUROLOGICAL APPLICATIONS
COVERAGE RATIONALE

Magnetoencephalography and magnetic source imaging (MEG/MSI) are proven for the following:

- presurgical evaluation in patients with intractable focal epilepsy
- presurgical evaluation of brain tumors and vascular malformations

Magnetoencephalography and magnetic source imaging (MEG/MSI) are unproven for the evaluation of brain function in patients with trauma, stroke, learning disorders, or other neurologic disorders and psychiatric conditions such as schizophrenia.

There is insufficient evidence to conclude that the use of MEG/MSI improves health outcomes such as improved diagnostic accuracy and treatment planning for patients with trauma, stroke, learning disorders, or other neurologic disorders and psychiatric conditions. Further clinical trials demonstrating the clinical usefulness of this procedure are necessary before it can be considered proven to have a benefit on health outcomes.

BACKGROUND
Policy Number: 2010T0172H
Effective Date: August 13, 2010

ACMEGS

Successes

CIGNA

CIGNA covers magnetoencephalography (MEG) or magnetic source imaging (MSI) as medically necessary when EITHER of the following criteria are met:
• presurgical evaluation of individuals with intractable focal epilepsy to identify and localize area(s) of epileptiform activity when other neurological imaging studies designed to localize a focus are indeterminate
• presurgical mapping of the eloquent cortex, as an alternative to invasive testing (e.g., the Wada test), in individuals being prepared for surgery for brain tumors and vascular malformations.

CIGNA does not cover MEG or MSI as a stand-alone test or as the first order of test after clinical And routine electroencephalography (EEG) diagnosis of epilepsy because it is considered experimental, investigational or unproven.
CIGNA does not cover MEG or MSI for any other condition because they are considered experimental, investigational or unproven.

Effective Date 12/15/2010
Next Review Date.....12/15/2011
Coverage Policy Number 0248

ACMEGS

Successes

TOP 20 Commercial Health Plans

Company	Enrollment
UnitedHealth Group	**32,702,445**
WellPoint Inc.	**30,622,381**
Aetna Inc.	**16,318,625**
Health Care Service Corp.	12,218,623
Cigna Healthcare Inc.	**9,922,135**
Kaiser Permanente	8,532,951
Humana Inc.	**8,486,913**
Health Net Inc.	**6,180,395**
Highmark Inc.	**5,182,186**
BlueCrossBlueShield of Michigan	5,011,359
Coventry Health Care Inc.	**4,762,000**
Emblem Health Inc.	4,035,710
Medical Mutual of Omaha	3,929,677
WellCare Group of Companies	3,537,777
Independent BlueCross	3,480,168
BlueShield of California	**3,474,951**
Horizon BlueCrossBlueShield	**3,474,951**
CareFirst Inc.	3,044,880
BlueCrossBlueShield of Massachusetts	**3,012,396**
BlueCrossBlueShield of Alabama	**2,971,869**

ACMEGS

Successes

CMS Manual System

Pub 100-04 Medicare Claims Processing

Transmittal 1927

Department of Health & Human Services (DHHS)
Centers for Medicare & Medicaid Services (CMS)
Date: March 5, 2010
Change Request 6882

REVENUE CODES
Added Revenue Codes
The following revenue code(s) were added to the list of valid revenue codes, **effective 04-01-10**

Revenue Code	Status Indicator
0860	N
0861	N

ACMEGS

Opportunity

Medical Society Recommendations
- American Academy of Neurology Policy
- ACMEGS Policy

Commercial Payers
- Aetna Medical Coverage Policy
- UnitedHealthcare Coverage Policy
- CIGNA Coverage Policy
- Wellpoint Coverage Policy
- Anthem BCBS Coverage Policy
- Highmark Coverage Policy
- BCBS of California Coverage Policy
- BCBS of Alabama Coverage Policy
- TriCare Coverage Policy

Challenges

CMS
- Obtain a fair calculation of reimbursement based solely on the MEG cost data
  - Medicare Cost Report
    - Line 54 - EEG
    - No CPT codes listed
  - OPPS - APC
    - UB-04 Revenue Code is same as EEG
    - MEG CPT codes

Challenges

ACR Appropriateness Criteria®

Radiologic Procedure	Rating	Comments	RRL
Variant 1: Chronic epilepsy, poor therapeutic response. Surgery candidate.			
MEG/MSI	5	Data probably equivalent to BOLD and SPECT	None
Variant 2: New onset seizure. ETOH, and/or drug related.			
MEG/MSI	2		None
Variant 3: New onset seizure. Aged 18-40 years.			
MEG/MSI	2		None
Variant 4: New onset seizure. Older than age 40.			
MEG/MSI	2		None

Rating Scale: 1=Least appropriate, 9=Most appropriate

Last review date: 2006

Activities

American Academy of Neurology Partnerships:

- Katie Kuechenmeister (Staff Liaison)
- Joel M. Kaufman, MD (Chair, Payment Policy Subcommittee)
- Robert C. Griggs, MD, FAAN (President, American Academy of Neurology)

Activities

- Comments; OPPS Proposed Rule
  - *Our request is for a fair calculation of reimbursement based solely on the MEG cost data provided.*
- Presentation; Advisory Panel on Ambulatory Payment Classification Groups August 23 & 24, 2010
  - Acknowledgment from the Advisory Panel on Ambulatory Payment Classification Groups that current methodology for calculating an appropriate reimbursement rate for MEG is flawed.
  - AAN Letter of Support

Activities

ACMEGS PR Committee

Susan Boyer, PhD

National Meetings: AES, AAN

Brochures, Table Cloth, Banner

Speakers Bureau

2010 Key Goals

1. CMS
   a. Medicare Cost Report Inclusion No
   b. Fair APC calculation of reimbursement Work In Progress
2. National Carriers; UnitedHealthcare and Cigna YES!
3. Commission Third Party Reimbursement Report No
4. Regional Carriers – Support YES!
5. Advocacy Groups – Increase utilization No
6. Represent ACMEGS in Washington, DC YES

2011 Key Goals

1. CMS - Fair APC calculation of reimbursement
2. National Carriers; BCBS TEC Association
3. Regional Carriers – Support
4. Advocacy Groups –
5. Represent ACMEGS in Washington, DC

ACMEGS in 2011

- What are your key concerns?
- Questions

ACMEGS in 2011

THANK YOU!

2nd ACMEGS POSTER PRESENTATION

Current Clinical MEG Practice In The USA: Does The Flag Identify The Cargo?

Anto Bagić, Department of Neurology, University of Pittsburgh Medical Center, Pittsburgh ,PA

Although MEG is a mature technology, clinical MEG is a growing field facing various challenges some of which may stem from clinical practice that was never assessed in any formal way.

This survey of 20 questions ("MEG Center Director Survey"), designed to investigate institutional practices in clinical magnetoencephalography (MEG) in the USA, was e-mailed to all clinically active centers in the USA (21) in 2008. A part of general data is presented here.

All participating centers (15) declared 106 (mean = 7, range = 2-21) years in operation, and performed 836 mappings [138 Auditory Evoked Magnetic Fields (AEFs), 211 Language-Related Brain Magnetic Fields (LRFs), 140 Movement-Related Magnetic Fields (MRFs), 317 Somatosensory Evoked Magnetic Fields (SEFs) and 30 Visual Evoked Magnetic Fields (VEFs)], 842 epilepsy and 1222 research studies in 2006, and 866 (110 AEFs, 228 LRFs, 149 MRFs, 347 SEFs, and 32 VEFs) , 880 and 1384 in 2007. All sites claimed using an EEG in conjunction with MEG for epilepsy studies, but used it very differently. The number of required accepted averages for various evoked modalities varied: AEF (100-400), LRF (50-930), MRF (80-740), SEF (100-768), VEF (100-512). In 2 centers MEG reports are signed by non-physicians and in 2 by non-neurologists. Epilepsy studies are reported within 9.3 days (1-30) and mapping studies within 4.1 (0.5-30).

USA MEG Centers vary considerably in experience and practice of clinical MEG, and these two elements don't seem to be strongly related. Clinical practice guidelines (CPG) are necessary to cultivate the growth of the field.

Significant Differences in the Location of MEG vs EEG Spike Dipoles: the Edge Effect?

Susan M. Ebersole[1] and John S. Ebersole[2]
Illinois MEG Center, Alexian Brothers Medical Center[1] and The University of Chicago[2]

Most of the time, MEG and EEG source modeling from simultaneous recordings of epileptiform spikes yield dipole models that are similar in location, but different in orientation, as would be expected. Occasionally, however, these source models of the same spike may be centimeters apart, raising the questions, "Why such discrepancy, and which is the true source?"

We have reviewed dipole models derived from simultaneously recorded MEG and EEG data in 100+ patients with focal epilepsy. In approximately 10 % of cases, the MEG and EEG dipoles of the same spike differed in location by three to ten centimeters, when modeled at the same latency.
These large discrepancies are difficult to understand and are at the same time troubling for clinical interpretations. We believe that the differential sensitivities of MEG and EEG to source orientation may be responsible. Furthermore, we posit that these differences in putative source location may be the result of the "edge effect", whereby MEG "sees" only the edge of a large cortical source, where there is asymmetrical sulcus or fissure activation to produce a tangential field.
Accordingly, we believe that the EEG should be subjected to source modeling, not simply recorded, along with MEG in any epilepsy evaluation.

MEG and EEG sensitivity - Dependence on source orientation and depth

Alexander Hunold[1,2], Michael Funke[2], Roland Eichardt[1] and Jens Haueisen[1]
Ilmenau University of Technology, Ilmenau, Germany[1], University of Utah, Salt Lake City, USA[2]

In simultaneous clinical recordings of MEG and EEG phenomena appear where both modalities show different sensitivity to interictal spikes. Most events can be perceived in MEG as well as in EEG recordings. Besides, there are situation where abnormal activity is detectable in one modality only. Referring to the physical methods and the anatomical structure it is not completely clear what determines the detectability of interictal spikes in MEG or EEG. Our aim was to investigate the influence of the source depth as well as the orientation of the source, to determine whether or not there is correlation to detectability of interictal spikes.
First, we build a realistic numerical head model and shaped point sources of different orientation and depth localization. Source depth is defined as distance to the outer scalp surface. A row of spike source points starts in the bottom of the sulcus centralis with radial orientation and goes up in the sulcus wall with tangential orientation. The row ends with a radially oriented dipole at the top of the accordant gyrus precentralis or gyrus postcentralis. The dipole strength for background activity as well as spike activity was set to produce physiologically reasonable MEG and EEG outputs. In simulated signals we analyzed the signal-to-noise ratio (SNR) as an amplitude ratio between spike and background activity.
Following a row of spike source points the SNR develops very different for MEG and EEG, respectively. EEG signals show a high SNR (around 4.5) for spikes produced by radially oriented (0 to 10 degrees) superior sources (20 to 25 mm). The SNR decreases by almost 50% for deeper (40 to 45 mm) radial sources. For tangential sources (80 to 90 degrees) the SNR in EEG is lower (around 2). EEG provides a higher sensitivity to deep sources than MEG. In contrast, MEG detects superior located spikes in tangentially oriented dipoles better than EEG. Furthermore the high SNR for tangential spikes in MEG is strongly dependent on the depth of the corresponding source which is why the

SNR decreases from 4 for upper sources (20 to 25 mm) to 1 for deeper sources (40 to 45 mm). Thus suggests that both MEG and EEG demonstrate weakness in sensitivity for deep tangential sources with SNR around 1 and 2 in MEG and EEG, respectively. In general we found the SNR of MEG and EEG in a comparable range between 1 and 4.5.
These results show the strength of MEG to detect tangentially oriented spikes. EEG shows advantages regarding spike detection from radially oriented sources. To take advantage of the strength of both modalities, it is advisable to combine MEG and EEG for clinical source localization. Since anatomical structures provide the entire range from radially to tangentially oriented as well as from superiorly to inferiorly located sources. To ensure the best detectability both modalities should be consulted.

Case-Based MEG-EEG Analysis of Interictal Epileptiform Transients (IET)

Fumisuke Matsuo, MD, Pegah Afra, MD, and Michael Funke, MD, PhD.
Neurology Department, University of Utah School of Medicine, Salt Lake City, UT, USA.

MEG and EEG: From Biophysics to Clinical Practice, an American Clinical Neurophysiology Society symposium (2009) helped to identify issues interfering with co-registration-analysis. This clinical case was initially examined for both MEG and EEG features. The protocol consisted of 3 phases; (1) identification by 2 independent reviews of first 50 IET, (2) joint review to define differences, and (3) modeling (reconciliation-synthesis) of potential epileptogenic foci.
Phase 1 yielded 64 IET (discordance of 14). Joint review (Phase 2) confirmed 36 IET with MEG-EEG agreement, 13 with minimal MEG correlates, and 9 with minimal EEG correlates. Last group included 5 MEG-IET with EEG-IET detected in a single basal derivation. Remaining 6 IET were judged without clinical relevance. Phase 3 involved a total of 94 IET (53 right- and 41 left-sided) after added sampling.
53 right-sided IET was fronto-temporal in EEG and frontal in MEG source location. 28 of 41 left-sided IET were basal fronto-temporal in EEG, and frontal in MEG, including 11 consisting of multiple peaks indicative of secondary sources. 13 left-sided IET were fronto-temporal in EEG, and frontal in MEG, associated with secondary sources over fronto-temporal regions.
We found that IET evaluation was complemented by use of co-registered MEG-EEG data. IET missed by independent review, were IET with unfavorable signal-to-background ratio but affected both EEG and MEG. EEG-IET waveforms were simpler, representing 3 generator locations, but failed to differentiate between frontal and temporal locations, while MEG indicated definite frontal sources. Complex MEG-IET suggested bi-directional propagation between distant sources; a feature that warrants further investigations in a larger number of clinical samples.

Pre-Surgical Mapping for Brain Tumor Patients: Initial experiences

Ajay Niranjan, MD, MBA; Erika Laing, MS; Anna Haridis, MPA, R.EEG/EP. T
UPMC- Brain Mapping Center, Pittsburgh, PA, USA

Considerable evidence supports that magnetoencephalography (MEG) can be a valuable noninvasive tool for presurgical mapping eloquent brain areas. In this study we present the UPMC Brain Mapping Center's initial experiences with presurgical brain mapping using MEG. Between September 2010 and Jan 2011, six patients (3 male) with malignant brain tumors (4 left lateralized) underwent presurgical mapping using MEG (whole-head 306 channel Neuromag® Vectorview System). Sensory (median nerve stimulation), motor (index finger lift), auditory, aurally-presented language, and visually-presented language paradigms were delivered using E-prime software or internally-driven Elekta software. Analysis was performed using the Neuromag Toolbox. Single dipoles were chosen to represent each identified average MEG peak, which were then projected on the coregistered MRI. The dipole selection was evaluated by examining the dipolar field configuration, the goodness-of-fit, and the confidence volume for each dipole. The results suggest that while somatosensory and auditory responses, found in all six patients, were robust and repeatable, motor and language localizations were more challenging. Motor activity was inconsistently localizable, found only in a subset of patients, but when identified the response bore a consistent localization pattern. However, the motor data showed a large degree of individual variability in the time course and an overall poor goodness-of-fit. Language localizations also exhibited a large degree of individual variability, but also depended on which pathway the paradigm targeted (visual or auditory). Areas thought of as Broca's and Wernicke's areas, and regions thought to be responsible for phonological and word-form processing, were all elicited in different patients and at different time points, but none consistently in all patients. Language processing is known to be accomplished by a vast inner-connected network of regions, and though it is uplifting that we have been able to view pieces of this network, much more work is required to enhance our ability to consistently map larger sections of this network and its pathways. Investigations into alternative paradigms and analysis techniques are ongoing for motor and language localizations. Overall, results presented here represent the successes and pitfalls of our initial experience with pre-surgical planning using MEG, as we optimistically move forward towards a robust presurgical mapping program.

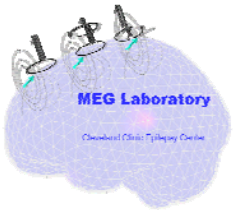
From the Clinic: Ramping up an MEG center from scratch: The Cleveland Clinics experience

Richard Burgess, M.D., Ph.D.
Department of Neurology, Cleveland Clinics, Cleveland, OH

Ramping Up a Clinical MEG Center from Scratch: Timelines, Challenges, and Results

Richard C. Burgess, MD, PhD

The Cleveland Clinic Epilepsy Center



Planning, Implementation, and Startup Considerations *

- Timeline
- Personnel
- Adaptations and Enhancements
- Clinical Results and Workflow

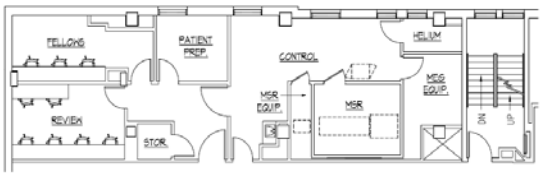
*Not including financial or remimbursement issues.

*Some considerations primarily applicable to Elekta Neuromag system.

Timeline --- Planning and Buildout

- May 2006
  - Architectural Conceptual Planning
- June – November 2006
  - Consultation with MEG and MSR vendor to refine site requirements
- September 2006
  - Final Site Drawings
- January 2007
  - Construction contract awarded
  - City permits submitted
- April 2007
  - Final equipment drawings and specifications from vendors
- April – September 2007
  - Construction and buildout
  - Site preparation

MEG Laboratory --- Layout



Timeline --- Installation, Cool-Down, Initial Training

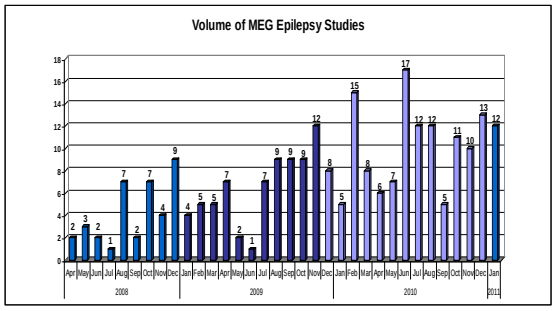
- October 2007
  - Magnetically shielded room installation
- December 2007
  - MEG equipment shipped and installed
  - Hardware connection
  - Cooldown
- January 2008
  - System administration and configuration
  - On-site system training

CCF MEG SUITE

Timeline ---
Clinical Testing, Overcoming Obstacles, Creating Efficiency

- February – April 2008
  - Volunteer testing
  - Contractor punchlist
  - Vendor punchlist
  - Software updates
  - Expand network connections
  - Bug correction
- April 2008
  - First clinical patients

CCF Epilepsy Center:
Gradual Increase in Volume of Clinical MEG Tests



Adapted from: Burgess RC, Comparison of MEG techniques for localizing and characterizing the epileptogenic focus: MEG Procedure at the Cleveland Clinic. American Clinical MEG Society Annual Meeting, San Diego, Febuary 4, 2010

Personnel

- Richard Burgess, MD, PhD: Clinical Neurophysiologist, Lab Director
- Andreas Alexopoulos, MD, MPH: Epileptologist
- John Mosher, PhD: MEG Scientist, Research Director
- Greg Wooledge: System Administrator
- Ping Liu: Software Engineer, Application Developer
- Anne-Sophie Dubarry: Engineer, Hardware & Software
- Shelly Simon, REEGT: MEG technologist
- Lourdes Colon, REEGT: MEG technologist
- Irene Wang, PhD: Post-doctoral research fellow
- Raghavan Gopalakrishnan: Research fellow
- Epilepsy Fellows: Part-time magnetoencephalographers & researchers

Personnel --- Percent Effort

- Richard Burgess, MD, PhD: Clinical Neurophysiologist, Lab Director 35%
- Andreas Alexopoulos, MD, MPH: Epileptologist 10%
- John Mosher, PhD: MEG Scientist, Research Director 100%
- Greg Wooledge: System Administrator 10%
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- Irene Wang, PhD: Post-doctoral research fellow 75%
- Raghavan Gopalakrishnan : Research fellow 75%
- Epilepsy Fellows: Part-time magnetoencephalographers & researchers ~%

Personnel --- Crucial Initial Functions

- Richard Burgess, MD, PhD: Clinical Neurophysiologist, Lab Director 35%
- Andreas Alexopoulos, MD, MPH: Epileptologist
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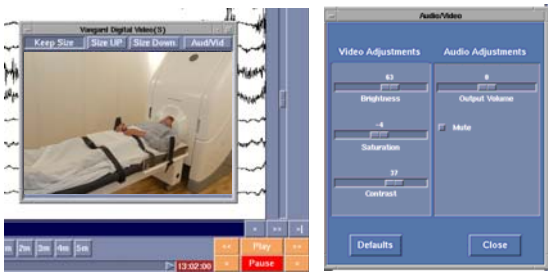
- Irene Wang, PhD: Post-doctoral research fellow
- Raghavan Gopalakrishnan: Research fellow
- Epilepsy Fellows: Part-time magnetoencephalographers & researchers ?

Adaptations and Enhancements --- Acquisition (1)

- Real-time simultaneous video-audio recording with frame-by-frame synchronization via NTP.
- Functional, high-voice-quality intercom, with output to AV recording, additional control desk mic for optional audio annotation.
- Real-time marker entry.
- On-line view of patient position.
- On-line, patient-customized SSP.
- Squiddler interface to facilitate selective sensor heating, all sensor heating, and resets without dropdowns.

Simultaneous, Time-locked Digital Video/Audio



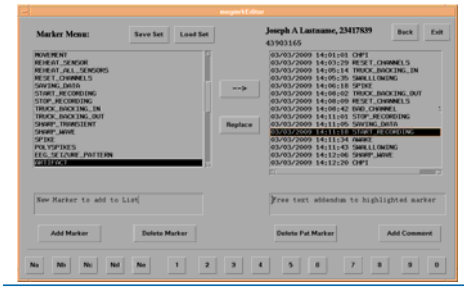
*Operator control of MPEG compression *Full-motion video, no dropped frames

On-Line Marker Entry

Marker entry program runs in real-time on the acquisition computer.

Provides precisely timed data tags.

Supplements the continuous video monitoring.



Adaptations and Enhancements --- Acquisition (1)

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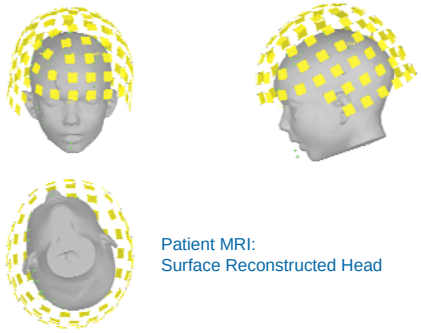
- Real-time marker entry.
- On-line view of patient position.
- On-line, patient-customized SSP.
- Squiddler interface to facilitate selective sensor heating, all sensor heating, and resets without dropdowns.

Alignment of Subject in MEG Array

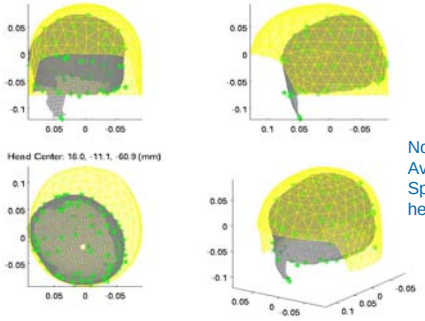
Generation of alignment image in real-time to insure good position



Patient MRI:
Surface Reconstructed Head

Alignment of Subject in MEG Array

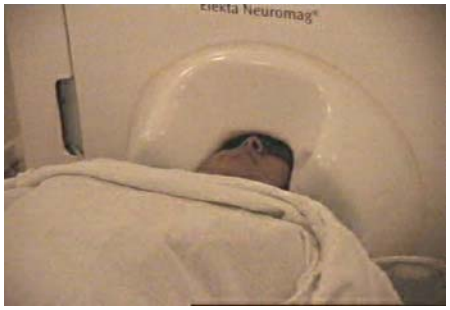
Generation of alignment image in real-time to insure good position



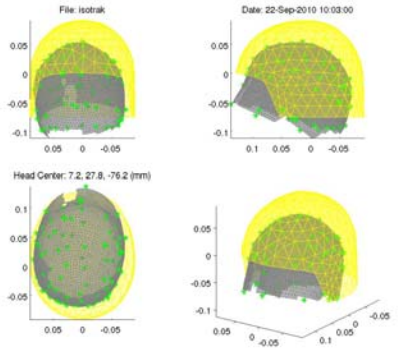
No MRI Available:
Spline fit head model

Patient with large head and copious hair

Is this patient in good position inside the MEG array?

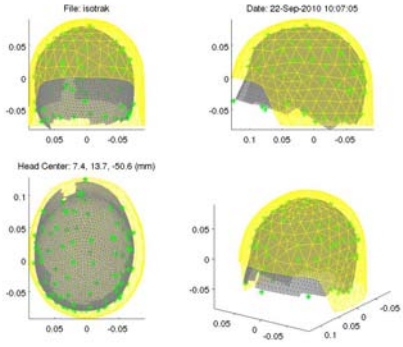


Initial position



rgess

After repositioning



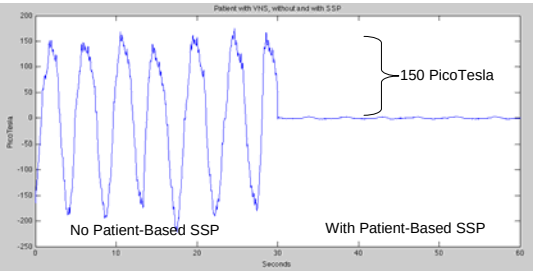
gess

Adaptations and Enhancements --- Acquisition (1)

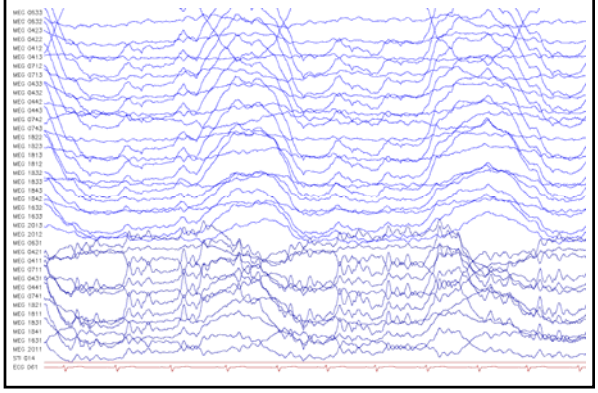
- Real-time simultaneous video-audio recording with frame-by-frame synchronization via NTP.
- Functional, high-voice-quality intercom, with output to AV recording, additional control desk mic for optional audio annotation.
- Real-time marker entry.
- On-line view of patient position.
- On-line, patient-customized SSP.
- Squiddler interface to facilitate selective sensor heating, all sensor heating, and resets without dropdowns.

Patient-Customized Real-Time Noise Rejection

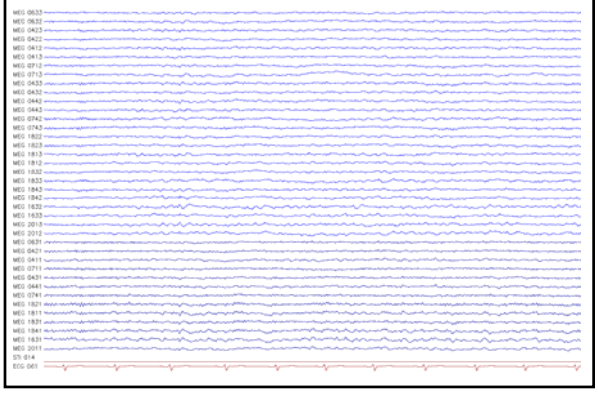
•Patient's VNS or other metal usually causes strong respiration artifact.
•At CCF, we generate a new "SSP" with patient in the array to allow easier real-time viewing of the data.



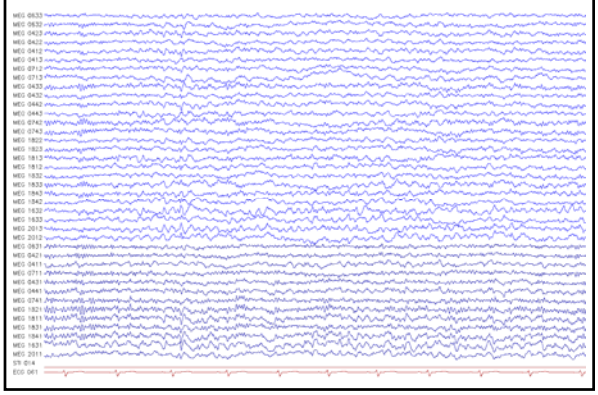
Live Display Using Standard, Empty Room SSP



Live Display Using Patient-Customized SSP
(same gain)



Live Display Using Patient-Customized SSP
(higher gain)



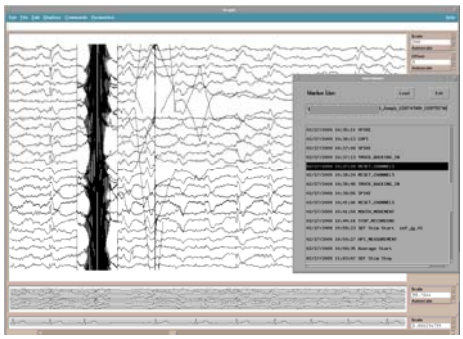
Adaptations and Enhancements --- Acquisition (2)

- Acquistion launch wrapper, a unifying application that starts the appropriate programs
  - Captures patient information
  - Manages database (e.g. patients returning for 2nd MEG)
  - Establishes patient-specific data directories and subfolders both locally and on the server
  - Writes files used by HPI preparation and other programs
  - Provides a systematic file naming convention
  - Launches patient marker file
  - Keeps track of associated files (e.g. empty room data)
  - Co-registers the outputs of separate applications (such as fif file and marker file timing)
  - Starts acquisition program
- Tuning tricks and other tweaks
  - Specialized daily tuning procedure

Adaptations and Enhancements --- Review (1)

- Markers
  - Acquisition-time markers review
  - Review-time marker entry
  - Synchronization of overall marker list to appropriate data file
  - Automatic marker navigation
- Review workstations
  - Multiple, infinitely expandable, networked workstations
  - Used for review, analysis, presentation, parallel processing
  - NFS, yellow pages, shells to insure access to the same data, setup files, and montages from every seat
  - Access to Radiology PACS, Hospital EMR, etc

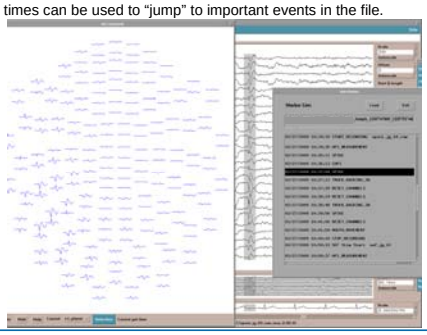
Acquisition-Time Markers Used for Navigation at Review-Time



Marker List Available at Review Time

Markers entered during acquisition are available to help navigate during review.

Marker times can be used to "jump" to important events in the file.



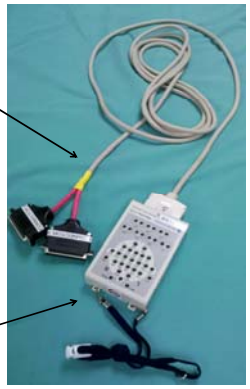
Adaptations and Enhancements --- Review (2)

- Integrated digital video review, especially important for ictal MEGs
- Review room projector for MEG rounds and research meetings
- Scheduling and results reporting system (EBase)

Adaptations and Enhancements --- System Architecture and Lab Workflow (1)

- Jackbox and cables:
  - Replace jackbox with standard EEG jackbox (NK)
    - Fabricate substitute cable for EEG and bipolar input
    - Facilitates standard electrode application and impedance testing
  - Fabricate special adaptor cables for 128 channel setups
    - Allows directly plugging high density or intracranial arrays into Neuromag system without jackbox
- Alternative stimulator:
  - Replace stock separate stimulators with integrated standard clinical neurophysiological device (Grass S88)
  - Allows more standard protocols
    - Permits recording of EEG simultaneous with MEG during SEFs
    - Permits alternating bilateral stimulation protocols
  - Optional pneumatic glove or airpuff tactile stimulator

Outpatient EEG Jackbox



Adaptations and Enhancements --- System Architecture and Lab Workflow (2)

- Outsmarting the automatic HPI digitization process
  - Modification to HPI measurement procedure to prevent errors (automatic but erroneous rotation, movement of the reference transmitter)
- Pressurized helium gas dewar filling procedure
- Data and file server
  - Conversion to patient-centric arrangement
  - File naming, folder organization, logical links
  - Security, backup, scalability
  - Default files and data field entries
  - Central administration (e.g. for printing)
- Workstation file maintenance
  - Log file rotation
  - Log file aging
  - Cleaning daemon

Clinical Results and Workflow

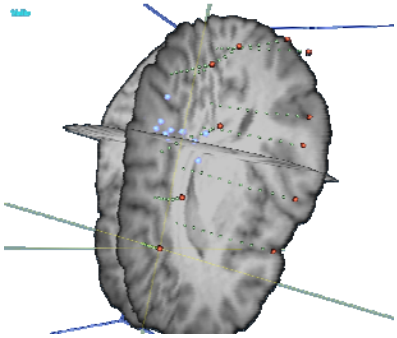
- Nine slots per week (8AM – 5 PM)
  - Outpatient MEG studies
  - Inpatient MEG studies
  - Research studies
- Stat / emergency MEGs[1]
- Fellowship training
  - Research fellows from outside (some self-funded)
  - Internal clinical and research fellows

([1] Burgess, Hantus, Cleary, Engle, Mosher, Alexopoulos. AES 2010, San Antonio TX)

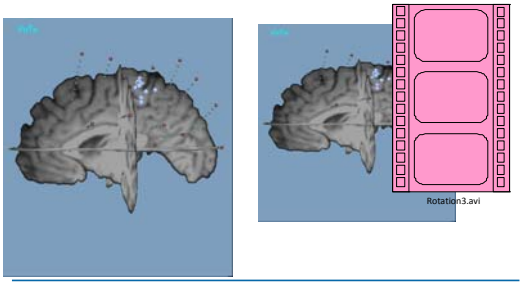
Illustrative Cases

- Utilize high volume of invasive cases at Cleveland Clinic
- Validation based on intra-cranial EEG
  - Stereo-EEG electrodes (typically 160 contacts)
  - Subdural electrodes (typically 300 contacts)
- Multimodality co-registration

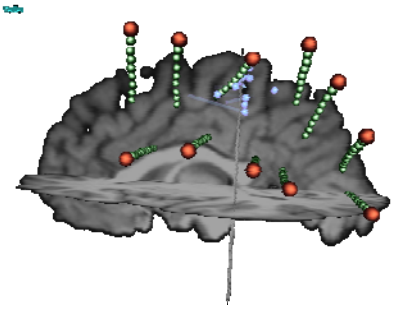
Comparison of MEG and ICEEG Localization



Display of Multimodality Data

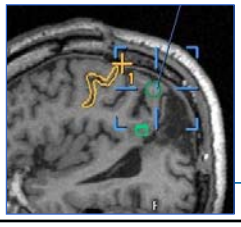


The MEG localization in this SEEG case suggests that activity must be coming from between the H and M electrodes.

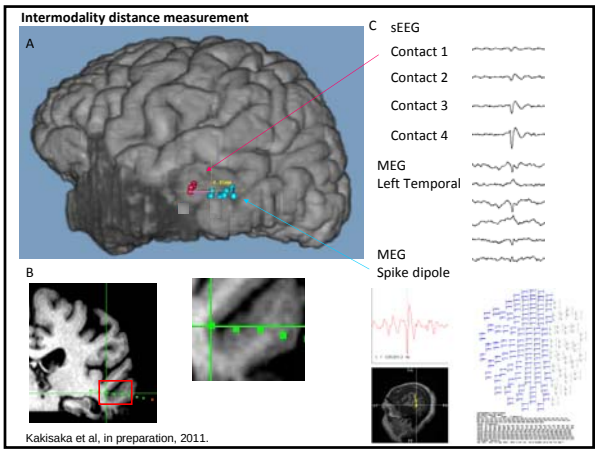


Spatial Relationship Questions

- For intraoperative neuronavigation or radiosurgery, how reliable and accurate are MEG localization results?
- Regarding sources identified by MEG, "how far are is this source from the activity picked up on SPECT or SEEG or other modalities?"

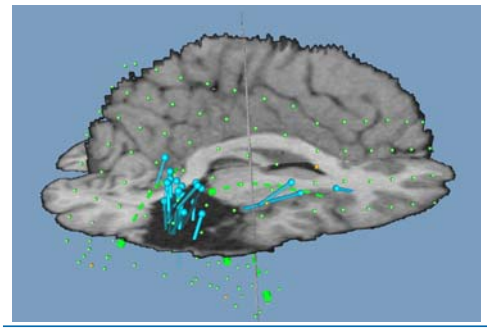


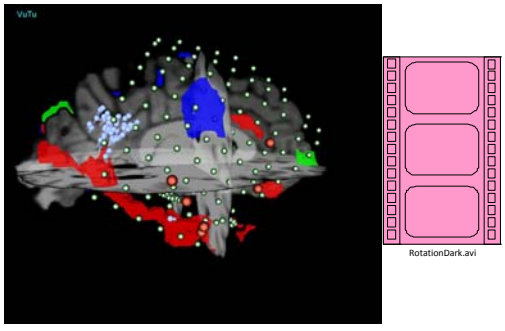
Fahlbusch, Nimsky, Ganslandt, Romstöck
2004, Clinic of Neurosurgery, Erlangen



Viewing Spatial Relationships

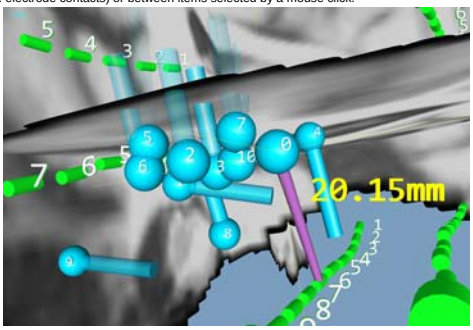
We have developed a multi-modality data coregistration and viewing program.





Determining Spatial Relationships

Users can request automated measurements (i.e. euclidean distance) between named items (e.g. electrode contacts) or between items selected by a mouse click.



Magnetic Source Imaging in Non-Lesional Neocortical Partial Epilepsy: Additional Value and Comparison with ICEEG

Felix Schneider, MD

Methods

- **All patients in the MEG database from February 2008 to July 2010 were reviewed**
- **Patients meeting inclusion criteria as following were extracted:**
  - **(1) diagnosis of medically refractory neocortical epilepsy**
  - **(2) MRI-negative**
  - **(3) resective epilepsy surgery was performed with a postoperative follow-up of at least 6 months**
  - **(2) Underwent ICEEG before surgery**
- **Of 178 patients 18 were enrolled in the study**

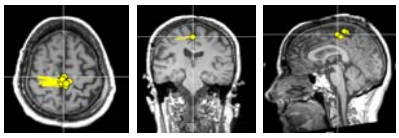


Fig 1: Preoperative sublobar MEG superimposed to the postoperative MRI; Excision superior frontal gyrus, MEG focus completely resected; Seizure-free outcome.

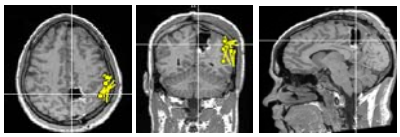


Fig 2: Preoperative multilobar MEG superimposed to the postoperative MRI; Excision superior parietal lobule, MEG focus not resected; Non seizure-free outcome.

Results

	ICEEG	MSI	ICEEG + MSI
Sublobar (concordant)	15 (83.3%)	11 (61.1%)	9 (50%)
Sublobar (concordant) + completely resected	15	9	9
Class 1 outcome (sublobar localizing group)	10 / 15 (66.6%)	8 / 11 (72.7%)	8 / 9 (88.9%)
Class 1 outcome (not sublobar localizing group)	1 / 3 (33.3%)	3 / 7 (42.9%)	3 / 9 (33.3%)
P - value * (Spearman correlation)	0.751	**0.007**	**0.014**

* focus completely resected or sublobar concordant results and complete focus resection / outcome

Main Findings

- **Clinical relevance:**

→ Combination of MSI and ICEEG increases the accuracy of localizing the EZ

→ Sublobar concordance of ICEEG and MSI results has the highest specificity, PPV and OR for exact localization of the EZ based on seizure-freedom after epilepsy surgery, compared with any single test alone.

→ Complete resection of both foci is significantly correlated with a favorable surgical outcome (p = 0.014).

Main Findings

→ Complete ICEEG focus resection is still considered as the most important predictor for a favorable surgical outcome (Kim DW et al. 2010; Stefan H et al. 2000)

→ ICEEG alone inferior compared to combined ICEEG and MSI findings (66.7% compared to 88.9% seizure-free rate)

Case Example: K S
MRI-Negative, Questionable Extended Source Left Parieto-Temporal

History

- 11 year old male
- Right-handed
- Onset: 2 years of age
- Episodes began after an ear infection (during which he was afebrile).
- Characterized as paroxysmal shrugging and wriggling around which were not initially recognized as seizures.
- Two days later he had his first generalized convulsion (also afebrile at this time).

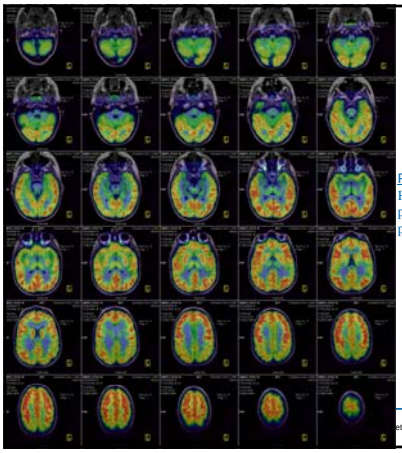
MRI

- 2000: Normal
- 2004: Normal
- 2006: Normal

Seizure description at time of referral

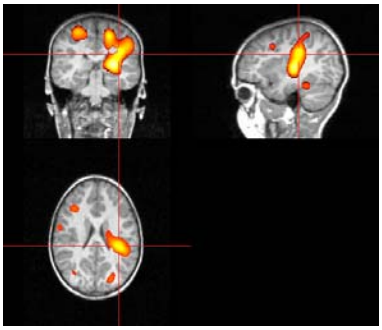
- Seizure type #1: Auditory Aura → Bilateral asymmetric tonic seizure → Complex motor seizure
- Aura: buzzing noise in his ears prior to his seizures.
- Motor: diffuse stiffening of body, with spreading of legs & arms, followed by thrashing movements of the arms and legs, L>R
- Seizure frequency: mainly nocturnal, typically 3-5 times/week, lasting 20-30 seconds

- Seizure type #2: Generalized tonic clonic motor seizure
- Motor: sometimes bites his tongue, head turns to one side (L or R?)
- Seizure frequency: 3 times per week, started more than a year ago.



PET: 04/07/06
Hypometabolism involving left posterior insular and adjacent parietal regions.

SPECT SISCOM z=1.5



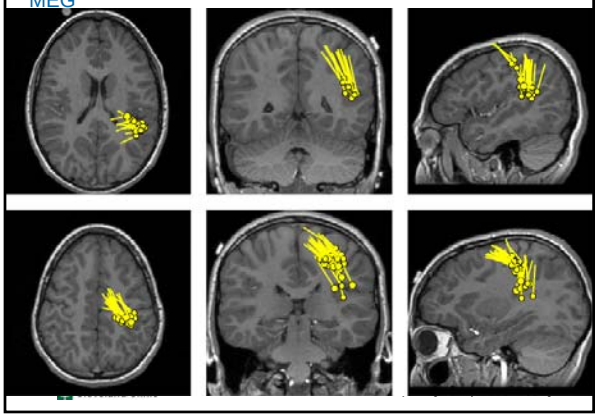
Limitation of SPECT

- Poor time resolution
- Cannot show which region initiated the epileptic discharge
- Subjective thresholding
  - Used z=1.5 in this case, instead of 2.0
  - Hot areas lit up by this threshold imply connectivity

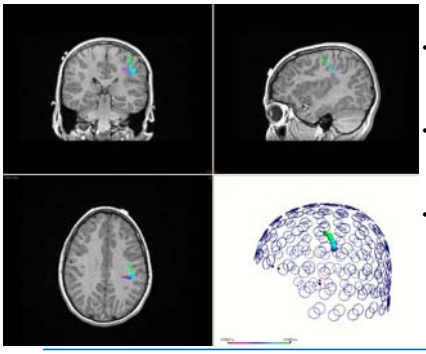
Propagation Question

- Ictal Spect shows regions possibly connected (hourglass).
- Can the MEG demonstrate connected regions, or two separate epileptic regions?

MEG



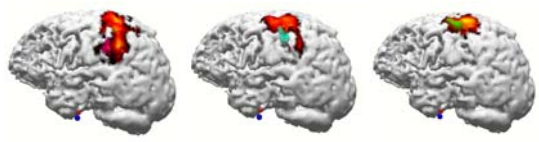
MEG – Sequential Dipole Analysis



- MEG showed consistent propagation pattern of interictal spikes.
- Interictal spikes started from the left parieto-temporal region;
- Then quickly propagated to the primary and supplementary motor cortex.

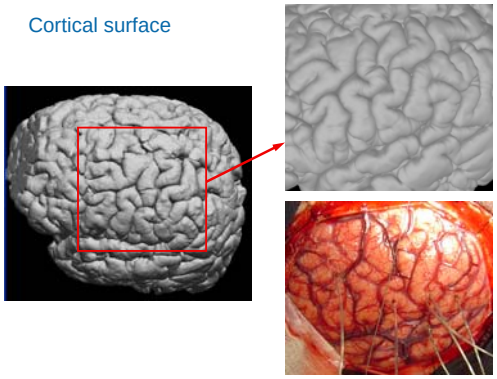
MEG Propagation Modeling

- The MEG sequential dipole analysis showed the involvement of both of these two areas
- Moreover, it showed the propagation from one to the other



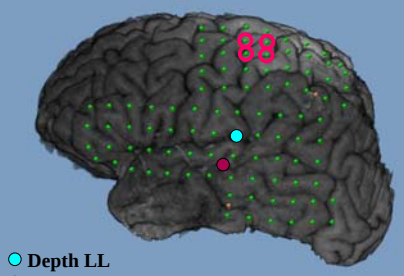
5ms 15ms 25ms

Cortical surface



Results of invasive recordings

- MEG sequential analysis fit with the triggering area and seizure spread demonstrated on the invasive recordings

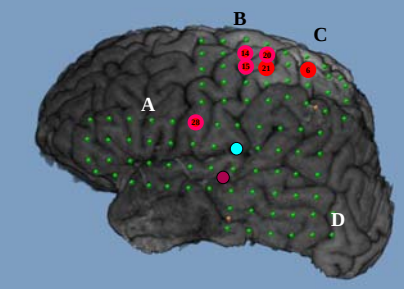


Depth LL
Depth LIL

Interictal discharges

→LIL3-6, LL3-6

B14,15, 20,21



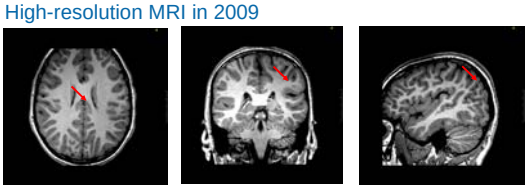
LL
LIL 3-6

Ictal onset

→Sz1P-4P B14,15,20,21 + A28+ sC6

→Sz 5P-6P LIL 3-6

High-resolution MRI in 2009

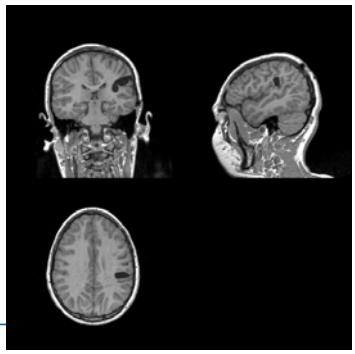


Upon further review:

- There is an abnormality in the gray white borders in the left supramarginal gyrus, with increased cortical and subcortical T2 and FLAIR signal intensity and decreased subcortical T1 signal intensity. There is no mass effect.
- This finding is most consistent with a small malformation of cortical development.

Patient Treatment

- Limited resection of the parietal operculum and posterior insula
- Seizure free 1 year post op



Cleveland Clinic

MEG Results

Number of spontaneous MEGs	211
Number of patients	205
Dates of study	7/2008 – 11/2010
Pediatric cases (age < 20)	81
No. of children accompanied into MSR by parents	6
No. of MEGs recorded with simultaneous scalp EEG	202
No. of MEGs recorded with simultaneous ICEEG	9
VNS (2 had only electrodes after removal of can)	38
Braces, permanent metallic bridge, or large fillings	28
Implanted Devices, including: pacemakers intracranial clips or plates SEEG electrodes depth and subdural electrodes	27 3 10 7 2
No. uninterpretable or aborted for technical reasons	2
Nl MEG (i.e. no epileptiform discharges recorded)	62
MEG studies during which seizures were recorded	18
MEG very helpful	83

MEG Clinical Utility

Category	Previous Video-EEG	EEG Simultaneous w/MEG*	MEG	No. of MEGS
A	Nl or non-localizable	Nl or non-localizable	Non-localizing	56
B	Nl or non-localizable	Nl or non-localizable	Localizing	32
C	Nl or non-localizable	Abnormal	Non-localizing	0
D	Nl or non-localizable	Abnormal	Localizing	5
E	Poorly localizing	Nl or non-localizable	Non-localizing	25
F	Poorly localizing	Nl or non-localizable	Localizing	52
G	Poorly localizing	Abnormal	Non-localizing	0
H	Poorly localizing	Abnormal	Localizing	17
I	Localized		Non-localizing	0
J	Localized		Nothing new	6

Non-localizable EEG = generalized, or obscured
Poorly localizing EEG = only lateralized, or bilateral focii, or multiple focii
Non-localizing MEG = normal, or too few spikes, or multi-focal
* ICEEG cases excluded

Why use MEG for language mapping?

Jeffrey Lewine, Ph.D.
MIND Research Network, Albuquerque, NM

Jeffrey Lewine

NOTES

NOTES

Language mapping using MEG: Practical considerations

Eduardo Castillo, Ph.D.
University of Texas Medical School, Houston, TX

Eduardo Castillo

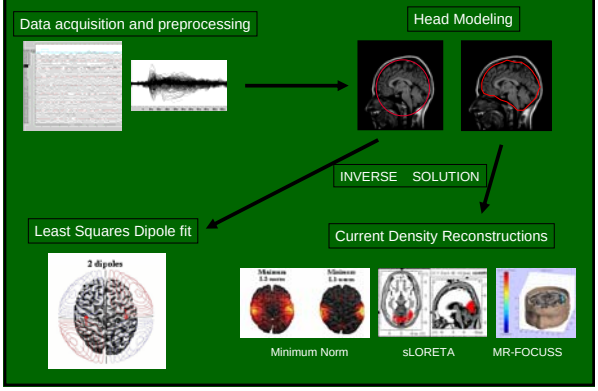
Language mapping using MEG: practical considerations

Eduardo M Castillo, PhD
MEG-Lab University of Texas-Houston

Clinical areas of interest:

- Language laterality.
- Localization of language-specific cortex.
- Dissociating linguistic operations.

Activation task, modeling approach and ROIs...



Activation tasks:

-Continuous recognition of Words

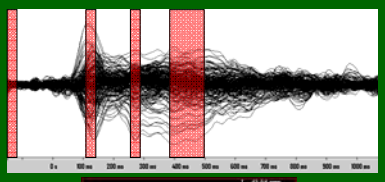
-Auditory and visual version of the same task.

- Always a replication.

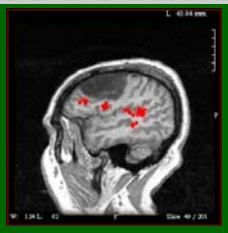
- Visual trigger: use a photo diode to ensure accurate time-locking.

MEG: Averaged Waveform

(Task: word recognition)

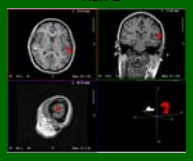


Magnetic Source Imaging

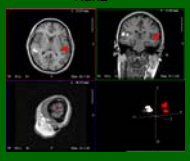


Automatic Clustering (time and space!)

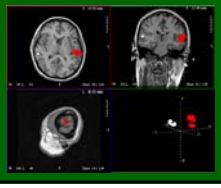
Run 1



Run2



Replicated (time and space) maps

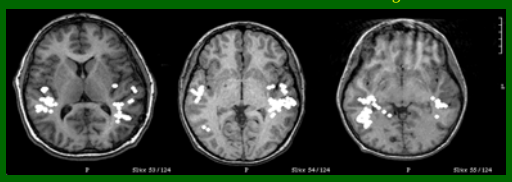


Classification of patients as bilaterally, left or right dominant for receptive language

MEG Laterality index as follows:

$$\frac{(\#\text{ of perisylvian ECDs in RH} - (\#\text{ of perisylvian ECDs in LH})}{(\#\text{ of perisylvian ECDs in RH}) + (\#\text{ of perisylvian ECDs in LH})}$$

Bilateral Left Right



Patient 1 (24 yrs) Patient 2 (15 yrs): Patient 3 (34 yrs):

Can we tell language laterality?

Wada Vs MEG (N = 84) **WADA**

		Left	Bilateral	Right
MEG	Left	56	2	0
	Bilateral	7	15	1
	Right	0	1	2

a) High degree of concordance between the two methods.

b) We currently use the procedure routinely as an adjunct to intra- and extraoperative language mapping in planning surgical resection for both adults and children.

* In our center we have consistently used the Wada procedure described by Loring et al., 1990

Papanicolaou et al., 2004. Journal of Neurosurgery, May;100 (5):867-76.

Exclusion criteria (Papanicolaou et al, 2004)

a) **N1 asymmetry**: Absence of N1. No ECDs (r > .9) in at least one hemisphere.
b) **Signal to noise ratio**: noise > 3/4 signal.
c) **Baseline**: Presence of ECDs (r>.9) in one hemisphere Vs the other in a ratio of 1 to 5 or higher (with more than 10 in one hemisphere*) in the 150 ms baseline.
d) **Combined criteria**: Noise > 2/3 signal and either…
   - N1 asymmetry (RMS) higher than 1/2.
   - N1 asymmetry (Latency) higher than 20 msecs.
   - Baseline asymmetry: hemispheric rate of ECDs (r>.9) is 1 to 2 or greater (with more than 10 dipoles in one hemisphere*).

* sample/rate 250 Hz

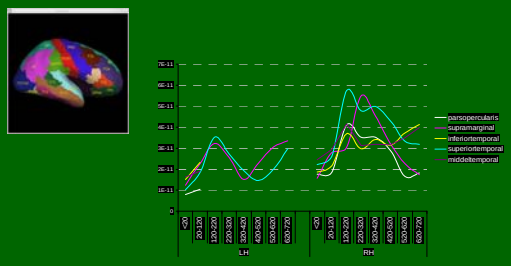
Replication using ECDs

- Epilepsia. 2009 Oct;50(10):2242-8. Epub 2009 Aug 7.
- **Lateralizing language with magnetic source imaging: validation based on the Wada test.**
- Doss RC, Zhang W, Risse GL, Dickens DL.
- Minnesota Epilepsy Group, P.A., St Paul, Minnesota 55102, USA. rdoss@mnepilepsy.net

- PURPOSE: Magnetoencephalography (MEG)/magnetic source imaging (MSI) is a noninvasive functional neuroimaging procedure used to localize language-specific regions in the brain. The Wada test, or intracarotid amobarbital procedure (IAP), is the gold standard in determining speech/language lateralization for presurgical planning, although it is invasive and associated with morbidity. The purpose of this study is to provide further validation on the use of MSI for presurgical language lateralization by comparing results against the IAP. METHODS: The sample consisted of 35 patients with epilepsy and/or brain tumor undergoing presurgical evaluation at the Minnesota Epilepsy Group. All patients received both an IAP and MSI to determine hemispheric language dominance. For MSI, a 148-channel MEG system was used to record activation of language-specific cortex by an auditory word-recognition task. RESULTS: The MSI and IAP were concordant in determining language in the hemisphere to be treated in 86% of the cases with sensitivity and specificity values of 80% and 100%, respectively. CONCLUSIONS: The results from this study are consistent with prior research findings comparing functional neuroimaging procedures to the IAP in determining language lateralization in presurgical patients. The current study provides an important replication and support for Papanicolaou et al.'s findings in 2004 using a consecutive clinical sample from a different institution. An unusually high rate of atypical IAP language cases in this sample and differences between the two procedures are believed to explain the noted discrepancies. MSI is a viable noninvasive alternative to the IAP in the presurgical determination of language lateralization.

MRI data reconstruction: FREESURFER

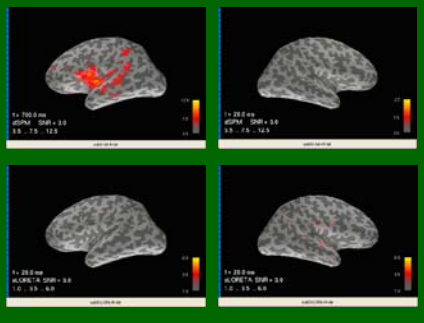
Auto Parcellation



Analysis procedures: distributed sources (MNE tool)

dSPM

sLORETA

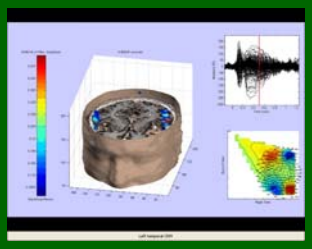


Task: Oral word comprehension.

MR-Focus…

- Epilepsy Behav. 2005 Mar;6(2):235-41.
- **Language laterality determined by MEG mapping with MR-FOCUSS.**
- Bowyer SM, Moran JE, Weiland BJ, Mason KM, Greenwald ML, Smith BJ, Barkley GL, Tepley N.
- Department of Neurology, Henry Ford Health System, Detroit, MI 48202, USA. drsusan@umich.edu
- Magnetoencephalography recordings were made on 27 patients with localization related epilepsy during two different language tasks involving semantic and phonological processing (verb generation and picture naming). These patients underwent the semi-invasive intracarotid amobarbital procedure (IAP), also referred to as the Wada test, to determine the language-dominant hemisphere. Magnetoencephalography (MEG) data were analyzed by MR-FOCUSS, a current density imaging technique. A laterality index (LI) was calculated from this solution to determine which hemisphere had more neural activation during these language tasks. The LIs for three separate latencies, within each language task, were calculated to determine the latency that correlated best with each patient's IAP result. The LI for all language processing was calculated for the interval 150-550 ms, the second LI was calculated for the interval 230-290 ms (Wernicke's activation), and the third LI was calculated for the interval 396-460 ms (Broca's activation). In 23 of 24 epilepsy patients with a successful IAP, the LIs for Broca's activation, during the picture naming task, were in agreement with the results of the IAP (96% agreement). One of three patients who had an undetermined or bilateral IAP had an LI calculated for Broca's activation (396-460 ms) that agreed with intracranial mapping and clinical testing. These results indicate an 89% agreement rate (24 of 27) for magnetoencephalographic LI determination of the hemisphere of language dominance.

Analysis procedures: current density (MR-Focuss)



Task: Oral word comprehension.

Laterality based on time-frequency analysis…

- Neuroimage. 2008 Oct 1;42(4):1499-507. Epub 2008 Jun 13.
- **Language lateralization using MEG beta frequency desynchronization during auditory oddball stimulation with one-syllable words.**
- Kim JS, Chung CK.
- MEG Center, Department of Neurosurgery, Seoul National University College of Medicine, Republic of Korea.
- Some patients with epilepsy have difficulty performing complex language tasks due to the long duration of the disease and cognitive side effects of antiepileptic drugs. Therefore, a simple passive paradigm would be useful for determining the language dominance lateralization in epilepsy patients. The goal of this study was to develop an efficient and non-invasive analysis method for determining language dominance in epilepsy patients. To this end, magnetoencephalography was performed while an auditory stimulus sequence comprised of two one-syllable spoken words was presented to 17 subjects in an oddball paradigm without subject response. The time-frequency difference between deviant and standard sounds was then analyzed in the source space using a spatial filtering method that was based on minimum-norm estimation. The laterality index was estimated in language-related regions of interest (ROI). The results were compared to the traditional lateralization method using the Wada test. Beta band oscillation activity decreased during deviant stimulation, and the lateralization of the decrease was in good agreement with the Wada test, in the posterior part of the inferior frontal gyrus in 94% of the subjects and in the posterior part of the superior temporal gyrus in 71% of the subjects. In conclusion, the ROI-based time-frequency difference between deviant and standard sounds can be used to assess language lateralization in accordance with the Wada test.

What ROI to use?....

- Epilepsia. 2009 Oct;50(10):2256-66. Epub 2009 Jun 22.
- **Distributed source modeling of language with magnetoencephalography: application to patients with intractable epilepsy.**
- McDonald CR, Thesen T, Hagler DJ Jr, Carlson C, Devinsky O, Kuzniecky R, Barr W, Gharapetian L, Trongnetrpunya A, Dale AM, Halgren E.
- Department of Psychiatry, University of California, San Diego, California, USA. camcdonald@ucsd.edu

- PURPOSE: To examine distributed patterns of language processing in healthy controls and patients with epilepsy using magnetoencephalography (MEG), and to evaluate the concordance between laterality of distributed MEG sources and language laterality as determined by the intracarotid amobarbital procedure (IAP).

- METHODS: MEG was performed in 10 healthy controls using an anatomically constrained, noise-normalized distributed source solution (dynamic statistical parametric map, dSPM). Distributed source modeling of language was then applied to eight patients with intractable epilepsy. Average source strengths within temporoparietal and frontal lobe regions of interest (ROIs) were calculated, and the laterality of activity within ROIs during discrete time windows was compared to results from the IAP.

- RESULTS: In healthy controls, dSPM revealed activity in visual cortex bilaterally from approximately 80 to 120 ms in response to novel words and sensory control stimuli (i.e., false fonts). Activity then spread to fusiform cortex approximately 160-200 ms, and was dominated by left hemisphere activity in response to novel words. From approximately 240 to 450 ms, novel words produced activity that was left-lateralized in frontal and temporal lobe regions, including anterior and inferior temporal, temporal pole, and pars opercularis, as well as bilaterally in posterior superior temporal cortex. Analysis of patient data with dSPM demonstrated that from 350 to 450 ms, laterality of temporoparietal sources agreed with the IAP 75% of the time, whereas laterality of frontal MEG sources agreed with the IAP in all eight patients.

Laterality based on event-related desynchronization…

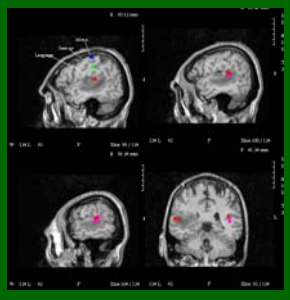
- J Neurosurg. 2009 Aug 14.
- **Language dominance and mapping based on neuromagnetic oscillatory changes: comparison with invasive procedures.**
- Hirata M, Goto T, Barnes G, Umekawa Y, Yanagisawa T, Kato A, Oshino S, Kishima H, Hashimoto N, Saitoh Y, Tani N, Yorifuji S, Yoshimine T.
- Department of Neurosurgery, Osaka University Medical School;
- Methods A statistical group analysis of 14 healthy volunteers was conducted to establish a normal control. Language dominance and localization were then evaluated in a larger population of 123 consecutive patients. Study participants were instructed to silently read 100 visually presented words. Using SAM, the spatial distribution of the oscillatory changes was obtained as the Student t statistic by comparing the current density for each voxel between 1 second before and 1 second after each word presentation. Group analyses of the healthy volunteers were performed using statistical nonparametric mapping. Language dominance in the patients was determined according to the laterality index (LI) calculated using peak t values of the left and right frontal desynchronizations. Language dominance was prospectively assessed, and the results were compared with those of the Wada test (63 patients). Language localization results were quantitatively compared with those of stimulation mapping (17 patients). Results Group analysis of the healthy volunteers indicated beta to low gamma band desynchronization in the left frontal area and alpha to beta desynchronization in the left parietotemporal areas. In patients, the frontal language areas were detected in 119 persons (95.9%). Lateralization of beta or low gamma desynchronization in the inferior or middle frontal gyri corresponded well with language dominance. The introduction of the LI resulted in a quantitative evaluation of language dominance, whose results were concordant with those of the Wada test in 51 (85.0%) of 60 cases. The distance between the estimated frontal language areas and stimulation-positive sites was 6.0 +/- 7.1 mm (mean +/- SD). Conclusions This study is the first in which magnetoencephalography (MEG) was used to determine language dominance in a large population, and the results were compared with those of the Wada test. Moreover, language localization results obtained using MEG were compared with those obtained by invasive mapping. The authors' method, which is based on neuromagnetic oscillatory changes, is a new approach for noninvasively evaluating the frontal language areas, a location that has been problematic using MEG dipole methods. Synthetic aperture magnetometry is a noninvasive alternative to Wada testing for language dominance and helps to determine stimulation sites for invasive mapping.

Study 2: Localization of language-specific cortex (N= 47)

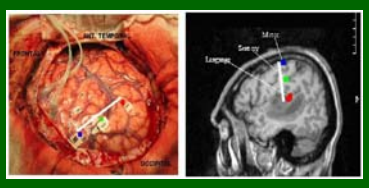
- 47 patients (21 female/26 male). Age 17 to 56 years
  - Intraoperative (14 cases)
  - Extraoperative (33 cases)
- Indication for surgery
  - Epilepsy (31 cases)
  - Tumor (16 cases)
- Wada (available in 27 patients)
  - Language dominance: 37 left/ 6 bilateral/ 4 right
- Area to be operated
  - 38 temporal lobe (32 left, 6 right)
  - 6 frontal (5 left, 1 right)
  - 3 parietal (3 left)

Optimal presurgical and postsurgical profiles…

Before surgery

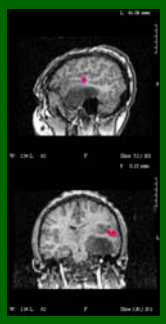


During surgery…

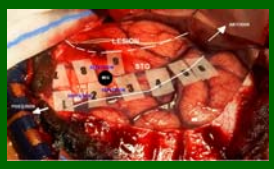


Postsurgery

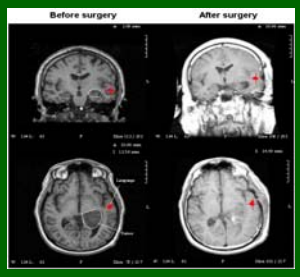
29 y old male



- Intraoperative mapping
- Brain tumor
- Normal language pre- and postop
- Left dominance for language (Wada)



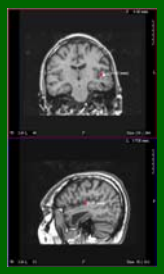
Language mapping and the surgical plan (tumor)



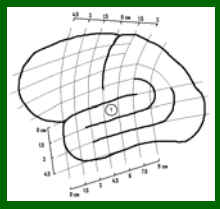
-Male patient, 27 years old
-Left Hemisphere tumor
-Postsurgical outcome without linguistic change.

Localization of MEG-derived language sites

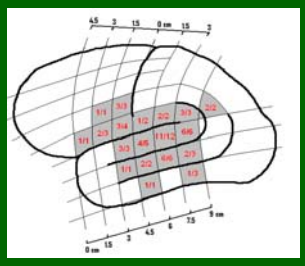
Individual profile



Drawing of MEG-derived localization



Results



Figure; *results in our 47 cases where 63 areas defined by MEG were tested with a sensitivity of 85%. For each quadrant the ratio of positive MEG sites verified by ECS.*

Predictions of MEG and ECS Vs language outcome (naming).

N= 14	Language-related sites found (EFFICIENCY)		Language related sites removed ?		Expected outcome (naming)		Real Outcome (naming)	Prediction accuracy	
	CSM	MEG	CSM	MEG	CSM	MEG		CSM	MEG
1	YES	YES	NO	NO	NORMAL	NORMAL	NORMAL	CORRECT	CORRECT
2	YES	YES	YES	NO	DEFICIT	NORMAL	NORMAL	INCORRECT	CORRECT
3	YES	YES	YES	YES	DEFICIT	DEFICIT	DEFICIT	CORRECT	CORRECT
4	YES	YES	NO	YES	NORMAL	DEFICIT	NORMAL	CORRECT	INCORRECT
5	NO	YES	----	NO	----------	NORMAL	DEFICIT	----------	INCORRECT
6	YES	YES	YES	YES	DEFICIT	DEFICIT	DEFICIT	CORRECT	CORRECT
7	YES	YES	YES	YES	DEFICIT	DEFICIT	DEFICIT	CORRECT	CORRECT
8	NO	YES	----	YES	----------	DEFICIT	DEFICIT	----------	CORRECT
9	YES	YES	NO	YES	NORMAL	DEFICIT	DEFICIT	INCORRECT	CORRECT
10	YES	YES	YES	YES	DEFICIT	DEFICIT	DEFICIT	CORRECT	CORRECT
11	YES	YES	NO	YES	NORMAL	DEFICIT	DEFICIT	INCORRECT	CORRECT
12	YES	YES	NO	NO	NORMAL	NORMAL	NORMAL	CORRECT	CORRECT
13	YES	YES	NO	NO	NORMAL	NORMAL	NORMAL	CORRECT	CORRECT
14	YES	YES	NO	YES	NORMAL	DEFICIT	NORMAL	CORRECT	INCORRECT
TOTAL	12/14	14/14			7 CASES AGREEMENT= 7 CASES CORRECT PREDICTIONS (100%)			9/12 = 75%	11/14= 78%

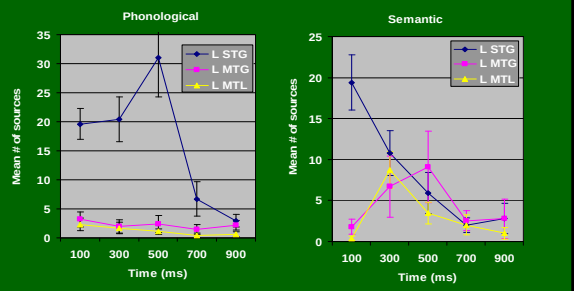
Table 1: *Prediction accuracy for ECS and MEG estimates to estimate postsurgical naming deficits in 14 patients based on linguistic performance and the removal/sparing of language-specific cortex as defined by these two techniques.*

Total agreement of MEG and ECS was achieved in 7 cases and the consensus decision was correct in all the cases (in yellow).

The independent predictive value (ECS and MEG) was 75% and 78% respectively.

Castillo et al., 2005. Epilepsia.46 (s8): 324.

Dissociation of linguistic operations…



- Thank you!

What to look for in a language study

Susan Bowyer, Ph.D.
Henry Ford Hospital, Detroit, MI

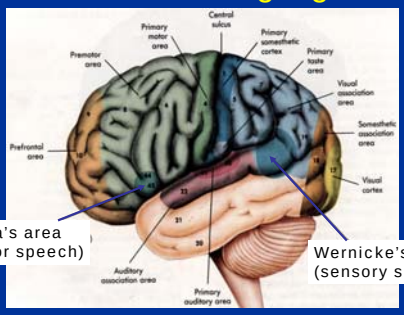
What to look for in a Language study?

Susan M. Bowyer, PhD
Biomedical Physicist

Neuromagnetism Lab
Henry Ford Hospital

www.megimaging.com

Localization of Language Areas



Objective: non-invasively localize functional language areas

ACMEG Guidelines

- Linguistic stimuli presented acoustically or visually result in language-related responses (late responses) in addition to primary auditory and visual responses (early responses)
- Laterality of the language areas, as measured by MEG, have been found to correlate between 80-95% with results from the Wada procedure and intracranial recordings.
- LEF studies of receptive language (comprehension) localize sources to the posterior aspects of the superior and middle temporal lobe and the temporoparietal junction
- LEF studies of expressive language (speech production) localize activity in frontal and basal temporal areas.
- The primary clinical application of LEFs is to determine the language-dominant hemisphere.
- The results from a multitude of studies show that MEG LEF studies are able to replace the language portion of the invasive Wada procedure

ACMEG Guidelines

- **Stimulation**
- ***Auditory presentation:*** Single word auditory stimuli are most commonly used, with fixed or random inter-stimulus-intervals, typically greater than 2 seconds. Stimuli are typically presented at normal listening levels (~60 dB above normal hearing levels) and subjects may be asked to either listen passively to the words, or to covertly (silently) think of an action word that goes with the word.
- ***Visual presentation:*** Visually presented words may also be used. Subjects can be asked to either read the words, or they can be asked to read the word and think of an action word that goes with the word.
- ***State variables:*** The subject must be awake and able to concentrate on the task. Distracters can be used to monitor wakefulness as well as alpha activity.

Language Tasks

Picture naming

Verb Generation

Book

Identical tasks used during intracranial mapping

Auditory stimuli

Initial Inspection of Early latency

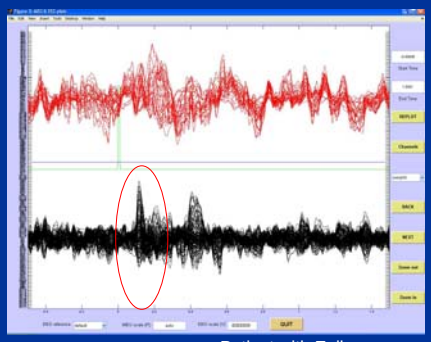
- Evoked LEF waveform will have several peaks
- Initial peaks (<150 ms) basic sensory processing
- It is important to evaluate the integrity of basic auditory/visual
- Early evoked fields can be used for quality control
  - Is the response clear (above the noise) and symmetrical
  - Is latency ~100 ms
  - Is location auditory cortex if stimuli are sounds
  - Is location visual cortex if stimuli are images

Verb Generation Task

EEG

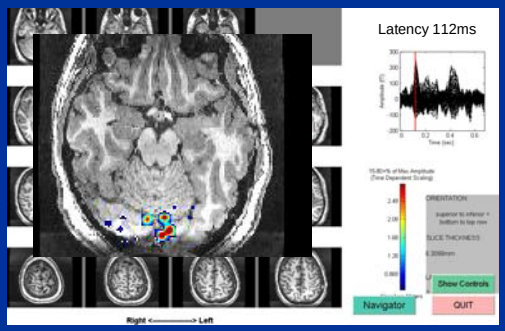
Trigger

MEG



Patient with Epilepsy

Visual peak



Initial Inspection of Long latency

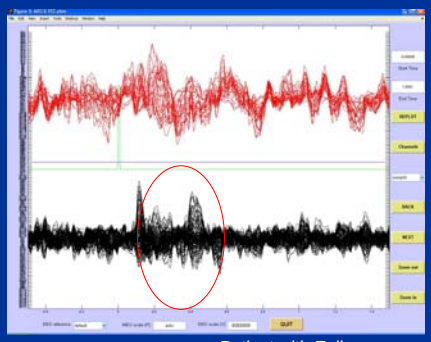
- Long latency responses (> 200 ms after stimuli onset) evoked by language stimulation
- Peaks will not be as clear or symmetrical as the early latencies as the Long latency contains activity arising from multiple language areas, independent of the method of stimulation, auditory or visual
- When subjects attend to the task the responses in the MEG waveform may become clearer
- The signals reflect varying contributions from multiple language areas including:
  - Wernicke's language area (superior temporal gyrus Brodmann's area (BA 22), the angular gyrus (BA 39), the supramarginal gyrus (BA 40)
  - Broca's language area (pars opercularis and pars triangularis of the inferior frontal gyrus (BA 44 and 45).
- Different tasks change which source regions dominate the evoked responses
- Regardless of the modality of stimulation and subtle details of the stimulation paradigms, linguistic stimuli evoke a large, typically lateralized, response which normally peaks between 400-500 ms
- The activity may begin as early as 250 ms and may extend to 750 ms or beyond

Verb Generation Task

EEG

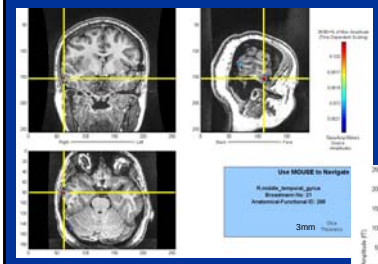
Trigger

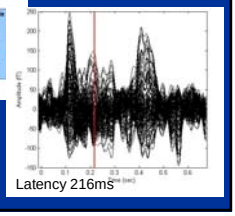
MEG



Patient with Epilepsy

Wernicke's activation peak

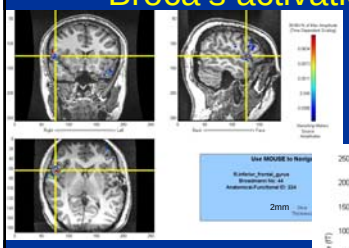


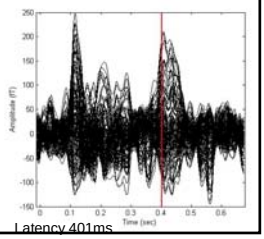


Laterality index = -17
Left lateralized

Latency 216ms

Broca's activation peak

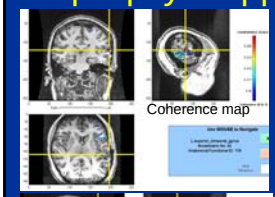




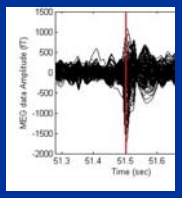
Laterality index = -32
Left lateralized

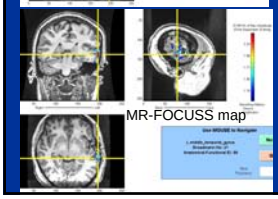
Latency 401ms

Epilepsy mapping

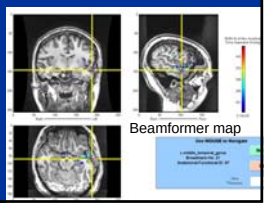


Coherence map





MR-FOCUSS map



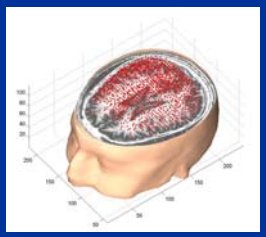
Beamformer map

MR-FOCUSS

- A non-linear current distribution imaging technique
- Images extended and compact sources of simultaneous neuronal activity.
- Incorporate a wavelet basis to obtain a multi-resolution description of the cortical source structure, to provide control of the distribution of the source amplitudes (focal vs extended) and suppress imaging error due to noise.
- Useful for studying the time evolution and sequence of overlapping neuronal source activity.
- For enhanced imaging MR-FOCUSS can utilize an initial estimate of source activity generated by fMRI, PET, and/or EEG.

Moran et al, Brain Topography, 2005

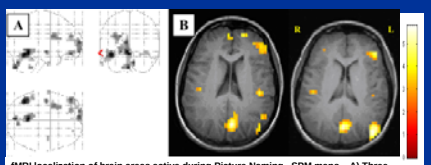
Cortical Model



- Created from Volumetric MRI Data
- ~4,000 cortical locations
- Distribution matches cortical gray matter

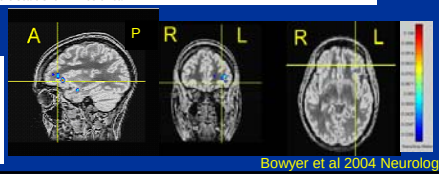
Picture Naming

fMRI



fMRI localization of brain areas active during Picture Naming. SPM maps. A) Three-plane Glass Brain (Fixed effect analysis corrected p<.001) B) Axial overlay shown. Z-score scale shown in color bar.

MEG

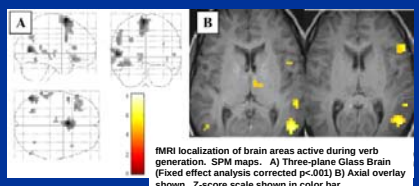


MEG localization at 437 ms after onset of Visual picture. This is the point at which the brain is telling the mouth to say the word. MR-FOCUSS results scale in nanoAmp-Meters.

Bowyer et al 2004 Neurology

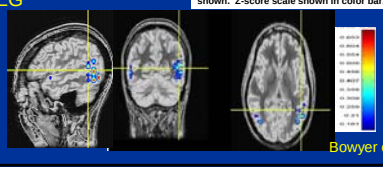
Verb Generation

fMRI



fMRI localization of brain areas active during verb generation. SPM maps. A) Three-plane Glass Brain (Fixed effect analysis corrected p<.001) B) Axial overlay shown. Z-score scale shown in color bar.

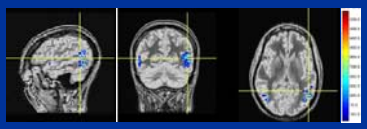
MEG



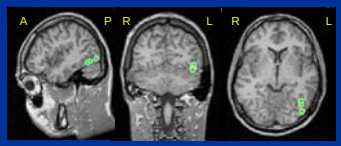
MEG localization at 235 ms after onset of Visual word. This is the point at which the brain is generating the verb. MR-FOCUSS results scale in nanoAmp-Meters.

Bowyer et al 2004 Neurology

Wernicke's Area



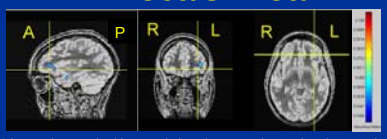
MR-FOCUSS localization images of cortical language processing areas during Verb Generation in control subject # 5. Verb Generation produced neuronal activation in the SMG, STG and AG at 235 ms after onset of visual stimuli. Red areas on MRI scan show most intense cortical activation. Scale in nAmp-Meters.



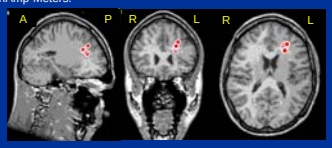
ECD localization of MEG data from same subject during Verb Generation produced STG activation at 235-239 ms after onset of visual stimuli. Three dipoles were found that fit the acceptable criteria.

Bowyer et al 2004 Neurology

Broca's Area



MR-FOCUSS images in control subject # 5 during Picture Naming produced neuronal activation in the IFG at 437 ms after onset of visual stimuli. Red color on MRI scan shows most intense cortical activity. Scale in nAmp-Meters.



ECD localization in same subject during Picture Naming produced MFG activation at 428-435 ms after onset of visual stimuli. Five dipoles were found that fit the acceptable criteria.

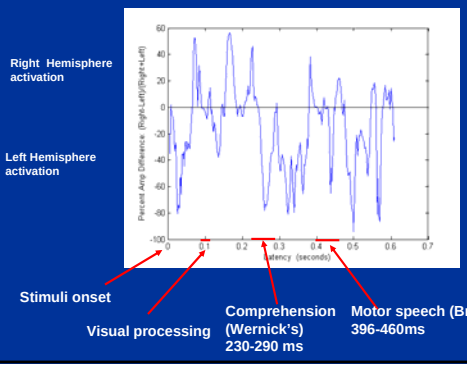
Bowyer et al 2004 Neurology

Language Laterality

- Picture naming task, brain activity between 396-460ms found closest concurrence with the WADA results (IAP).
- In 23 out of 24 epilepsy patients with a successful IAP, the Index for Broca's activation were in agreement with the results of the WADA (96% accuracy).
- In 1 of the 3 patients who had an undetermined or bilateral IAP, MEG lateralized language to the same hemisphere as clinical findings making our overall accuracy 89%.

Bowyer et al 2005 Epilepsy & Behavior

Language Laterality



Language Laterality Table

Subjects	Handedness		Gender	Age	Laterality Verb Generation			Laterality Picture Naming			WADA
Epilepsy	R +100	L -100		(Yrs)	LI 150-550	LI 230-290	LI 396-460	LI 150-550	LI 230-290	LI 396-460	Dominant Hemisphere
1	100	F	34	**-20**	33	53	**-27**	20	**-60**	Left
2	100	F	16	**-4**	86	4	47	100	**-9**	Left
3	-59	F	43	-2	**20**	-76	**24**	-60	**3**	Right
4	-100	M	32	**-29**	47	**-88**	**-65**	**-73**	**-100**	Left
5	100	F	43	**-55**	**-60**	**-50**	**-53**	**-20**	**-88**	Left
6	25	M	35	**-38**	**-93**	**-33**	**-42**	**-100**	**-21**	Left
7	100	F	31	**-68**	**-87**	**-38**	**-47**	**-29**	**-76**	Left
8	100	F	21	**-67**	**-7**	**-100**	**-33**	**-60**	**-100**	Left
9	70	M	51	**-53**	**-87**	33	**-56**	20	**-82**	Left
10	100	F	33	**-25**	**-93**	21	**-23**	50	**-33**	Left
11	70	M	20	**47**	-33	**58**	**67**	**100**	-33	Bilateral* (R)
12	90	M	27	**-28**	**-60**	**-94**	40	53	**-24**	Left
13	100	F	21	**-30**	27	**-46**	**-17**	**-13**	**-93**	Left
14	-100	M	59	**-23**	80	**-87**	**-34**	7	27	Indeter* (Left)
15	100	M	24	**-18**	**-20**	**-3**	22	100	**-45**	Indeter* (Left)
16	100	M	10	**68**	**100**	**87**	**10**	-93	**100**	Right
17	100	F	51	**-30**	**-13**	33	**-42**	**-100**	**-100**	Left
18	80	M	37	33	60	58	**-20**	**-100**	33	Left
19	100	F	46	**-20**	**-20**	**-81**	**-44**	26	**-27**	Left
20	100	F	41	**-16**	**-93**	**-15**	**-42**	23	**-70**	Left
21	80	F	33	45	7	33	**-16**	7	**-27**	Left
22	100	F	23	28	40	76	**-22**	**-100**	**-70**	Left
23	-100	M	21	**-100**	100	**-3**	**-13**	**-27**	**-45**	Left
24	100	M	39	**-25**	53	**-65**	**-29**	27	**-70**	Left
25	100	F	48	**-53**	**-100**	**-76**	**-35**	**-100**	**-21**	Left
26	70	F	35	**-26**	**-7**	**-100**	6	**-73**	**-51**	Left
27	100	M	21	16	47	**-70**	14	53	**-94**	Left
Correctly match				**22**	15	18	21	12	**24**	

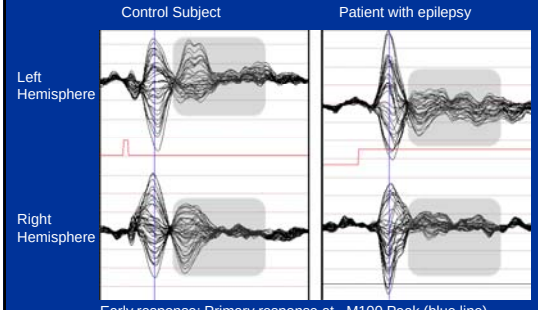
Rethinking clinical language mapping approaches:
Discordant receptive and expressive hemispheric language dominance in epilepsy surgery candidates

Gage, Nicole M, (1, 6), Eliashiv, Dawn S, (2, 3), Isenberg, A. Lisette (1), Fillmore, Paul (4), Kurelowech, Lacey (5), Quint, Patti (5), Chung, Jeffrey M (2, 3), and Otis, Shirley M. (6)

In Press Journal of Clinical Neurophysiology

Results provide evidence that receptive and expressive language may have divergent hemispheric dominance in patients with Epilepsy.

Averaged MEG Waveforms



Early response: Primary response at ~M100 Peak (blue line)
Late response: 130-380ms is shaded in gray

Results

- They found that 3/6 patients were discordant
  - Receptive language was right-dominant
  - Expressive language was left-dominant
- These results are in accordance with previous MEG studies by Breier and colleagues in patients with intractable seizures and TBI where reorganization of language function probably occurs and results in atypical language lateralization.
- Our findings are similar to a recent finding in a case study where receptive language function showed right-dominance in MEG scans and expressive showed left-dominance in fMRI scans (Kamada et al., 2006).
- Therefore for patient populations it may be necessary to map both receptive and expressive language function

Thank you for your attention!

Thank you to all my Colleagues:

Karen Mason REEG/MEG

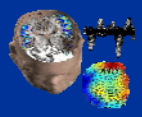
Gregory L Barkley MD
Brien Smith MD
Dave Burdette MD

Kost Elisevich MD, PHD

Norman Tepley PhD
John Moran PhD

Valia Gumenyuk PhD
Renee Lajiness O'Neill PhD
Margaret Greenwald PhD

Special Thank you
Nicole Gage PhD and
All of her Collaborators



Identification of pathological high frequency oscillations in epilepsy using MEG.

Julia Stephen, Ph.D.
The MIND Research Network, Albuquerque, NM

Julia Stephen

Identification of pathological high frequency oscillations in epilepsy using MEG

Julia M. Stephen, PhD

February 3, 2011

Why are we interested in high frequency oscillations (HFOs) in epilepsy?

We know that interictal spikes are not always representative of the seizure onset zone (SOZ). With multiple independent foci, how does one determine the SOZ? Therefore, a better interictal marker for the SOZ would facilitate epilepsy treatment.

Recent studies have suggested that HFOs may provide a better marker for the SOZ than interictal spikes.

- HFOs can occur in the presence and absence of seizures and interictal spikes (e.g. Jacobs et al. 2008, 2010).
- HFOs appear to originate more frequently from SOZ than from other areas (Staba et al. 2002, and many more).

Except, most of these results are from animal work or invasive recordings in humans

The *challenge* is:

Can we effectively apply the intracranial results to non-invasive recordings?

Challenges in using HFOs clinically

Ideally, we want a noninvasive marker for the SOZ.

What are HFOs?

- Pathological versus nonpathological HFOs
- Ripples versus fast ripples

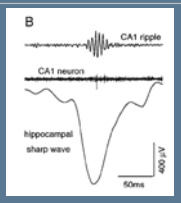
Can we identify HFOs noninvasively?

How do we identify HFOs noninvasively?

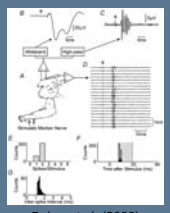
Can we distinguish HFOs from artifacts?

Normal HFOs

- Chrobak and Buzsaki (1996) reported normal ripples (200 Hz) from hippocampal/entorhinal network activity.
- Especially important for working memory



Chrobak & Buzsaki (1996)

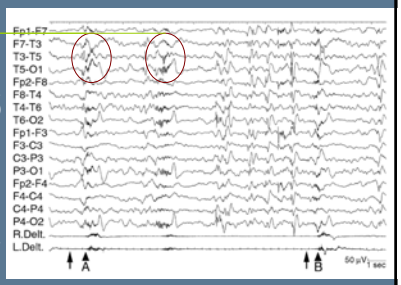


Baker et al. (2003)

- 600 Hz activity elicited by median nerve stimulation (Baker et al. 2003)
- Curio et al. (1994) Measured this 600 Hz noninvasively with MEG.

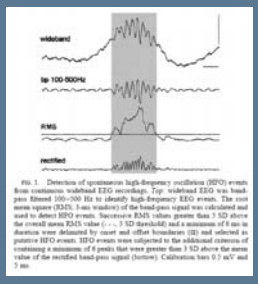
High Frequency Oscillations in Epilepsy

- High frequency activity has been observed during *ictal* activity (Bancaud 1975, Alarcon 1995, Allen 1992, Fisher 1992, Panzica 1999 – infantile spasms, Akiyama 2006)
- Ictal HFOs were often discounted due to the confounder of muscle artifact.
- Primarily reported on "fast activity" greater than 20 Hz. (40-50 & 80-120Hz – Fisher 1992, 51-98 Hz – Kobayashi, 2004)

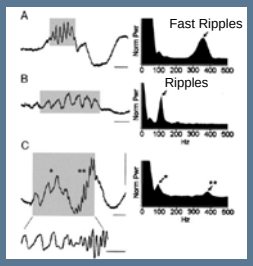


Kobayashi et al. (2004) Epilepsia

High frequency oscillations during *interictal* activity (Engel et al.)



Staba et al. 2002



Engel et al. proposed that fast ripples were pathological

Ripples 80-250 Hz, Fast ripples >250 Hz

Are HFOs measureable noninvasively?

- **We know that some groups have identified ictal HFOs noninvasively (e.g. Kobayashi et al. 2004).**
  - This suggests, at least, that the recording parameters and SNR are sufficient to detect some pathological HFOs.
- **Recent studies have shown evidence of the sensitivity of MEG to HFOs.**
  - Rampp et al. (2010) used iEEG-triggered averaging to identify HFOs in MEG.
  - Xiang et al. (2010) used short FFT to identify HFOs, but this did not allow for direct correlation with interictal spikes. It also averages across HFO events.

Testing for HFOs noninvasively using babySQUID

- **Is the HFO amplitude large enough to measure at a distance?**
- **Collected data from 8 children with epilepsy using babySQUID**
- **babySQUID system designed specifically for measuring signals from infant brains**
  - Hemispherical design with 76 axial gradiometers
  - Outer dewar surface to pick-up coil distance ~6 mm compared to 20-30 mm in commercial adult systems

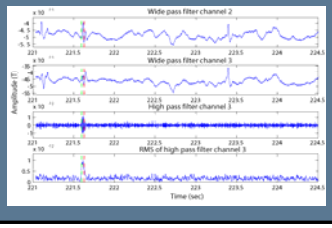
Used the Staba (2002) approach to define an HFO event

Preprocessing of the data:
- **Perform high pass filtering >80 Hz**
- **Obtain RMS average over a 6 ms time window of the high passed data**

To qualify as an HFO event
1. **the RMS value must be > 5 SD of the average RMS for that channel for at least 6 ms.**
2. **There must be at least 6 contiguous peaks that remain > 3 SD of the average RMS.**
3. **The event must be seen in at least 3 contiguous channels.**

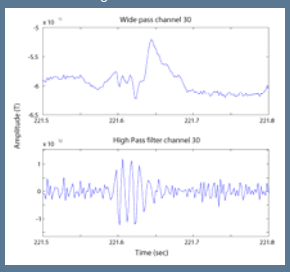
16-month old child with epilepsy

HFOs are not present with each spike suggesting possible selectivity.

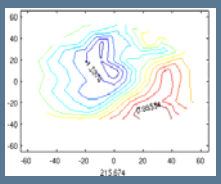


A closer look…

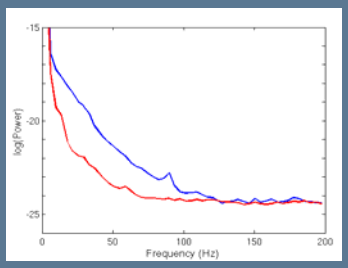
Single event with HFO



Contour map from one peak of the HFO event

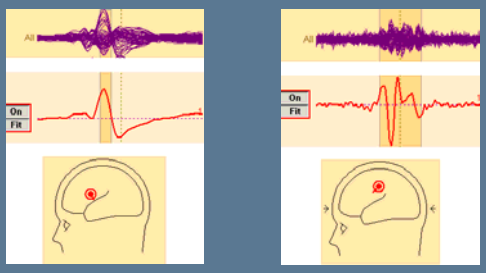


Relative to healthy controls



- We have not yet found evidence of equivalent HFO events in healthy control children.
- This is a unique contribution for noninvasive MEG/EEG.

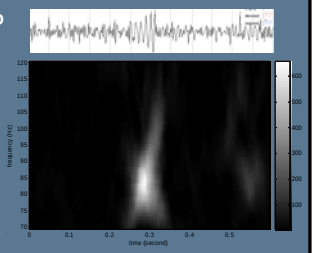
Consistency in source localization



General location is consistent between interictal spike and HFOs. Variability may be due to differences in SNR or real differences in location.

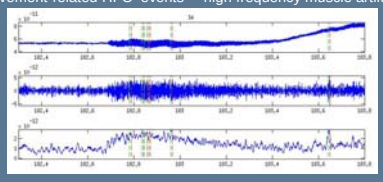
This looks perfectly consistent with the timing and morphology of the Engel HFOs, however…

- Engel identified fast ripples and ripples -- Our babySQUID child data ranged from 80-120 Hz (ripples)
- We identified HFO events in 2/8 children (caveat: most of the other children did not show spikes during the MEG).
- The child with frequent HFOs had multi-focal epilepsy with no conclusive clinical SOZ.



HFO artifacts

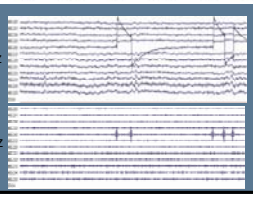
Movement-related HFO 'events' – high frequency muscle artifact



Flux jumps

0-200 Hz

80-200 Hz

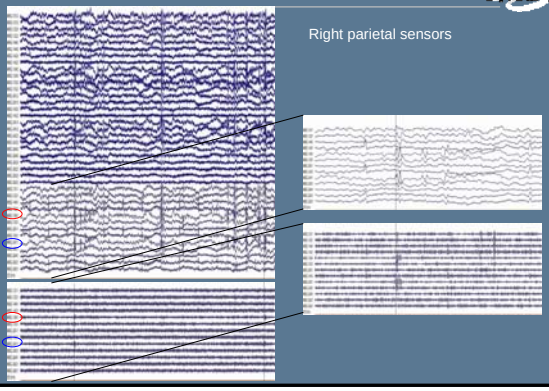


Duration of HFO events is important

Artifacts discussed by Benar et al. 2010

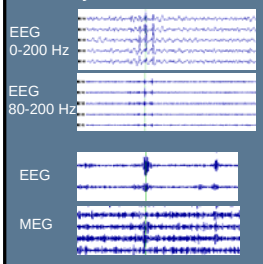
HFOs using Elekta Neuromag 306 channel MEG system

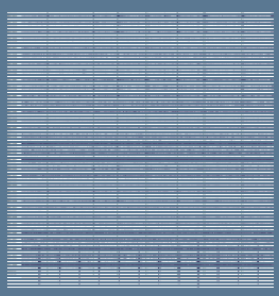
Right parietal sensors



Simultaneous EEG and ECG

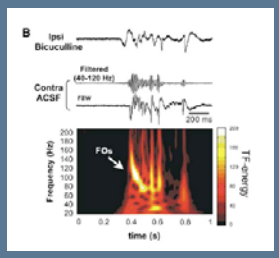
5 ½ year old EEG HFOs





Developmental rat model of epileptogenesis

- Khalilov et al. 2005 found that GABA-A receptors are necessary for HFOs in developing rat hippocampus contralateral to ictal zone
- If HFOs were blocked (by blocking GABA-A receptors) there was not epileptogenesis
- Le Van Quyen et al. (2006) suggested the epileptogenesis does not occur without HFOs.



Conclusions

- HFOs have been identified in both temporal lobe (Engel et al.'s work) and neocortical epilepsy (Shevon et al. 2009, Brazdil et al. 2010)
  - SNR may play a role in identifying HFOs non-invasively with a bias towards neocoritcal epilepsy. But neocortical epilepsy has the worst surgical outcome so HFOs may help out.
- HFOs correlated well with surgical outcome (e.g. Jacobs et al. 2010). Amount of HFO-generating tissue removed correlated better with outcome than amount of spike-generating tissue removed.
- Worrell et al. (2008) used both microwire and macro-electrodes invasively and found more sensitivity to FR and R, respectively.
  - Perhaps either R or FR can be used to identify the SOZ. MEG is likely more sensitive to Ripples.

Acknowledgements

MRN Collaborators
- Jeff Lewine, PhD
- Amanda Peters
- Lucinda Romero
- Nirupama Sharadamma

Children's Hospital of Boston
- Yoshio Okada, PhD

UNM Collaborators
- Bruce Fisch, MD
- John Phillips, MD
- Jennifer Vickers, MD
- Tongsheng Zhang, PhD

UCLA
- Pete Engel, MD
- Anatol Bragin, PhD
- Richard Staba, PhD

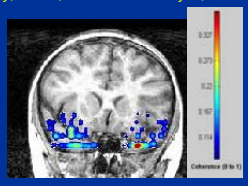
MEG coherence imaging for lateralizing temporal lobe epilepsy

Susan Bowyer, Ph.D.
Henry Ford Hospital, Detroit, MI

Susan Bowyer

MEG Coherence Imaging For Lateralizing Temporal Lobe Epilepsy

Kost Elisevich, M.D., Ph.D. Neetu Shukla, M.S., John Moran, Ph.D., Brien Smith, M.D., Lonni Schultz, Ph.D., , Karen Mason, R.EEG/MEG T., Gregory L Barkley, M.D., Norman Tepley, Ph.D. , Valentina Gumenyuk, Ph.D. and Susan M. Bowyer, Ph.D.



www.megimaging.com

Purpose

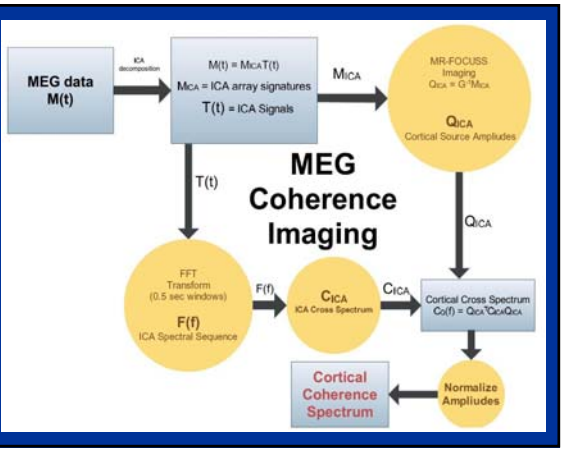
This study examines the capability of magnetoencephalographic (MEG) coherence imaging to lateralize the site of epileptogenicity in patients with drug resistant temporal lobe epilepsy (TLE).

Methods

- An archival review of single equivalent current dipole (ECD) MEG analyses from
- 30 presurgical TLE patients
- Postoperative outcome was assessed by Engel class.
- MEG coherence images were generated from 10 minutes of spontaneous brain activity
- MEG coherence images were compared to surgically resected brain areas outlined on each subject's MRI.
- Coherence values were averaged independently for each hemisphere to ascertain the laterality of the epileptic network.
- Reliability between runs was established by calculating the correlation between runs.

Coherence

- The analysis of coherence between EEG electrode site and MEG sensors has been performed for many years. However, at best only regional inference of cortical connectivity can be estimated without **first imaging brain activity.**
- Transients and oscillations of brain electric activity are found in MEG, EEG and ICEEG recordings of spontaneous brain activity. These transient waveforms and oscillations can be quantified by applying a time-frequency decomposition technique such as the short-time Fourier transform (SFFT).
- After transformation to a time frequency representation, the strength of network interactions can be estimated by calculation of coherence, which is a measure of synchrony between signals from different brain regions for each FFT frequency component.
- Advanced network evaluation techniques (Granger causality, narrow band filtering or Essential Mode Decomposition with Hilbert transforms, wavelets) can be applied to non-stationary data.
  - Determine the direction of network interactions
  - Quantify significance of network structures

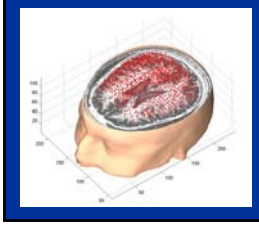


Coherence Imaging Methods

- 10 to 15 minutes of MEG data at 508 Hz sampling rate
- Filtered 3-50 Hz and Heart artifact removed
- Divided into 7.5 second intervals for imaging and coherence calculations
  - ICA for extracting neuronal bursts of activity (epileptic signals)
  - MR-FOCUSS/Coherence imaging for determining the global extent of the epileptic network and the local spectrum of overall network coherence and connectivity. (Very, numerically efficient compared to other MEG methods)
- FFT with 256 point hanning window and 25% overlap
- Coherence results for all 7.5 second interval are averaged.
- Multiple runs processed to check for stability of results

Extracting real time neural networks from MEG data

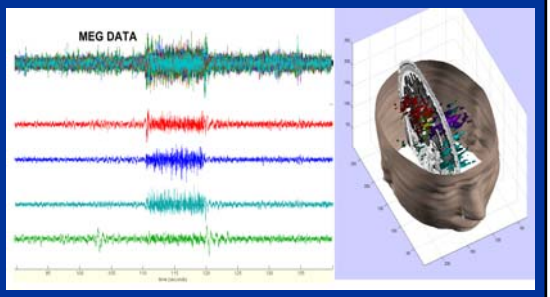
- Oscillations or rhythmic activity
- Synchronization of oscillatory activity



Cortical Model

- Created from Volumetric MRI Data
- ~4000 cortical locations
- Distribution matches cortical gray

ICA signal separation MR-FOCUSS Imaging

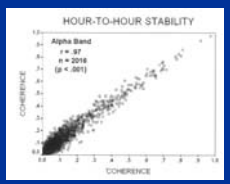


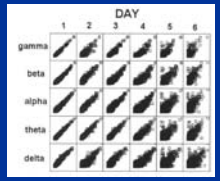
Coherence and Epilepsy

ECoG studies:

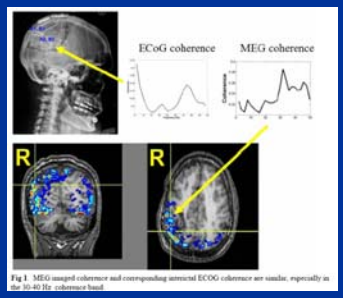
Coherence is very stable over time

V.L Towle, et.al., Frequency Domain Analysis of Human Subdural Recordings. J. Clin. Neurophysiology, Vol. 34 No. 2, pp 205 – 213, 2007





MEG Imaged Coherence Mapping
Compared to Electrocortical Recordings



Moran J. et al. *2006, MEG Coherence Imaging Compared to Electrocortical Recordings from NeuroPace Implants to Determine the Location of Ictal Onset in Epilepsy Patients*, in *15th International Conference on Biomagnetism*.

Results

- The ECD method provided an overall match rate of 43% (13 cases/30) for Engel class I outcomes with 37% (11 cases) found to be indeterminate (i.e., no spikes identified on MEG)
- Coherence analysis provided an overall match rate of 67% (20 cases 30)
- Using only the class I outcome results (i.e., absence of disabling seizures) as a measure of success, the mean coherence value was found to be 0.26 ± 0.03.
- Control subjects demonstrated no area of high coherence, as expected, and a lower mean coherence value (0.17 ± 0.09).

Table 3

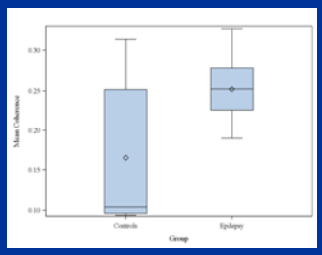
Table 3: Summary of Engel classes with ECD and MEG analyses

Engel Class	EC D		Coherence analysis	
	Match*	No Match	Match*	No Match
Ia	9	13	16	6
Ib	1	0	1	0
Ic	1	0	1	0
Id	2	0	2	0
IIa	0	1	1	0
IIb	1	0	1	0
IIIa	2	0	1	1
Total	**16**	**14**	**23**	**7**

*A match indicates agreement of MEG analysis with the laterality of the surgical resection and, therefore, the result of standard investigation.

Elisevich et al, Epilepsia 2011

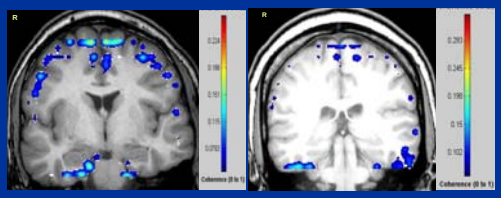
Coherence Levels



Box plots showing mean (1), median, interquartile range and minimum and maximum values of coherence for control subjects and epilepsy patients. The difference between the two populations was significant (p=0.007).

Elisevich et al, Epilepsia 2011

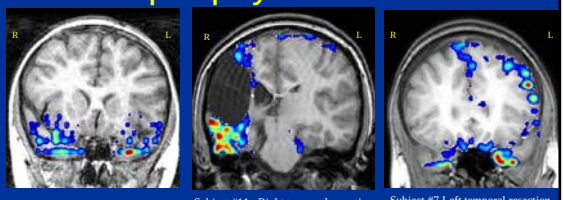
Healthy Normal Control subjects



Control subject. Magnetic resonance image showing coronal MR images overlaid with the results of coherence analysis. No areas of high coherence are identified.

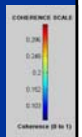
Elisevich et al, Epilepsia 2011

Epilepsy Patients



Subject #1: Left temporal resection | Subject #11: Right temporal resection | Subject #7 Left temporal resection

- Increased coherence (presurgical) was localized to the concordant area of resection in 19/24 temporal lobe epilepsy cases. All of whom were seizure-free longer than 1 year postoperatively.
-
- 5/6 cases with a **normal** presurgical MRI were correctly localized by coherence measures.



Results

- Sensitivity of the ECD method was 41% (indeterminate cases included) and that of the coherence method 73% with a positive predictive value of 70% for an Engel class Ia outcome

Sensitivity and specificity

of ECD and coherence analysis methods.

ECD and Engel class outcome			
	Ia	Not Ia	Total
Match*	9	7	16
Not Match	13	1	14
Total	22	8	30
Sensitivity of Engel class Ia		41	
Specificity of Engel class Ia		13	

Coherence and Engel class outcome			
	Ia	Not Ia	Total
Match*	16	7	23
Not Match	6	1	7
Total	22	8	30
Sensitivity of Engel class Ia		73	
Specificity of Engel class Ia		13	

*A match indicates agreement of MEG analysis with the laterality of the surgical resection and, therefore, the result of standard investigation.

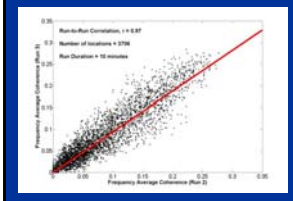
Elisevich et al, Epilepsia 2011

Results

Intrasubject coherence imaging reliability was consistent from run-to-run (correlation >0.90)

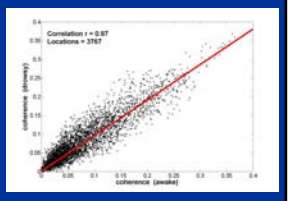
MEG Coherence and Epilepsy

- MEG Coherence imaging is stable



Run-to-Run Correlation

(A) Run-to-run coherence imaging measurements for two 10 minute studies in one epilepsy patient indicates the local variance at each whole brain location (3706 sites) is consistent (i.e., highly correlated) between each run.



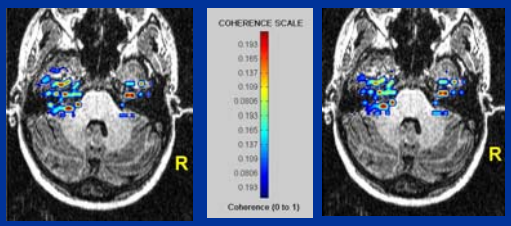
Awake-Drowsy Correlation

(B) Comparison of coherence imaging results in the awake state versus drowsiness state of brain activity in a single control subject shows the reliability of coherence imaging between the two runs.

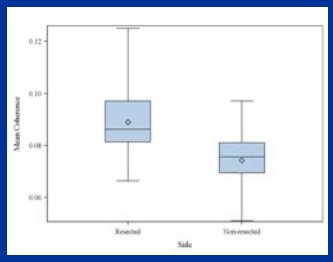
MEG Coherence and Epilepsy

- MEG coherence run-to-run stability

Run 2 Run 3

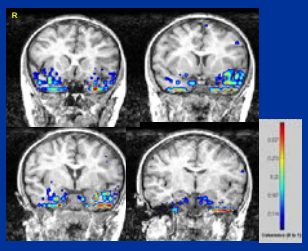


Hemispheric Coherence Levels



Box plots showing mean (◇), median, interquartile range and minimum and maximum values of coherence for the resected and nonresected hemispheres. The difference between the two sides was significant ($p<0.001$).

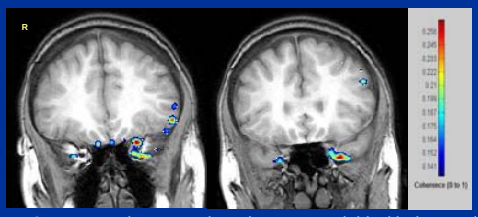
Epilepsy Patient



Case 1. Preoperative coronal MR images overlaid with the results of coherence analysis. The study identifies an asymmetry in signal intensity (inset) weighted towards the left temporal lobe despite the absence of MTS. The patient remains seizure-free following resection of the inferopolar and mesiobasal portions of the left temporal lobe.

Elisevich et al, Epilepsia 2011

Epilepsy Patient



Case 6. Preoperative coronal MR images overlaid with the results of coherence analysis in a case wherein the ECD method was indeterminate. The study identifies an asymmetry in signal intensity weighted toward the mesiopolar region of the left temporal lobe despite the absence of MTS. The patient remains seizure-free following resection of the inferopolar and uncal portions of the left temporal lobe.

Elisevich et al, Epilepsia 2011

Discussion:

- MEG coherence analysis has greater sensitivity than the ECD method for lateralizing TLE,
- Coherence imaging demonstrates reliable stability from run-to-run
- Provides unique functional information for clinical decision-making where the laterality of TLE is questioned.

Future Direction

The Clinical Questions

Where does a patient's epilepsy start?

Where is the best location for intervention?

Epileptic Activity is not Focal

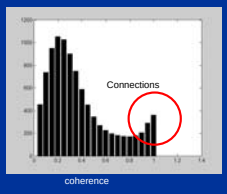
- Rapid spread throughout a well established, well connected, often global network
- Amplitude and frequency depends on connectivity
- Amplitude of activity and network behavior is distinctly different from normal brain network behavior
- Epileptic network activity is similar across patients
- Generators of abnormal brain activity have different behaviors than other network components
- Components of the epileptic network have different ictal and interictal activities.

Next Step

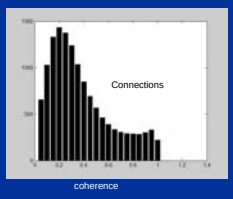
- Coherence imaged results
- Discriminant analysis is well suited for utilizing differences in coherence and connectivity to create discriminant functions that can be used to identify active generator sites when applied to new patient data.
- Further, discriminant analysis can provide predictors of surgical outcome.
- Discriminant analysis performed to train and to predict
  - Multiple discriminant functions applied and results averaged in predict mode (use the training MEG data samples to estimate the values of the parameters)
  - Data base of discriminant functions constructed in train mode such that individual variations are well accommodated (the MEG data samples to estimate a classifier based on the values of parameters)

Coherence-Connectivity distribution

- The coherence distribution: one site with all other sites
- It is distinctly different for sources that have different connectivity.



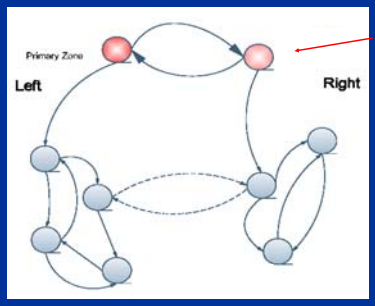
Within Epileptic Zone

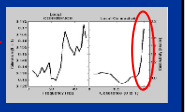


Outside Epileptic Zone

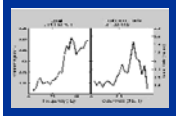
These are coherent sites that are well connected

Epileptic Network

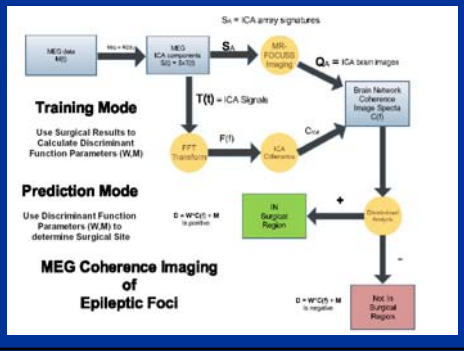




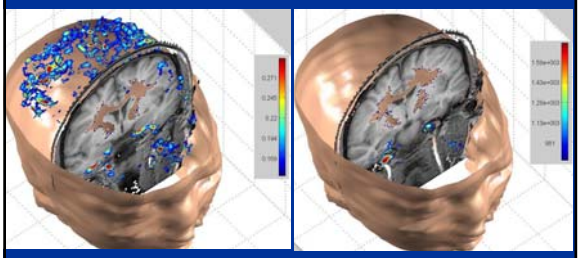
Unique spectra will be the area that drives the network



Coherence Imaging and Discriminant Analysis



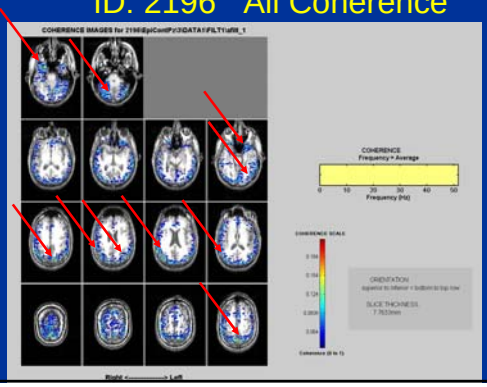
Discriminant Image Results



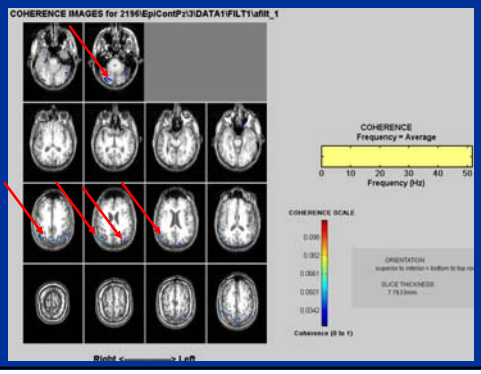
Coherence results

Discriminant Score

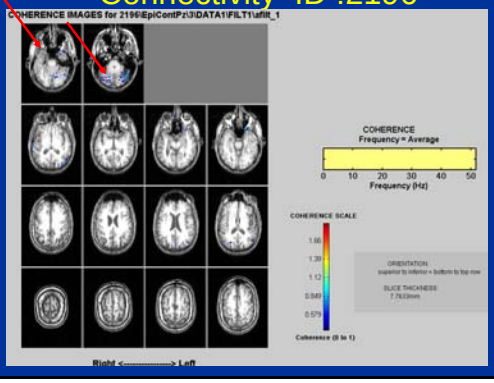
Patient with Right Temporal Epilepsy ID: 2196 All Coherence



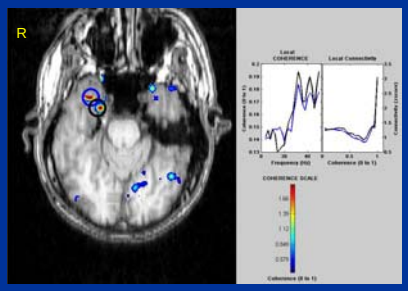
Discriminant Analysis on Coherence ID :2196



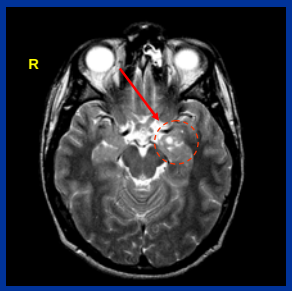
Discriminant Analysis on Connectivity ID :2196



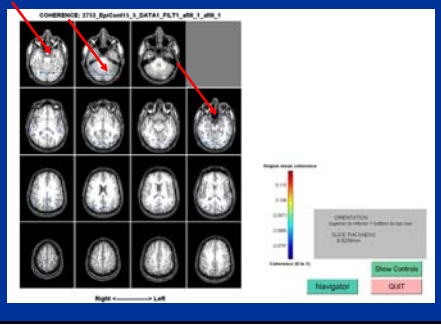
ID 2196 Discriminant Analysis on Connectivity show activity in the Right temporal region



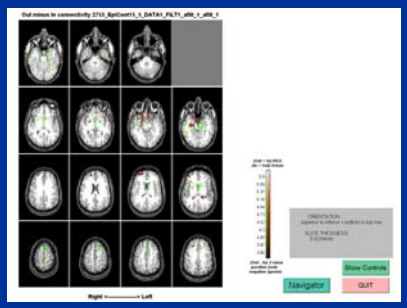
Epilepsy Patient with Lesions in Left Temporal Area - ID 2753



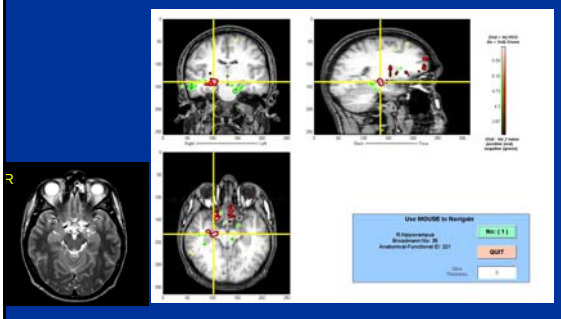
Mean Regional Coherence (72 regions) ID 2753



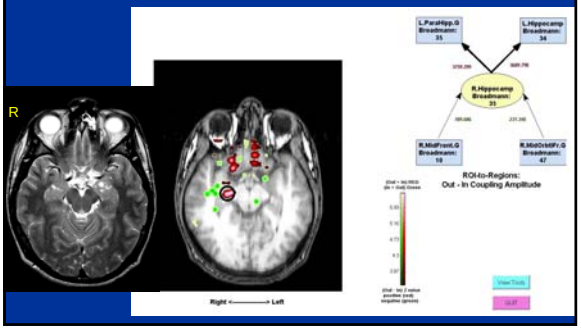
IN OUT Coupling Grainger Causality



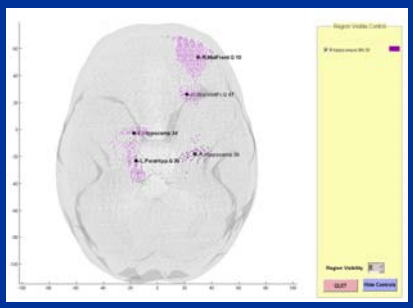
Top location



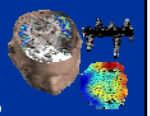
Locations that are communicating



Locations plotted in brain



Thank you for your attention!



My Collaborators:
Gregory L Barkley, MD
Brien Smith, MD
David Burdette, MD
Amit Ray, MD
Veba Wasada, MD
Panos Mitsias, MD
Brian Silver, MD
Michael D Seidman, MD
Kost Elisevich, MD, PhD

Karen M Mason, REEG/MEG

Norman Tepley, PhD
John E Moran, PhD
Stephen Robinson, PhD
Quan Jiang, PhD
Barbara Weiland, PhD
Valentina Gumenyuk, PhD
Jinsheng Zhang, PhD

Renee Lajiness-O'Neill, PhD
Margaret Greenwald, PhD

Neetu Shukla Grad Student
Reza Farjam Grad Student

Acknowledgement

Research supported by NIH/NINDS Grant RO1-NS30914

Making the invisible wounds of war visible: multimodal imaging in TBI, PTSD, and Depression

Jeffrey Lewine, Ph.D.
MIND Research Network, Albuquerque, NM

Jeffrey Lewine

Making the Invisible Wounds of War Visible: Advanced Imaging in mTBI, PTSD, and Depression

Presented by: Julia M. Stephen, Ph.D.
for
Jeffrey David Lewine, Ph.D.

Associate Professor of Translational Neuroscience

Invisible Wounds of War: The Numbers

- Approximately 2.5 million troops have been deployed in Operations Enduring Freedom and Iraqi Freedom.
- The Rand Corporation estimates that >300,000 returning servicemen and women will show signs of the "Invisible Wounds of War" – mild traumatic brain injury, post-traumatic stress disorder, and depression.

The Challenge

- Differential diagnosis of mTBI, PTSD, and depression is essential to effective treatment.
- Knowing when TBI is co-morbid with PTSD and depression is especially important because TBI alters the brain's response to medications and cognitive-behavioral therapy. When TBI is also present, the treatment of the other conditions may need to be altered.
  - >40% of servicemen with documented head injury are showing signs of PTSD
  - >50% of servicemen with PTSD show cognitive, emotional, and somatic symptoms suggestive of mild TBI
  - >40% of servicemen show signs of depression. Depression may be associated with cognitive symptoms similar to those seen in mTBI and PTSD

Objective diagnosis of mild-TBI is a major clinical and scientific challenge, in both the semi-acute phase and especially in the chronic phase.

- Questionnaires are inadequate
  - Based on questionnaires, >50% of patients with major depression and no history of head trauma meet diagnostic criteria for a post-concussive syndrome and mild-TBI.
- Neuropsychological/Cognitive testing is inadequate
  - Because adequate baseline data are not available, testing is based on population norms. Deficits from mild TBI are often subtle, and scores often do not fall significantly outside of the normal range. As a result, for example, an engineer with an initial [but undocumented] IQ of 140 might show an IQ of 100 following head trauma. This is an average score and the individual is likely to be told that there is nothing wrong, but clearly post-trauma abilities will not match the pre-trauma baseline.
- Structural Brain Imaging is inadequate
  - Routine CT and MRI are normal in the vast majority of patients believed to have mild traumatic brain injury

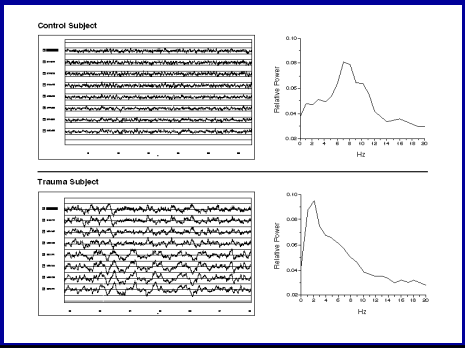
Advanced Brain Imaging Techniques Show Promise, But the Following Considerations Must Not Be Ignored.

- The method has to work for individual subjects
- The method has to be more sensitive to mTBI than other methods
- The method has to be specific to mTBI with respect to other clinical conditions including: normal controls, PTSD, depression, substance abuse, ADHD, and sleep disorder.
- Many imaging methods work on group data, but few studies actually demonstrate high sensitivity and specificity for the evaluation of individuals.
  - e.g., fMRI, DTI

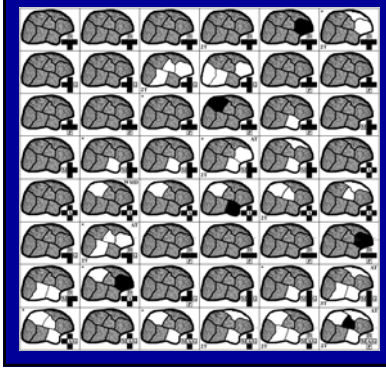
One Last Challenge

- There is no gold standard against which to judge advanced methods. Therefore examine
  - "dose response"
  - History and Symptom profile

Spectral Abnormalities



Increased Delta Activity in mTBI

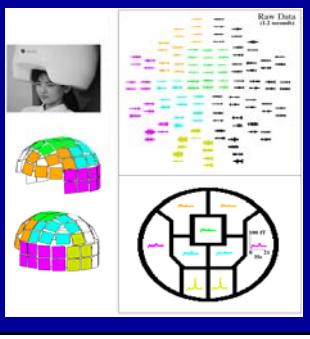


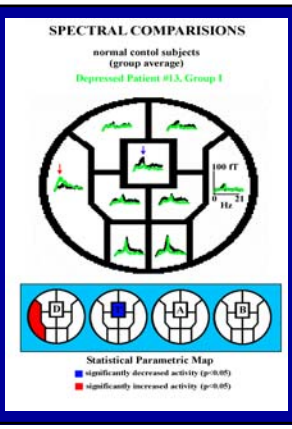
- Data are collapsed across hemispheres. White shows increased delta, black decreased delta, relative to a normative control database [n=105].
- Spectral abnormalities are most prominent in patients with cognitive symptoms.

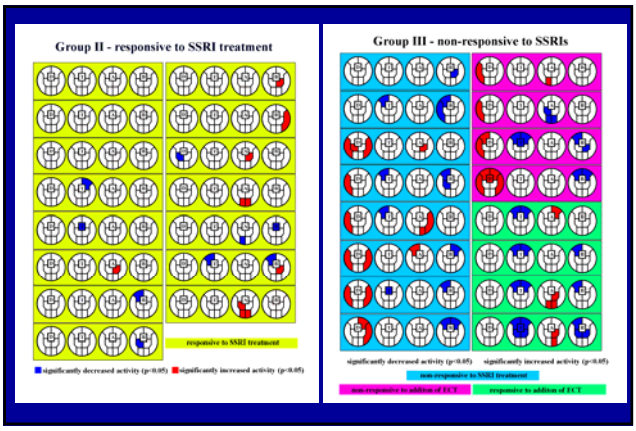
Specificity

- Many Conditions Show Increased Low Frequency Activity in Power Spectra, Including Depression, Substance Abuse, and Sleep Deprivation

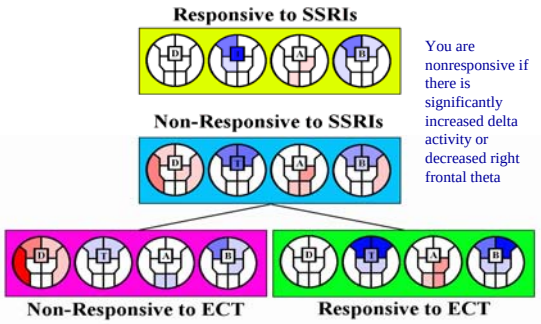
MEG in Major Depressive Disorder



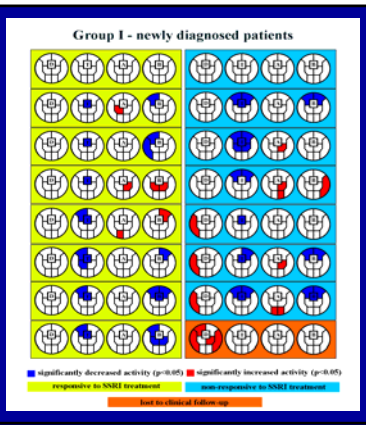




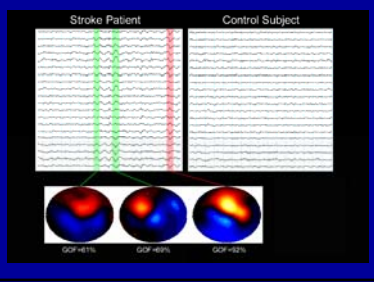
MEG profiles in Major Depressive Disorder



You are nonresponsive if there is significantly increased delta activity or decreased right frontal theta

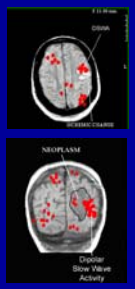


Brain Damage Is Associated with Dipolar Abnormal Low Frequency Magnetic Activity and Slow Waves



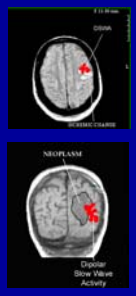
All Slow Wave Activity

- Most slow waves are non-dipolar. If you model all events the following happens:
  - Most fits are of poor quality
  - Dipole locations seem to have little to do with clear pathology. This holds using multiple dipole models as well.
  - High false positive rate in normal control subjects if drowsiness or sleep is present

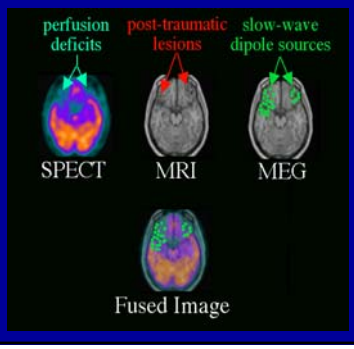


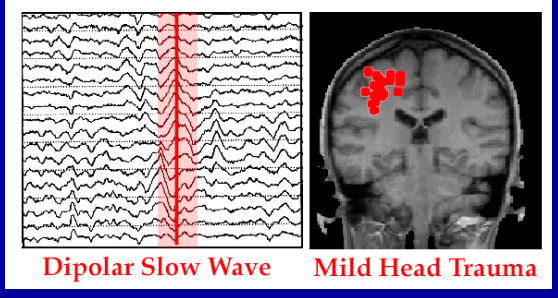
Dipolar Slow Wave Activity (DSWA)

- If you focus only on dipolar events there is a good correlation with pathology, although some additional clusters may be seen
  - But, you have 'thrown away' most of the data – less than 1% of slow waves are dipolar.
  - Low false positive rate in normal control subjects. Slow waves for drowsiness and sleep are non-dipolar.
- The situation for distributed source models is presently unclear.
  - Algorithms like VESTAL may be very useful if it can be demonstrated that identified regions show real pathology.

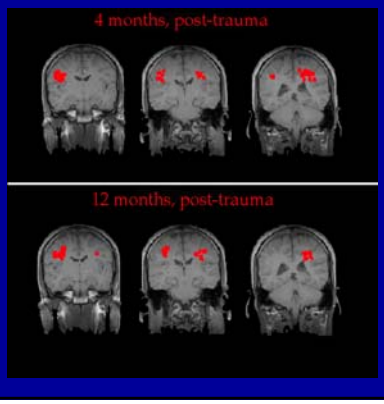


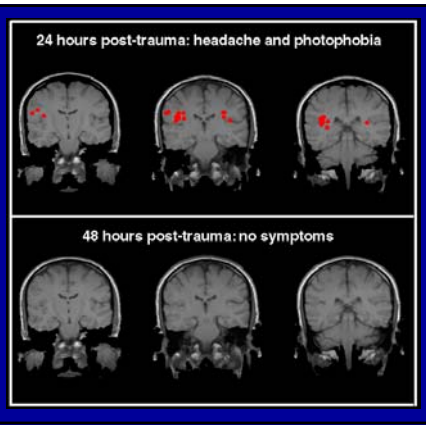
Moderate Trauma





Dipolar Slow Wave Mild Head Trauma





Type of Subject	Number of Subjects	DSWA
Normal Control	106	5.7%
Mild TBI no PCS	33	15.2%
Mild TBI with PCS	68	64.7%
Moderate TBI with PCS	30	80.0%

Method	Number of Subjects	Abnormalities
MEG - DSWA	68	64.7%
Routine MRI	68	13.3%
Clinical EEG	68	20.6%
SPECT	30	40.0%

Regional MEG abnormalities correlate with specific cognitive symptoms in a pattern that is consistent with general observations in behavioral neurology

MEG and SPECT are complementary: Lewine et al., 2007

Table 3: Odds-ratios for finding specific imaging abnormalities given that a specific post-concussive symptom was present.

		Psychiatric	Somatic	Cognitive			
		all	all	Memory	Attention	Executive	Speed
MRI	atrophy	2.7	1.1	5.7	0.7	4.8	4.8
SPECT	atrophy	2.7	1.7	3.4	1.2	2.9	–
SPECT	frontal	4.7	2.7	1.0	0.5	–	0.8
SPECT	temporal	0.8	1.1	5.7	2.7	1.4	4.8
SPECT	parietal	2.5	0.8	1.5	–	–	–
SPECT	occipital	–	0.0	–	–	–	–
SPECT	sub-cortical	3.0	58.0	0.7	1.2	1.4	0.6
MEG	frontal	2.1	0.5	1.2	0.9	–	2.1
MEG	temporal	0.4	0.3	13.0	1.4	2.3	8.0
MEG	parietal	1.3	0.3	1.0	12.0	4.0	4.0
MEG	occipital	2.5	0.0	0.4	2.5	1.3	–

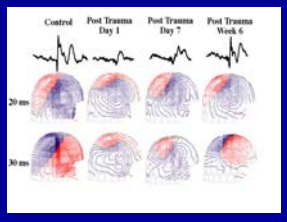
– indicates infinite odds-ratio because one of the cells in the calculation was 0.

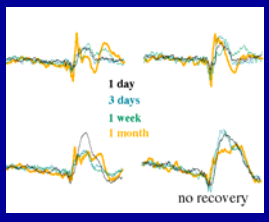
p<0.050 by Fishers Exact Test
p<0.010 by Fishers Exact Test
p<0.005 by Fishers Exact Test
p<0.001 by Fishers Exact Test
All other observations are non-significant

Condition	N	Abnormalities	comments
TBI	68	64.7%	
Normal Control	106	5.7%	
PTSD	30	15.0%	
Substance Abuse	12	25.0%	Only with atrophy
Depression	16	25.0%	↓theta
ADHD	20	10.0%	↓beta/theta
Sleep Disorder	8	12.5%	

Addition of Evoked Responses Can Improve Diagnostic Sensitivity and Specificity

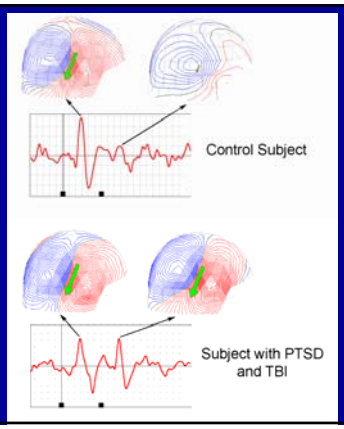
Median Nerve Stimulation

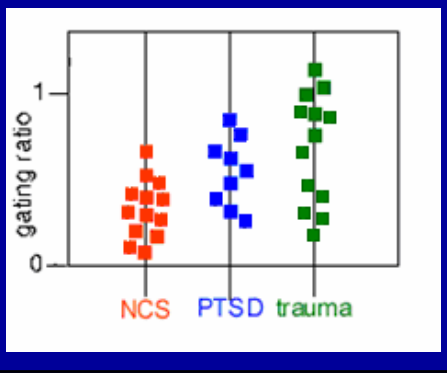




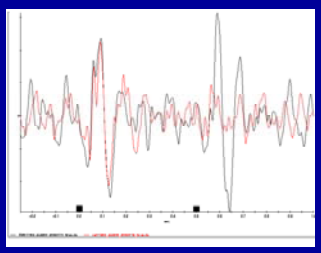
M30/M20 ratio is abnormal in TBI: sensitivity ~ 60%, specificity ~85%

Sensory gating paired tones

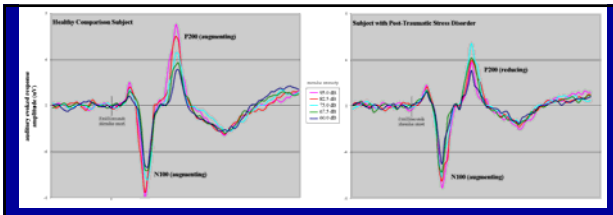




Aricept improves sensory gating and attention in mTBI



- Black – baseline
- Red – with Aricept



Loudness Dependent Auditory Evoked Response -- Database of 20 controls

Control Subjects [N=10] – 90% augment

TBI [N=10] – 10% reducer, 80% augment, 10% over augment

PTSD [N=36]– 60% reducer, 40% augment

Depression [N=16] – 37.5% augment, 62.5% over augment

P3a, P3b

- XXXXOXXXXXOXXX1XXXOXXXXXXXXOXXX2X

- Novel (P3a) – numbers, Target (P3b) – O.
- P3a - orienting response to novel stimuli
  - Augmented in PTSD, reduced in other conditions
- P3b - memory up-dating
  - Reduced in PTSD, TBI, Depression

	DSWA	Median	LDAER	Gaiting	P3a	P3b
mTBI	+++	+++	wnl	+++	wnl/-	-
PTSD	wnl	wnl	60%R	++	++	-
Dep	+ [<theta]	wnl	60% OA	+	-	-
Sub Abuse	+	wnl	wnl	+	-	-
ADHD	wnl	wnl	?	+	-	-
Sleep	wnl	wnl	?	?	-	-

Discrimination of mTBI, PTSD, mTBI+PTSD, and Depression

- Control Subjects = 14/14
- mTBI = 10/14 [4 wnl]
- PTSD = 6/7 [1 wnl]
- mTBI + PTSD = 6/7 [1 PTSD]
- Depression = 6/9 [3 wnl]

- Overall 42/51 [82%] correctly classified

Special Thanks To:
NSF, NIH, A-VAMC, IDVA, Alexian Brothers Medical Center, Mind Research Network

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Chris Amick
Jose Canive
Chris D'Agostino
John Davis
Carly Demopoulos
Kaitlyn DePlonty
Chris Edgar
Brandon Kopald
Tim Lazicki
Patrick McGrath
William Orrison
Sherri Provencal
Robert Thoma

Roland Lee

Diagnostic Value of an Automated MEG Slow-wave Imaging Approach for Mild TBI (mTBI) Patients

Roland Lee, M.D.
University of California San Diego, San Diego, CA

An Automatic MEG Low-Frequency Source Imaging Approach for Diagnosing Mild and Moderate TBI Patients with Blast and Non-Blast Causes

Mingxiong Huang, PhD, Roland R. Lee, MD
mxhuang@ucsd.edu, rrlee@ucsd.edu

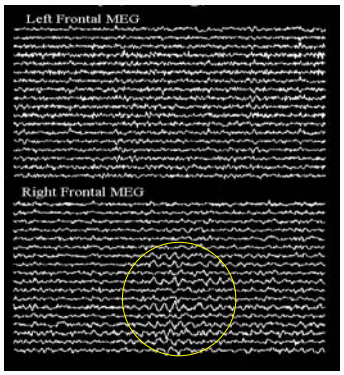
Department of Radiology, University of California, San Diego, CA
VA San Diego Healthcare System, San Diego, CA

Examining Traumatic Brain Injury Patients: Diagnostic Value of an Automatic MEG Slow-wave Imaging Approach for Mild and Moderate TBI Patients with Blast and Non-Blast Causes

- Traumatic brain injury (TBI) is a leading cause of sustained impairment in military and civilian populations.
- However, mild (and some moderate) TBI can be difficult to diagnose because the injuries are often not visible on conventional acute MRI or CT.
- Injured brain tissues in TBI patients generate pathological low-frequency neuronal magnetic signal (peaked at 1-4 Hz) that can be measured and localized by magnetoencephalography (MEG) (Lewine et al., 1999, Huang, et al., 2009).
- Our first study examined 10 patients with mild TBI (ages 25 ± 11), 9 of whom had normal CT/MRI. 14 normal age-matched control subjects.

Abnormal MEG Slow-waves (1-4 Hz, delta-waves) are Characteristic of Neurological Injuries in the Brain

- Stroke
- Brain tumor
- Epilepsy
- Traumatic brain injury



MEG Data Acquisition and Analysis for Detecting Abnormal Slow-waves

Resting state spontaneous MEG recording for 15 minutes

↓

MaxFilter [1] and Independent Component Analysis to remove artifacts (heart, eye, etc.) and reduce noises

↓

Use VESTAL and DCBF to localize MEG slow-wave generators [2] with real-shape boundary element model as the forward solution

↓

Non-parametric statistical analysis for controlling the multiple comparison problem and obtain statistical significances

[1] Taulu S and Simola. Phys. Med. Biol. 51: 1759-1768, 2006.
[2] Huang, et al., NeuroImage 31(3):1025-1037, 2006.

DTI Data Acquisition and Analysis

1.5T GE MRI system: TR=15.1 sec, TE = 80.4 ms, FOV = 24 cm, 54 oblique slices AC/PC-aligned encompassing the whole brain, and 2.5 mm slice thickness). b-value=1000 s/mm^2 and along 51 directions

↓

An affine linear registration and Diffusion Toolbox (FDT) in FSL software package [1] to obtain the diffusion parameters (FA, eigen-values, eigen-vectors, etc.)

↓

FA , L1, L2, L3 asymmetry analysis

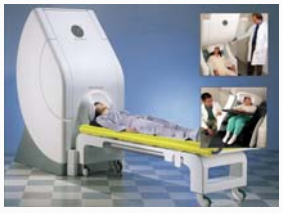
↓

Probabilistic Tractography to trace the white-matter tracts to the gray-matter

Conventional Clinical MRI
- T1-weighted
- T2*-weighted
- T2-weighted with ASSET
- FLAIR
- DWI

[1] Behrens et al., Magn Reson.Med. 50: 1077-1088, 2003 -- fsl.fmrib.ox.ac.uk/fsl/fdt/
[2] Smith et al., Neuroimage 31: 1487-1505, 2006.

Whole-Head 306-channel MEG System and 1.5T MRI System

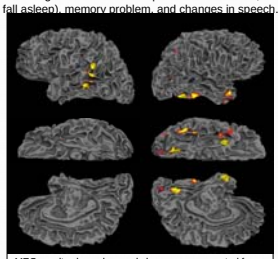


MRI field strength: 1.5 T

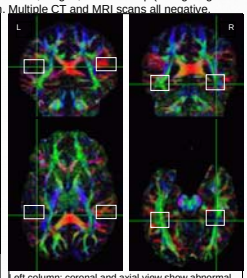
MEG SQUID sensor sensitivity: ~ fT (10^{-15} T)

Mild TBI due to Sport-related Accidents with NO Visible Lesion on CT or MRI, but with Abnormal MEG Slow-waves and DTI

•History: 17-year old, male football player, who suffered 3 mTBIs while playing football. 1st and 2nd concussions separated by a few weeks, and 3rd a few months later. After the 1st injury: headaches. After the 2nd injury: headaches, dizziness, and extreme fatigue while performing any mental task. Following the 3rd concussion: pressure headaches, dizziness, fatigue, altered sleep (taking longer to fall asleep), memory problem, and changes in speech. Multiple CT and MRI scans all negative.



MEG results show abnormal slow-waves generated from two regions in a TBI patient: 1) left column -- left lateral superior-posterior temporal region, 2) right column --- right inferior-temporal areas. Color threshold p<0.01. The top, middle, and bottom rows are lateral-view, ventral-view, and middle-view, respectively.

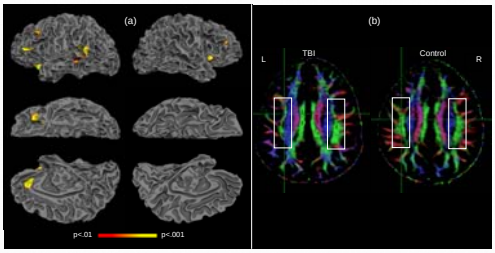


Left column: coronal and axial view show abnormal DTI in superior-posterior temporal lobe of the left hemisphere in a TBI patient. Right column: abnormal DTI in inferior-temporal lobe as part of the inferior longitudinal fasciculus of the right hemisphere.

Huang, ..., Lee, J. NeuroTrauma 2009; 26: 1213-1226.

Mild TBI patient with blast injury with NO Visible Lesion on CT or MRI, but abnormal MEG slow-waves and DTI findings in a Major white-matter tract

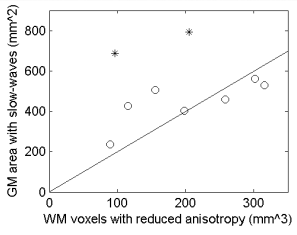
History: blast-induced mTBI patient (male, age 27) caused by an IED. He experienced a loss of consciousness for several seconds and he experienced post-concussive symptoms of fatigue, disordered sleep, dizziness, irritability, anxiety, psychosocial and personality disturbances, and memory loss since the incident. His clinical MRI and CT scans were negative.



Multiple neuronal sources that generated MEG slow-waves in a mild TBI patient. Bilateral LPFC, left OFC, left ACC, and left temporal areas regions showed abnormal slow-wave activities. DTI reveals profound abnormality of left SLF in the TBI patient. The normal control showed much thicker anterior-posterior oriented diffusion in SLF (green color) than the TBI patient in the left hemisphere. The white boxes are used for ROI analysis.

Huang, ..., Lee, J. NeuroTrauma 2009; 26: 1213-1226.

MEG and DTI correlation



Huang M.X, ..., Lee R.R. J. NeuroTrauma 2009; 26: 1213-1226.

Summary of Integrated MEG-DTI Study of TBI Patients

- The multimodal imaging approach with MEG and DTI is substantially more sensitive than conventional CT and MRI in detecting subtle neuronal injury in mild TBI.
- MEG slow-waves accrue from de-afferentation in cortical gray-matter neurons that connect to white-matter fibers with axonal injury.
- MEG slow-waves in TBI patients can show a focal, multi-focal, and/or diffuse pattern with multiple generators, indicating more diffuse cortical de-afferentation due to axonal injury.
- Reduced anisotropy in local (non-major) white-matter fiber tracts (as measured by DTI) will lead to focal abnormal delta-waves (as measured by MEG) from cortical gray-matter overlaid with these local tracts. On the other hand, reduced anisotropy in major white-matter fiber tracts will lead to multi-focal or distributed patterns of abnormal delta-waves generated from multiple cortical gray-matter areas that can be remote in location but functionally and structurally linked by the injured major white-matter fiber tracts.
- In some cases, abnormal MEG slow-waves were observed in mild TBI patients with no visible DTI abnormality
- MEG slow-wave findings were consistent with the clinical symptoms of the mTBI patients.

Two Key Issues of using MEG Slow-wave exam for diagnosing TBI

- Q1: What is the neurophysiology for slow-wave generation (1-4 Hz) in TBI?
- A1: MEG-DTI integration shows: De-afferentation
- Q2: Is there a way to develop an automated MEG slow-wave source imaging approach for objective diagnosis of TBI?
- A2: Frequency-domain VESTAL MEG slow-wave source imaging method

Examining Traumatic Brain Injury Patients: Diagnostic Value of an Automatic MEG Slow-wave Imaging Approach for Mild and Moderate TBI Patients with Blast and Non-Blast Causes

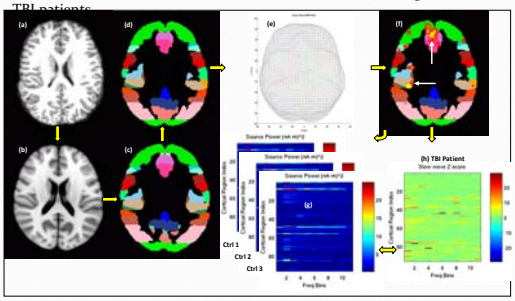
- Injured brain tissues in TBI patients generate pathological low-frequency neuronal magnetic signal (peaked at 1-4 Hz) that can be measured and localized by magnetoencephalography (MEG) (Lewine et al., 1999, Huang, et al., 2009).
- Our second study examines the diagnostic value (successful diagnostic rate) of our new automated and operator-independent MEG slow-wave source imaging method in 45 mild TBI (23 caused by blast and 22 with non-blast causes) and in 10 moderate TBI patients.

Research Subjects

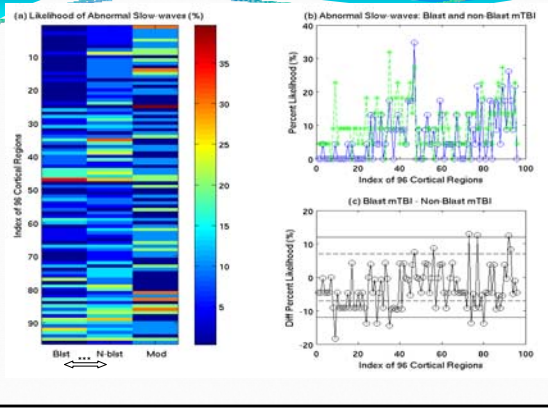
- Resting-state MEG data (spontaneous recording for slow-wave detection) were collected using a whole-head MEG system with 306 MEG channels at the UCSD MEG Center.
- Group 1 contains 23 military mild TBI patients whose injuries were caused by blast.
- Group 2 contains 22 civilian mild TBI injured by non-blast causes (i.e., motor vehicle accident, sports, and falls).
- Group 3 contains 10 moderate TBI that were not blast-related.
- Group 4 contains 28 age-matched healthy control subjects.

MEG Slow-wave Source Imaging

Resting-state MEG data were analyzed using our new improved frequency-domain VESTAL [2] method to obtain the source images for the low-frequency range (1-4Hz). Normative Database from healthy control subjects were used as baseline threshold to detect abnormal slow-wave generation in TBI patients.



Pattern of Injuries for Different TBI Groups



Blast versus Non-Blast TBI

- The percent likelihood of slow-wave generation in mild blast TBI group is highly correlated with that of the mild non-blast TBI group ($r=0.62$, $p< 10^{-10}$, $df=94$): asterisks and double-headed arrow.
- The percent likelihood of slow-wave generation in the moderate TBI group does not correlate with those from either the mild blast TBI or mild non-blast TBI groups.
- Fig. (c) shows the *difference* of percent likelihood measure between mild blast versus mild non-blast TBI groups (i.e., the first column minus the second column in Figs. (a)(b)).
- Only 6 cortical regions showed > than 7% in the measure of likelihood difference, indicating higher likelihood of slow-wave generation in mild blast TBI group than the mild non-blast TBI group.
- In contrast, 29 cortical areas showed < than -7% in the measure of likelihood difference which indicates that more regions in the mild non-blast TBI showed slow-waves than in the mild blast TBI group.

MEG Slow-wave Exam Correlates with Post-concussive Symptoms

- The PCS were coded as "1"s for existence of symptoms and "0"s for absence of symptoms in 28 categories: 1) headaches, 2) dizziness, 3) fatigue, 4)… from ~ the HISC battery.
- The total PCS scores (summing up over all categories) were: 6.4 ± 1.5 for mild blast TBI, 6.6 ± 3.1 for the mild non-blast TBI, and 5.4 ± 2.6 for the moderate TBI groups. No significant group differences were observed.
- $N_{slow\text{-}wave\_sum}$ is significantly correlated with N_{PCS_sum} ($r=+0.28$, $p<0.05$, $df=53$) in 55 TBI patients
- Regarding Individual PCS, $N_{slow\text{-}wave\_sum}$ significantly correlated with blurred vision ($r=+0.27$, $p<0.05$, $df=53$), other visual difficulties ($r=+0.35$, $p<0.01$, $df=53$), and depression ($r=+0.35$, $p<0.01$, $df=53$). In addition, trends towards significance were observed between $N_{slow\text{-}wave\_sum}$ with memory difficulty ($r=+0.22$, $p=0.09$, $df=53$) and with coordination problems ($r=+0.23$, $p=0.08$, $df=53$) in these TBI patients.

Summary: MEG for TBI

- Diagnostic Rates: Our new automated MEG source imaging approach for localizing abnormal slow-waves in TBI patients has 90% successful diagnostic rate in mild TBI and 100% for moderate TBI groups, substantially higher than the conventional neuroimaging methods (CT and MRI at ~10% in these patients). Threshold for delta-wave power was set for NO false positives in normal controls.
- Injury Patterns: The patterns of slow-wave generation between mild blast TBI and mild non-blast TBI patients were highly correlated, but they do not definitely correlate with that from the moderate TBI patients.
- Vulnerability: The (military) mild blast TBI patients show lower likelihood of abnormal slow-wave generation than mild non-blast TBI patients, suggesting that the helmet and armor have a protective effect in military personnel.

Acknowledgments:

This work was supported in part by Merit Review Grants from the Department of Veterans Affairs to MX Huang (051455 and 060812) and RR Lee (E4477-R), and by a research grant from the McDonnell Foundation via the Brain Trauma Foundation (PI: Jamshid Ghajar, site PIs: Lee and Huang).

VASDHS

Sharon Nichols, Ph.D.
Rebecca Theilmann, Ph.D.
Dewleen Baker, M.D.
Michael Levy, M.D.
Raul Coimbra, M.D.
John D'Andrea, M.D.
Doris Trauner, M.D.
Tao Song, Ph.D.
Annemarie Angeles
Ashley Robb

Angela Drake, Ph.D.
Robert McLay, M.D.
Paul Hammer, M.D.
Martin Holland, M.D.
Sarah Asmussen, Ph.D.
Catherine Cheung

John Gates Lecture 2011

Use of MEG/MSI interictal spikes in presurgical ICEEG planning

William Sutherling, M.D.
Huntington Memorial Hospital, Pasadena, CA

William Sutherling

NOTES

NOTES

AKNOWLEDGMENT

Grateful acknowledgment is made to the following organizations for their generous support of this workshop in the form of unrestricted educational grants.

EVALUATION

Please identify yourself: ☐ Neurologist ☐ Neurosurgeon
☐ Radiologist ☐ Technologist
☐ Other _____

Please rate the effectiveness using the following scale:
1 = poor 2 = below average 3 = average 4 = above average 5 = excellent

	clarity of the information presented	relevance of the information to your clinical practice	objectivity, balance & scientific rigor
Michael Longacre	① ② ③ ④ ⑤	① ② ③ ④ ⑤	① ② ③ ④ ⑤
Jefrey Lewine	① ② ③ ④ ⑤	① ② ③ ④ ⑤	① ② ③ ④ ⑤
Eduardo Castillo	① ② ③ ④ ⑤	① ② ③ ④ ⑤	① ② ③ ④ ⑤
Susan Bowyer	① ② ③ ④ ⑤	① ② ③ ④ ⑤	① ② ③ ④ ⑤
Richard Burgess	① ② ③ ④ ⑤	① ② ③ ④ ⑤	① ② ③ ④ ⑤
Julia Stephen	① ② ③ ④ ⑤	① ② ③ ④ ⑤	① ② ③ ④ ⑤
Susan Bowyer	① ② ③ ④ ⑤	① ② ③ ④ ⑤	① ② ③ ④ ⑤
Jefrey Lewine	① ② ③ ④ ⑤	① ② ③ ④ ⑤	① ② ③ ④ ⑤
Roland Lee	① ② ③ ④ ⑤	① ② ③ ④ ⑤	① ② ③ ④ ⑤
William Sutherling	① ② ③ ④ ⑤	① ② ③ ④ ⑤	① ② ③ ④ ⑤

Rate your overall satisfaction with the opportunity to network with colleagues.	① ② ③ ④ ⑤
Rate your overall satisfaction with the quality of this conference/workshop.	① ② ③ ④ ⑤
Please rate your satisfaction with the organization of the conference/workshop.	① ② ③ ④ ⑤
How would you rate the cost of registration versus what you personally got out of the conference?	① ② ③ ④ ⑤

What other topics should ACMEGS address in future conferences?

1) _____

2) _____

3) _____

Additional comments?_____

_____

Did you perceive commercial bias in any of the presentations? ☐ No ☐ Yes

Explain: _____

ACMEGS DOCUMENTS

- ACMEGS presentation to APC Panel
- AAN letter to APC Panel regarding MEG cost report
- AAN letter to CIGNA regarding MEG policy review

List the financial relationship of presenter(s), if any, with any company whose product, services, or procedures are under consideration.
I am the Director of the MEG Department at the University of Utah Medical and President of the American Clinical MEG Society. I am not affiliated nor represent with any manufacturer.
Physicians' Current Procedural Terminology (CPT) code(s) involved:
95965, 95966, 95967
APC(s) affected
067, 065
Description of the issue(s)
Current reimbursement does not reflect actual cost of procedure
Clinical description of the service under discussion *(with comparison to other services within the APC)*
MEG, spontaneous
Recommendations and rationale for change
Allow line on Cost Report or Hand Calculate Reimbursement for MEG
Expected outcome of change
A reimbursement that reflects actual costs
Potential consequences of not making the change
Lack of patient access due to unsustainable economic resources

Michael E Funke, MD, PhD
President
American Clinical MEG Society
729 Arapeen Drive, Salt Lake City, UT 84108
email: michael.funke@hsc.utah.edu
phone (801) 585-6840

American Clinical MEG Society

- ACMEGS appreciates the opportunity to address the Meeting of the Advisory Panel on Ambulatory Payment Classification Groups and commends CMS on its efforts to evaluate and improve the APC groups under the hospital outpatient prospective payment system.
- ACMEGS is a non-profit 501c6 trade association with a membership of more than 20 specialized clinical MEG centers in the United States. Founded in 2006 by physician-leaders committed to setting a national agenda for quality epilepsy care, ACMEGS educates public and private policymakers and regulators about appropriate patient care standards, reimbursement and medical services policies.

American Clinical MEG Society

- ACMEGS is committed to ensuring patient access to life-saving and life- enhancing devices in the most appropriate settings and supports a system with payment weights and payment rates that include sufficient resources to account for the costs of the medical technologies associated with hospital outpatient care.

Today's Objectives

- Acknowledgment from the Advisory Panel on Ambulatory Payment Classification Groups that current methodology for calculating an appropriate reimbursement rate for MEG is flawed.
- Recommend to CMS appropriate means to mitigate the situation.

Magnetoencephalography Reimbursement History

In 2005, MEG transitioned from a new technology APC to a clinical APC. The reimbursement for MEG has declined significantly since 2005. The actual reductions are:

CPT 95965 by 35% (2005: $5,250; 2011: $3,414) APC 67
CPT 95966 by 35% (2005: $1,450; 2011: $940) APC 65
CPT 95967 by 1% (2005: $950; 2011: $940) APC 65

2005 APC Advisory Panel Meeting

- In August 2005 MEG was brought to the attention of the APC Panel. It was our contention then, as it is now, that the cost data utilized to determine an appropriate reimbursement rate for MEG is not correct.
- At the conclusion of the presentation the panel recommended that *CMS maintain CPT codes 95965, 95966 and 95967, magnetoencephalography (MEG), in their 2005 new technology APCs. The panel also recommended that CMS collect more external data hospital data and provide a detailed review of the data for the Panel's consideration at its next meeting.*

CMS Responds to 2005 APC Panel Recommendation

- Regrettably CMS did not agree with the panel's decision and placed MEG in a clinical APC at a significantly lower reimbursement
- CMS further stated, "*As suggested by the APC Panel, we will continue to study the APC assignments for these procedures over the coming year and invite members of the public to submit any information they believe will be helpful to us.*"
- Those of us who presented that day felt that the panel agreed that there were disparities in the cost data and had challenged us to determine the reason for these errors.

CMS Responds to 2005 APC Panel Recommendation

CMS-1427-FC

Federal Register / Vol. 70, No. 217 / Thursday, November 10, 2005, page 685768579

In addition to the written comments we received on our proposed rule, hospital and manufacturer representatives made presentations to the APC Panel during its August 2005 meeting. At the time, the Panel recommended that CMS retain the MEG procedures in their current New Technologies APCs and that we collect more external data and provide a detailed review of the data for the Panel's consideration at its next meeting.

Problem

MEG & EEG costs are indistinguishable as they share the same:

- Cost Line on the Medicare Cost Report
- Revenue Code on the UB-04

MEG & EEG costs are indistinguishable!

- Medicare Cost Report
  - Line 5400
    - Noridian (MAC) granted MEG Line 54.01 as a remedy
- Revenue Code on UB-04
  - 0740 EEG (prior to April 1, 2010)
  - 086x – Magnetoencephalography (MEG) by National Uniform Billing Committee (NUBC)
    - NUBC also recommended that we request a separate line on the Medicare Cost Report

CMS 2008 Claims Data

The chart below contains claims data (2008) referenced by CMS in calculating the 2010 OPPS proposed rule.

Procedure	EEG	EEG	EEG	EEG	MEG
APC	0213	0213	0213	0213	0067
CPT	95816	95819	95812	95813	95965
Utilization	37,894	40,938	3,401	1,180	25
Costs	$151.88	$164.06	$175.63	$257.73	$2945.61

CCR Calculations

Facility	EEG CCR	MEG CCR
University of Utah Med Center	0.3199	0.7345
Wake Forest University Med Cnt	0.3370	0.8691
University of Pittsburg Med Cnt	0.0974	0.5844
Alexian Brothers Neuro Institute*	0.2138	0.4516
Average	0.2420	0.6599

* MEG operation is a joint venture, therefore only 50% of personnel cost are included

CMS Responds to Comments; Calculation of Reimbursement for MEG

CMS-1414-FC

Federal Register / Vol. 74, No. 223 / Friday, November 20, 2009 / Rules and Regulations / page 60448

*We initially assigned MEG services to New Technology APCs based on the information available to us at the time about the expected hospital costs. For CY 2006, **we believed** that we had sufficient claims data to enable us to make informed decisions regarding the proper clinical APCs for assignment of MEG services. We note that the volumes of claims for MEG services have remained stable since we moved them to clinical APCs in CY 2006. We have **no reason to believe** that the costs that we have derived from our standard cost estimation process for the CY 2010 OPPS fail to appropriately reflect the relative costs of MEG services in relation to the costs of other services paid under the OPPS, **nor do we have reason to believe** that payment at the rates under which these services were paid under the New Technology APCs in CY 2005 are justified.*

CMS Responds to Request for Separate Cost Line

CMS 1498-P

Federal Register / Vol. 75, No. 85 / Tuesday, May 4, 2010 / Proposed Rules / page 23880

Finally, with respect to MEG services, the extremely low volume of claims for MEG services furnished to Medicare beneficiaries in the hospital outpatient setting and the extremely low number of hospitals that report these codes relative to the volumes we typically have considered in adding both standard and nonstandard cost centers to the cost report lead us to conclude that a specific cost center for MEG is not justified at this time.

Questions for Panel

Have we presented enough evidence to document that the current methodology of calculating an appropriate reimbursement for 95965 (MEG) is flawed?

Does the Panel agree that the currently calculated reimbursement rate for 95965 (MEG) does not fairly represent its actual costs?

Thank You

ACMEGS appreciates the opportunity to bring this matter to the attention of **Advisory Panel on Ambulatory Payment Classification Groups** and ask that you recognize the unique challenges associated with MEG and support a fair calculation of an appropriate reimbursement rate.

American Academy of Neurology

American Academy of Neurology
Professional Association

1080 Montreal Avenue
St. Paul, Minnesota 55116

Tel: (651) 695-1940
Fax: (651) 695-2791

www.aan.com

August 10, 2010

E. L. Hambrick, MD, JD, CMS Medical Officer
Chair, Ambulatory Payment Classification Advisory Panel
7500 Security Boulevard
Mail Stop C4-05-17
Baltimore, Maryland 21244-1850
Email: CMS APCPanel@cms.hhs.gov

RE: Appropriate Payment Calculation for MEG by Adding a line on the MCR

Dear Dr. Hambrick,
The American Academy of Neurology ('AAN' or 'Academy') is the premier medical specialty society for more than 22,000 neurologists and neuroscience professionals dedicated to providing the highest quality patient-centered care for patients suffering from complex, chronic neurologic disease such as Alzheimer's, Parkinson's disease, ALS, and epilepsy. The AAN writes in support of the presentation by the American Clinical Magnetoencephalography (MEG) Society (ACMEGS) during the August meeting of the APC Advisory Panel to respectfully ask that CMS add a specific line for Magnetoencephalography (MEG) on the Medicare Cost Report (MCR) and recalculate an appropriate payment for MEG.

MEG, also known as Magnetic Source Imaging (MSI) is the noninvasive measurement of the magnetic fields generated by brain activity: it is one of several neurophysiological tests used to localize brain function**.** EEG, like MEG, measures brain activity with millisecond resolution. Both are far more sensitive than PET and SPECT to rapid changes in brain activity. Such rapid changes occur during the propagation of a seizure. EEG can be recorded noninvasively like MEG but surface EEG has limited resolution: it usually has inadequate sensitivity for pre-surgical decisions. The value of MEG lies in its ability to provide either new and non-duplicative or supplemental information to existing localizing technologies. For AAN's complete review of the technology, visit: http://www.aan.com/globals/axon/assets/7052.pdf.

Currently, there is no specific line item for MEG on the Medicare Cost Report (MCR) and MEG costs are combined with EEG on line 54 of the MCR. Therefore, the cost-to-charge ratio (CCR) for MEG cannot be distinguished. This has resulted in the costs for MEG—which are significantly higher—being diluted by the much lower costs (and much higher utilization) of EEG.

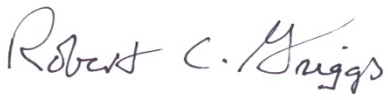
The isolation of MEG on the MCR results in a significant impact on its calculated cost-to-charge ratio (CCR). One facility petitioned Noridian (a Medicare Administrative Contractor), requesting a subscript to line 54 to account for MEG. The appeal was granted and line 54.01 was generated. The recalculated CCR for 2008 went from 0.3199 to 0.7345. In another institution, the recalculated CCR went from 0.3370 to 0.8691. In yet another institution the recalculated CCR was

0.5844. The delta in all instances is significant and would have a dramatic effect in determining the final Medicare reimbursement as well as setting future years payment rates. These differences prove the current methodology for calculating fair reimbursement for MEG is flawed.

Until recently, the recommended revenue code for MEG was the same revenue code for EEG. However, effective April 1, 2010, the National Uniform Billing Committee (NUBC) created a new revenue code category for MEG (086x). After creating the new revenue code, the NUBC—which included CMS representatives—highly recommended that ACMEGS and other interested groups also request that the APC Panel make the proposed modification above to the Medicare hospital cost report. Therefore the AAN respectfully requests that the APC panel create a separate line item for MEG on the MCR. Combined, the two changes will go a long way toward ensuring fair reimbursement for this procedure.

Thank you for your attention to these comments. Should you have questions or require further information regarding this issue, please contact Katie Kuechenmeister, AAN staff, by phone at (651) 695-2783 or by email at kkuechenmeister@aan.com.

Sincerely,



Robert C. Griggs, MD, FAAN
President, American Academy of Neurology

Cc: **Catherine M. Rydell, CAE**
Executive Director and CEO, American Academy of Neurology
American Academy of Neurology Foundation
AAN Enterprises, Inc.

Rod Larson
Chief Health Policy Officer, American Academy of Neurology

American Academy of Neurology
American Academy of Neurology Professional Association

1080 Montreal Avenue
St. Paul, Minnesota 55116

Tel: (651) 695-1940
Fax: (651) 695-2791

www.aan.com

November 16, 2010

Julie B. Kessel, MD
Medical Director, Emerging Health Care Technology and Medical Policy

Patricia Loudis, MD, MBA
Medical Director, Blue Bell

Victoria Springer
Coverage Policy Research Nurse

Douglas R. Hadley, MD
Medical Officer, Coverage Policy Unit

RE: Further AAN Comments on Cigna's MEG Coverage Policy (# 0248)

Dear Dr. Kessel, Dr. Loudis, Ms. Springer, and Dr. Hadley;

In follow up to our September 21, 2010 discussion regarding Cigna's medical coverage policy #0248 for Magnetoencephalography (MEG) services, the American Academy of Neurology (AAN) is pleased to submit the following additional comments. The AAN provides careful reviews of medical policies for a number of insurers and, as such, we welcome this opportunity to address Cigna's conclusions surrounding this technology.

The AAN subject matter experts hope that the initial conversation succeeded in facilitating a higher level of mutual understanding in terms of the AAN's view of accountable utilization of MEG technology in the process of delivering the best care to patients at a lower cost; an undisputed common goal among our organizations. As you requested during that call, the remainder of this letter will provide further comments on the current Cigna coverage policy for MEG and will outline common practice with respect to the ordered MEG studies.

It is our understanding that, although Cigna's is a non-coverage policy, MEG is still approved with and without prior-authorization. In the majority of cases where an independent medical review has been performed by a qualified neurologist or neurosurgeon on behalf of Cigna, MEG examinations have been approved as exceptions to the standing policy.

Our review of Cigna's current MEG coverage policy has found some discrepancies, especially when taking into account the current clinical literature:

1. Functional mapping of eloquent cortical areas prior to tumor resection
2. Pre-surgical evaluation of patients diagnosed with intractable epilepsy

First, in regards to functional mapping of eloquent cortical areas prior to tumor resection:
The current gold-standard for identifying eloquent areas of the brain that should be spared during the surgical resection is electro-cortical stimulation (ECS). ECS is a time intensive procedure whereby electrical current is applied directly to cortex.

Generally, the patient is awake and participatory (speech mapping). Functional mapping of the cortex through ECS significantly extends the duration of anesthesia and time in the operating room. The AAN's recent medical policy for MEG, notes that such direct recording and mapping procedures [e.g., ECS and intracranial EEG or monitoring (ICEEG or ICM), please see later] have significant risks. These procedures extend the duration of surgery (and hence anesthesia), are uncomfortable to the patient, and carry increased risk of morbidity. The AAN model policy further concludes that MEG mapping has been directly compared to ICEEG/ICM and the two procedures produce equivalent results in regards to localization of eloquent cortex. Finally, in general, only very circumscribed areas of cortex (e.g., part of one lobe) are evaluated with invasive procedures like ICEEG/ICM or even electrocorticography (ECoG, please see below) due to significant increase in the risk of morbidity (hemorrhage, infection, etc). Thus, even when these invasive procedures are unavoidable, their risks may be decreased with the guidance from non-invasive·procedures like MEG or functional magnetic resonance imaging (fMRI).

The current Cigna policy relies entirely on three independent studies in making a decision that MEG is "investigational" for this indication (Korvenoja et al. 2006; Ganslandt et al. 2004; Schiffbauer et al. 2001; see pg 8 of Coverage Policy #0248-December 2009 revision). The Cigna policy states:

(a) "*Results indicated that MEG enabled more reliable localization of the central sulcus compared with fMRI*". In 100% of patients, MEG localized the central sulcus correctly and the results were concordant with those at intra-operative mapping, whereas fMRI correctly localized the central sulcus in 73 % of cases (Korvenoja et al. 2006).

(b) "*Functional MRI may be an alternative more readily available but this method may not to be as accurate in localizing neuronal activity as MSI*" (Ganslandt et al. 2004).

(c) (c) "*To safely maximize tumor resection, preoperative functional imaging using MSI or other techniques and intra-operative electrophysiological mapping of the cerebral cortex and the white matter tracts is necessary*" (Schiffbauer et al. 2001).

Cigna does not consider fMRI an investigational technique. According to Medical Policy Number #0478, "*CIGNA covers fMRI as medically necessary when it is being used as part of a preoperative evaluation for a planned craniotomy and is required for localization of eloquent areas of the brain such as those responsible for speech, language, motor function and senses, which might potentially be put at risk during the proposed surgery*".

Nevertheless, Cigna's MEG coverage policy describes MEG/MSI as superior to fMRI, and then concludes that MEG procedures are investigational and not covered, while fMRI procedures are standard (non-investigational) and covered. We believe this to be a discrepancy worthy of correction.

Second, we would like to address issues of the current policy regarding the presurgical evaluation of patients diagnosed with intractable epilepsy:

The current gold-standard for localizing epileptic foci involves long-term intracranial monitoring (ICM) of seizures with surgically placed subdural grids and/or depth electrodes also known as intracranial EEG (ICEEG). Such ICEEG utilizes the same cortical contacts that are often used to stimulate cortex in the case of ECS and thus the techniques carry similar risks. Again, the AAN's recent MEG policy statement notes that such direct recording and mapping procedures (e.g., ECS and ICEEG/ICM) have significant risks. The review further concludes that MEG localization of the epileptogenic zone (an area of the brain that has to be removed in order to deem a patient seizure-free) has been directly compared to ICEEG/ICM and the two procedures produce equivalent results in regards to localization of epileptiform activity. As stated above, in general, only very circumscribed areas of cortex (e.g., part of one lobe) are evaluated with invasive procedures like ICEEG/ICM. Thus, even when these invasive procedures are necessary, they typically require guidance from non-invasive·procedures like MEG or, at times, fMRI.

Of the available non-invasive methods for guiding grid placement, magnetic source imaging (MSI) is the most well-established in the clinical literature. MSI involves integration of functional information from MEG with structural information from magnetic resonance imaging (MRI). The resultant magnetic source localization images provided two and three dimensional structural-functional blue-prints of brain. These allowed the neurosurgical team to determine the most effective approach to resection of the tumor and epileptic focus. In short, MEG/MSI provides—non-invasively—a neuro-navigational map that enables a neurosurgeon to accurately access and safely resect a lesion or epileptic focus. As recently stated by the AAN, fMRI, PET, Wada, SPECT, and other functional tests are useful in the evaluation of patients prior to surgery, but none of these techniques has been as rigorously and prospectively tested by evidence-based methodology as MEG.

When it comes to patients with epilepsy, only a tiny fraction will ever be considered as surgical candidates (i.e., patients that have failed multiple anti-epileptic drugs and have severe symptoms). In fact, according to the best estimates, this only potential cure for epilepsy is offered to not more than 1 in 30-50 patients in whose life it could make a drastic difference and considerably cut the cost of care over their lifetime.

The current Cigna MEG policy places heavy of emphasis on localizing brain tissues that are generating the seizure activity (i.e., epileptic foci). The document reviews approximately 30 epilepsy studies that evaluated MEG's clinical utility. All of the cited peer-reviewed epilepsy articles in this policy statement universally indicate MEG to be of utility in the identification of epileptic foci. The positive views held by authors of these articles are, with but one exception, included in the policy statement, yet the policy finally concludes MEG is an investigational procedure. Thus, there is a notable discrepancy between outcomes cited in the peer-reviewed literature and the conclusions of the policy writers.

In a review of MEG technology, one would hope that assigned professionals with a solid understanding of the relevant diseases and evaluating technologies would participate in the review process. This however does not appear to have been the case for the current MEG assessment. MEG is a technology most relevant to the practice of epileptologists, neurologists and neurosurgeons. The way that Cigna applied standards to MEG technology shows a bit of a lack of understanding of the technology and the relevant disease conditions, especially with respect to the pre-surgical evaluation of patients with tumors and/or epilepsy. It seems that no practicing epileptologist or neurosurgeon with an understanding of and experience with using MEG were consulted in the crafting of the current policy.

For example, (Cigna policy for MEG, page 11): the MEG literature is criticized for a lack of a randomized trial comparing outcomes of epilepsy patients that receive versus do not receive MEG. The concluding sentence of the policy reads, "*More definitive data from large, randomized, prospective controlled studies will help evaluate MEG's efficacy and clarify patient selection.*" It is a well known fact in the epilepsy community that the National Institutes of Health (NIH) has, during peer review of grants proposing this type of randomized trial, explicitly indicated that it would be unethical to deny patients access to a technology that the Food and Drug Administration (FDA), American Medical Association (AMA) and CMS have already judged to have clinical utility based on the peer-reviewed literature.

With respect to selection and ascertainment biases, these are inherent in research on the medical management of patients with epilepsy. In the policy's final summary, it seems as if Cigna is arguing that there is a patient selection problem whereby not all patients that receive MEG mapping procedures undergo neurosurgery. However, in many studies that the policy cites, the MEG results, in combination with other clinical and imaging data, indicate surgery to be a poor option. Following the logic of the policy's criticism, one could come to the impression that these patients should undergo surgery so that one can prove the MEG results were useful in demonstrating surgery was unlikely to be successful. We all agree that this is not a rational approach. The value of diagnostic technology is not only that it leads to

certain procedures, but that it helps patients achieve their optimal outcome(s). In the case of epilepsy, this may mean an exclusion from unnecessary or inappropriate surgery that remains the only potential cure for the right candidates.

The current Cigna MEG policy (page 10) states that the AAN and the American Epilepsy Society (AES) do not mention MEG in their practice parameters for neuroimaging in patients with an apparently unprovoked first time seizure. According to the policy statement, this serves as further evidence that MEG procedures are not considered standard of care. This conclusion is clear evidence that no epileptologists or epilepsy neurosurgeons were consulted in the process of formulating the policy. Of course, MEG imaging is not standard practice for these patients; such patients would not be *surgical* candidates so it would not be appropriate for these patients to undergo MEG procedures. At this point, MEG is a recommended study only for patients undergoing pre-surgical evaluation and this takes place much later after the initial diagnosis once patients meet the criteria for intractable epilepsy.

The most important question in reviewing the literature surrounding MEG should be: "Does inclusion of MEG in the pre-surgical evaluation of a patient significantly improve the quality of outcome?" The answer to this question, universally agreed upon by the directors of comprehensive epilepsy and brain tumor programs throughout the United States is a resounding ***yes.***

As early as 2000 and 2001, technology reviews led major professional organizations to conclude that MEG had established clinical utility in several clinical situations. Subsequently, these organizations sought CPT® codes for MEG from the AMA. These codes were issued by the AMA, and CMS determined MEG medically necessary in 2001. The very fact that the AMA and CMS have recognized the value of MEG/MSI indicates that the method is not investigational, since, in the development of new CPT codes, the CPT Advisory Committees and Editorial Panel require that the “clinical efficacy of the service/procedure is well established in the US peer-reviewed literature."

Conclusion

Once again, thank you for the opportunity to submit additional comments to you regarding the current Cigna medical policy for MEG. We look forward to hearing back from Cigna regarding your decisions, if any, to modify the current policy. Please contact Katie Kuechenmeister, AAN staff, by email at kkuechenmeister@aan.com or by phone at (651) 695-2783 if we may be of further service in the upcoming review of your coverage policy on this technology.

Sincerely,

Joel M. Kaufman, MD
Chair, Payment Policy Subcommittee
American Academy of Neurology Professional Association

ACMEGS BYLAWS

BYLAWS
OF
AMERICAN CLINICAL MAGNETOENCEPHALOGRAPHY SOCIETY, INC., A NON-PROFIT CORPORATION

ARTICLE I
ORGANIZATION

1.1 The name and charitable purposes of the organization shall be as set forth in its Articles of Organization. In addition to the charitable purposes as set forth in the Articles of Organization, the organization may work cooperatively with other national and international magnetoencephalography (MEG), neurology, neurosurgery, and radiology organizations in determining how best to meet the clinical needs of MEG sites within the United States. These Bylaws, the powers of the organization and of its directors and officers, shall be subject to the Articles of Organization as in effect from time to time. The principal office of the organization in the Commonwealth of Massachusetts shall initially be located at the place set forth in the Articles of Organization.

1.2 The organization may have a seal which shall be in such form as the Board of Directors may, from to time to time, adopt or amend.

1.3 The organization may at its pleasure by a vote of the Members (as hereinafter defined) change its name.

1.4 The pronoun “he” or “his,” when appropriate, shall be construed to mean also “she” or “her” and the word “chairman” shall be construed to include a female.

ARTICLE II
MEMBERSHIP

2.1 Membership in this organization shall be open to those who support the purpose statement of the organization as set forth in the Articles of Organization and meet the qualifications set forth in Section 2.2. Continuing membership is contingent upon being up-todate on membership dues which shall be paid annually on or before September 1st of each year.

2.2 There shall be three (3) classes of membership in the organization; namely, a Site-Designated Member class, a General Member class and an Associate Member class.

A. “Site-Designated Members” are those individuals so designated by each clinical site that has paid its membership dues. Each site may designate up to 2 members. Only site-designated members are eligible to be members of the Board of Directors”.

B. "General Members" shall include those individuals involved in the clinical use of magnetoencephalography (MEG) alone or in combination with electroencephalograms (EEGs), magnetic resonance imaging (MRI) or computerized axial tomography (CAT) scans and possessing a medical degree (M.D.), a Ph.D. in one of the aforementioned fields, or some equal equivalent degree.

C. "Associate Members" shall include clinicians, or their clinical assistants, involved with the use of magnetoencephalography (MEG) alone or in combination with electroencephalograms (EEGs), magnetic resonance imaging (MRI) or computerized axial tomography (CAT) scan equipment and students with an interest in any of those fields.

2.3 Individuals wishing to join the membership of this organization for either the General or Associate class of membership shall apply for admission and be nominated by two (2) existing members of the member class for which membership is sought; provided, however, that those individuals identified as directors in the Articles of Organization as originally filed with the Massachusetts Clerk of the Commonwealth shall be automatically admitted into the Member class of this organization without further application. The Membership Committee shall review and recommend either admission or denial into the membership of this organization for each application submitted, after which the entire Board of Directors shall vote to accept or reject the Membership Committee's recommendation. The vote of the Board of Directors shall be final.

2.4 The dues for each membership class shall be reviewed and set annually by the Board and any proposed changes shall be voted on at the annual membership meeting.

2.5 Only those members who are current on their membership dues and are in the Members class shall be eligible to vote at any annual or special meetings of the membership.

ARTICLE III
MEMBERSHIP MEETINGS

3.1 The first annual membership meeting of this organization shall be held on August 26, 2006 and thereafter shall be held on such date as determined by vote of the membership at the prior year's annual membership meeting.

3.2 The Clerk shall cause to be mailed to every member in good standing at its address as it appears in the membership roll book in this organization a notice telling the time and place of such annual meeting.

3.3 Meetings of the membership may be held at such time and place, within or without the Commonwealth of Massachusetts, as shall be stated in the notice of the meeting or in a duly executed waiver of notice thereof. Notices of meetings shall be sent

to all members at their addresses as they appear in the membership roll book at least ten (10) days before the scheduled date set for such meeting. If mailed, notice is given when deposited in the United States mail, postage prepaid, directed to the member at such member's address as it appears on the records of the organization. Without limiting the manner by which notice otherwise may be given effectively to members, any notice to members given by the organization shall be effective if given by a form of electronic transmission consented to by the member to whom the notice is given. Any such consent shall be revocable by the member by written notice to the organization. Any such consent shall be deemed revoked if (1) the organization is unable to deliver by electronic transmission two consecutive notices given by the organization in accordance with such consent and (2) such inability becomes known to the Clerk or an Assistant Clerk of the organization, or other person responsible for the giving of notice; provided, however, the inadvertent failure to treat such inability as a revocation shall not invalidate any meeting or other action.

3.4 The presence of not less than a majority of the Members class shall constitute a quorum and shall be necessary to conduct the business of this organization; but a lesser percentage may adjourn the meeting for a period of not more than four (4) weeks from the date scheduled by these Bylaws and the Clerk shall cause a notice of this scheduled meeting to be sent to all those members who were not present at the meeting originally called. A quorum as herein before set forth shall be required at any adjourned meeting.

3.5 Special meetings of the members may be called by the President when he deems it for the best interest of the organization. Such notice shall state the reasons that such meeting has been called, the business to be transacted at such meeting and by whom it was called. At the request of a majority of the members of the Board of Directors or a majority of the Members class, the President shall cause a special meeting to be called but such request must be made in writing at least ten (10) days before the requested scheduled date.

3.6 No other business but that specified in the notice may be transacted at such special meeting without the unanimous consent of all present at such meeting.

ARTICLE IV
VOTING

4.1 When a quorum is present at any meeting, or electronically between meetings, the vote of a majority of the Members class present in person or represented by proxy shall decide any question brought before such meeting, unless the question is one upon which by express provision of the statutes or of the Articles of Organization a different vote is required in which case such express provision shall govern and control the decision of such question.

4.2 Unless otherwise provided in the Articles of Organization or these Bylaws, each member of the Members class shall at every meeting of the membership be entitled to

one (1) vote in person or by proxy, but no proxy shall be voted on after three (3) years from its date, unless the proxy provides for a longer period.

4.3 Unless otherwise provide in the Articles of Organization, any action required to be taken at any annual or special meeting of the membership of the organization, or any action which may be taken at any annual or special meeting of such members, may be taken without a meeting, without prior notice and without a vote, if a consent in writing, setting forth the action so taken, shall be signed by the members of the Members class having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which such members of the Members class were present and voted. Prompt notice of the taking of the action without a meeting by less than unanimous written consent shall be given to those members who have not consented in writing.

ARTICLE V
BOARD OF DIRECTORS

5.1 The business of this organization shall be managed by a Board of Directors consisting of six voting Directors plus the past president who is eligible to vote only in case of ties.

5.2 Only site-designated members will be eligible to serve on the Board. A site-designated member is a member that has been designated as eligible by a site that has paid its site-membership dues.

5.3 Each Board member will serve a three year term. Terms will be staggered accordingly, with new members voted into office during each year's annual business meeting as needed.

5.4 All members will be eligible to vote for the Directors.

5.5 During presidential years, the Board of Directors will internally choose who the next president shall be. The presidential term shall be three years, starting from the date of appointment.

5.6 The Board shall appoint, on an annual basis, a Treasurer and Clerk from among the current board members.

5.7 An individual may serve only one term as president. Members of the Board may serve two consecutive terms, if so voted by the general membership.

5.8 The Board of Directors shall have the control and management of the affairs and business of this organization. Such Board of Directors shall only act in the name of the organization when it shall be regularly convened by its president after due notice to all the directors of such meeting.

5.9 A majority of the members of the Board of Directors shall constitute a quorum and the meetings of the Board of Directors shall be held regularly as such dates and times as the Board of Directors may determine, but no less than quarterly. The Board of Directors may hold meetings, both regular and special, either within or without the Commonwealth of Massachusetts.

5.10 Each active director shall have one (1) vote and such voting may not be done by proxy. The past-president will cast the deciding vote in the case of a tie.

5.11 Special meetings of the Board may be called by the President on five (5) days' notice to each director by mail or forty-eight (48) hours notice to each director either personally or by electronic means of communications, including electronic mail and facsimile transmission; special meetings shall be called by the President or Clerk in like manner and on like notice on the written request of one (1) director.

5.12 Unless otherwise restricted by the Articles of Organization or these Bylaws, any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting, if all members of the Board or committee, as the case may be, consent thereto in writing, and the writing or writings are filed with the minutes or proceedings of the Board or committee.

5.13 Unless otherwise restricted by the Articles of Organization or these Bylaws, members of the Board of Directors, or any committee designated by the Board of Directors, may participate in a meeting of the Board of Directors, or any committee, by means of conference telephone or similar communications equipment by means of which all persons participating in the meeting can hear each other, and such participation in a meeting shall constitute presence in person at the meeting.

5.14 Unless otherwise restricted by the Articles of Organization or these Bylaws, any director may be removed, with or without cause, by a majority of the members entitled to vote on such directorship. Any director may resign at any time by giving written notice of resignation to the Board of Directors, to the President or to the Clerk. Any such resignation shall take effect upon receipt of such notice or at any later time specified therein. Unless otherwise specified in the notice, the acceptance of a resignation shall not be necessary to make the resignation effective.

5.15 Vacancies in the Board of Directors shall be filled by the members entitled to vote on such directorship.

ARTICLE VI
OFFICERS

6.1 The officers of the organization shall be chosen by the Board of Directors and shall be a President, a Clerk and a Treasurer, all of whom shall be site-designated Members. The Board of Directors may also choose one or more Assistant Clerks and

Assistant Treasurers. Any number of offices may be held by the same person, unless the Articles of Organization or these Bylaws otherwise provide.

6.2 The Board of Directors at its first meeting after each annual meeting of the membership shall choose a Clerk and a Treasurer from those members of the Board of Directors, and may elect one or more Assistant Clerks and Assistant Treasurers as the Board of Directors shall deem to be in the organization's best interests. Presidential appointments are for three (3) years.

6.3 The Board of Directors may appoint such other officers and agents as it shall deem necessary who shall hold their offices for such terms and shall exercise such powers and perform such duties as shall be determined from time to time by the Board.

6.4 No officer shall for reason of his office be entitled to receive any salary or compensation, but nothing herein shall be construed to prevent an officer or director for receiving any compensation from the organization for duties other than as a director or officer.

6.5 The officers of the organization shall hold office until their successors are chosen and qualify. Any vacancy occurring in any office of the organization shall be filled by the Board of Directors. Any officer elected or appointed by the Board of Directors may be removed at any time by the affirmative vote of a majority of the Board of Directors. Any officer may resign at any time by giving written notice of resignation to the Board of Directors, to the President or to the Clerk. Any such resignation shall take effect upon receipt of such notice or at any later time specified therein. Unless otherwise specified in the notice, the acceptance of a resignation shall not be necessary to make the resignation effective.

6.6 The President shall be the chief executive officer of the organization, shall have general and active management of the business of the organization and shall see that all orders and resolutions of the Board of Directors are carried into effect. The President shall preside at all meetings of the membership and of the Board of Directors at which he is present. The President shall have all powers and duties usually incident to the office of the President except as specifically limited by a resolution of the Board of Directors. T he President shall have such other powers and perform such other duties as may be assigned to him from time to time by the Board of Directors.

6.7 The Clerk shall attend all meetings of the Board of Directors and all meetings of the membership and record all the proceedings of the meetings of the organization and of the Board of Directors in a book to be kept for that purpose and shall perform like duties for the standing committees when required. He shall give, or cause to be given, notice of all meetings of the membership and special meetings of the Board of Directors, and shall perform such other duties as may be prescribed by the Board of Directors or President, under whose supervision he shall be. He shall have custody of the corporate seal of the organization and he, or an Assistant Clerk, shall have authority to affix the same to any instrument requiring it and when so affixed, it may be attested by his signature or by the

signature of such Assistant Clerk. The Board of Directors may give general authority to any other officer to affix the seal of the organization and to attest the affixing by his signature.

6.8 The Assistant Clerk, or if there be more than one, the Assistant Clerks in the order determined by the Board of Directors (or if there be no such determination, then in order of their election) shall, in the absence of the Clerk or in the event of his inability or refusal to act, perform the duties and exercise the powers of the Clerk and shall perform such other duties and have such other powers as the Board of Directors may from time to time prescribe.

6.9 The Treasurer shall have the custody of the corporate funds and shall keep full and accurate accounts of receipts and disbursements in books belonging to the organization and shall deposit all monies and other valuable effects in the name and to the credit of the organization in such depositories as may be designated by the Board of Directors. He shall disburse the funds of the organization as may be ordered by the Board of Directors, taking proper vouchers for such disbursements, and shall render to the President and the Board of Directors, at its regular meetings, or when the Board of Directors so requires, an account of all his transactions as Treasurer and of the financial condition of the organization. He shall exercise all duties incident to the office of Treasurer.

6.10 The Assistant Treasurer, or if there shall be more than one, the Assistant Treasurers in the order determined by the Board of Directors (or if there be no such determination, then in the order of their election) shall, in the absence of the Treasurer or in the event of his inability or refusal to act, perform the duties and exercise the powers of the Treasurer and shall perform such other duties and have such other powers as the Board of Directors may from time to time prescribe.

ARTICLE VII
COMMITTEES

7.1 The Board of Directors may create committees as needed, such as executive, audit, and public relations. There shall be one standing committee – the Membership Committee. Except for members of the Membership Committee, membership in any committee created by the Board of Directors may contain such numbers of Members and Associate Members as the Board of Directors may reasonably determine.

7.2 No less than three (3) directors of the Board of Directors shall be appointed by the Board of Directors and shall serve as the members of the Membership Committee.

7.3 The Membership Committee shall have responsibility for reviewing applications for admission and making recommendations with respect such applications to the full Board of Directors.

ARTICLE VIII

GENERAL PROVISIONS

CHECKS

8.1 All checks or demands for money and notes of the organization shall be signed by such officer or officers or such other person or persons as the Board of Directors may from time to time designate.

FISCAL YEAR

8.2 The fiscal year of the organization shall be fixed by resolution of the Board of Directors.

BOOKS AND RECORDS

8.3 The books of the organization shall be kept at such place as the Board of Directors shall designate by resolution.

ARTICLE IX
INDEMNIFICATION; LIMITATION ON LIABILITY

9.1 Each director and officer of the organization shall be indemnified to the fullest extent now or hereafter permitted by law in connection with any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he is or was a director or officer of the organization or is or was serving at the request of the organization as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise. Without limiting the generality of the foregoing, the organization shall indemnify each person within the scope of the foregoing to the extent to which it is given the power to do so by Section 8.56 of the Massachusetts Business Corporations Act of the Commonwealth of Massachusetts as in effect on the effective date of these Bylaws or as thereafter amended. To the extent permitted by applicable law, the organization shall have power to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the organization, or is or was serving at the request of the organization as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against any liability asserted against him and incurred by him in any such capacity or arising out of his status as such whether or not the organization would have the power to indemnify him against such liability under applicable law.

9.2 A director of the organization shall not be personally liable to the organization or its members for monetary damages for breach of fiduciary duty as a director except for liability (i) for any breach of the director's duty of loyalty to the organization or its members, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 8.56 of the Massachusetts Business Corporations Act of the Commonwealth of Massachusetts, as the same exists or

hereafter may be amended, or (iv) for any transaction from which the director derived an improper personal benefit. If the Massachusetts Business Corporations Act hereafter amended to authorize the further elimination or limitation of the liability of directors, then the liability of a director of the organization, in addition to the limitation on personal liability provided herein, shall be limited to the fullest extent permitted by the amended Massachusetts Business Corporations Act. Any repeal or modification of this Article IX by the members of the organization shall be prospective only, and shall not adversely affect any limitation on the personal liability of a director of the organization existing at the time of such repeal or modification.

ARTICLE X
AMENDMENTS

10.1 These Bylaws may be altered, amended, repealed or added to by an affirmative vote of not less than a majority of the members entitled to vote thereon.