Welcome Letter
Brain Program Workshop 3, 2011

Dear Colleagues,

Welcome to the Foundation’s third workshop on focused ultrasound and the brain. This invitational event is being held at the request of the community with the anticipation of building on the foundation laid by two previous, highly productive workshops.

Our purpose for this workshop is to rapidly advance the development and adoption of reimbursable applications that either fulfill an unmet need or are significantly better than existing therapies in terms of outcomes, cost and convenience. Considerable time as has been set aside for informal discussion, relationship building, establishment of collaborations, and problem solving. Our specific goals for the workshop are to:

1) Produce a white paper documenting the state-of-the-art of MR guided focused ultrasound and the brain.
2) Develop action plans for one to two years including technical projects, preclinical studies, and clinical trials leading to reimbursable indications including essential tremor, Parkinson’s disease, temporal lobe epilepsy, and brain tumors.
3) Create a collaborative environment and infrastructure to facilitate achieving the above as rapidly as possible.

We believe that brain indications will be sentinel applications for the clinical use of focused ultrasound. If the brain can be treated safely and effectively with this technology then the road will be paved for the development and adoption of many other clinical applications.

You are here because you are an integral part of this community. We trust that you will take advantage of the great collaborative opportunity this workshop affords. Thank you for being an indispensable part of our efforts to bring hope, healing and better lives to patients around the world.

NEAL F. KASSELL, M.D.
Chairman
Focused Ultrasound Surgery Foundation
Professor of Neurosurgery
University of Virginia

JOHN W. SNELL, PH.D.
Brain Program Technical Director
Focused Ultrasound Surgery Foundation
Today, researchers and manufacturers around the world are developing focused ultrasound therapies for many deadly and debilitating medical conditions. Since its founding in 2006, the Focused Ultrasound Surgery Foundation has been dedicated to accelerating the development and adoption of these new, noninvasive treatments so that they become a standard of care worldwide. Motivating the Foundation’s work is the belief that every day without access to focused ultrasound treatments is a day of needless death, disability and suffering for countless patients.

Thanks to the support of philanthropic and corporate donors, the Foundation funds a variety of research and educational initiatives. We also promote collaboration, coordination and communication among researchers, clinicians and others who are pioneering this exciting and rapidly emerging area of medicine.

Our key initiatives include:

- Organizing, coordinating and funding research leading to new applications
- Establishing global collaboration between the research and development initiatives in academia and industry
- Funding training fellowships for clinicians and scientists
- Establishing new Centers of Excellence—luminary sites for research, training and patient care
- Supporting meetings, symposia and workshops
- Facilitating regulatory approval and third-party reimbursement
- Increasing awareness of what has been termed “medicine’s best kept secret”

To learn more about focused ultrasound and the Focused Ultrasound Surgery Foundation, visit the Foundation’s website: [www.fusfoundation.org](http://www.fusfoundation.org)
General Information

Registration

<table>
<thead>
<tr>
<th>Day</th>
<th>Time</th>
<th>Location</th>
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<tbody>
<tr>
<td>Sunday</td>
<td>6:00-8:00 PM</td>
<td>Hearth Room</td>
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<tr>
<td>Monday</td>
<td>7:00-8:00 AM</td>
<td>Ballroom</td>
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</table>

Contact Information

- The Boar's Head Inn: 434.296.2181
- FUSF Staff:
  - John Snell: 434.326.9836 (m)
  - Jade Faulkner: 434.882.1442 (m)
  - Chris Faulkner: 434.760.1170 (m)

Daily Events

*Please see Overview for detailed schedule*

Sunday, October 23

- 6:00 PM: Welcome Reception, Hearth Room
  - Includes drinks and hors d'oeuvres

Monday, October 24

- 6:30 AM – 8:15 AM: Breakfast - Old Mill Room
- 8:30 AM – 3:30 PM: Clinical Sessions - Ballroom
- 7:00 PM: Dinner – Pavilion

Tuesday, October 25

- 6:30 AM – 8:15 AM: Breakfast - Old Mill Room
- 8:30 AM – 3:30 PM: Technical Sessions – Ballroom
- 7:00 PM: Dinner – Hearth Room

Wednesday, March 23

- 7:00 AM – 7:45 AM: Breakfast - Old Mill Room
General Information

Key:
- Welcome Reception
  Hearth Room, ground floor
- Workshop Sessions
  Tuesday:
  Lower Level-Ballroom
  Wednesday:
  Lower Level-Ballroom
  Upper Level-Albemarle, Blue Ridge & Commonwealth Rooms
- Meals
  Tuesday:
  Lunch-Meeting Pavilion
  Dinner-Meeting Pavilion
  Wednesday:
  Lunch-Hearth Room

Focused Ultrasound Surgery Foundation | Brain Workshop 3, 2011
<table>
<thead>
<tr>
<th>Indications</th>
<th>Technical Challenges</th>
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<tbody>
<tr>
<td>Trigeminal Neuropathy</td>
<td>Treatment Planning</td>
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<td>Obsessive Compulsive Disorder</td>
<td>Skull Correction</td>
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<td>Ischemic Stroke</td>
<td>Volumetric MR Imaging</td>
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<td>Intracerebral Hemorrhage</td>
<td>Treatment Planning</td>
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<td>BBB + Drug Delivery</td>
<td>Skull Database without CT</td>
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<td>Neuropathic &amp; Cancer Pain</td>
<td>Volumetric MR Imaging</td>
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<td>Epilepsy</td>
<td>RF Head Coil</td>
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<td>Temporal Lobe</td>
<td>Thermoanometry</td>
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<td>Brain Tumors</td>
<td>Treatment Planning</td>
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<td>Neuromodulation</td>
<td>Frameless Stereotaxis</td>
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<td>Parkinson's Disease</td>
<td>Phantom &amp; Models</td>
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<td>Essential Tremor</td>
<td>Treatment Planning</td>
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</tbody>
</table>
Workshop Overview

Contact Numbers
The Boar’s Head 434.296.2181
John Snell 434.326.9836 (m)
Jade Faulkner 434.882.1442 (m)
Chris Faulkner 434.760.1170 (m)

Description of Events

Sunday, October 23
Registration and Welcome Reception will take place in the Hearth Room. Cocktails and hors d’oeuvres will be provided.

Monday, October 24
Clinical Indications - Presentations and discussion of MRgFUS brain indications will take place throughout the day in the Ballroom. Time has been set aside in the afternoon for impromptu discussions and collaborative opportunities. Dinner for all participants concludes the day.

Tuesday, October 25
Technical Issues – Presentations and discussions of high priority MRgFUS technical issues related to brain applications will take place throughout the day in the Ballroom. Time has been set aside in the afternoon for impromptu discussions and collaborative opportunities. Dinner for all participants concludes the day.

Wednesday, October 26
A farewell breakfast closes the program.

Sunday, October 23, 2011

| 6:00p | Reception | Hearth Room |

Monday, October 24, 2011

| 6:30a | Breakfast | Mill Room |
| 8:30a | Welcome and Introduction | Ballroom |
| 8:45a | Session 1: Clinical Indications | Ballroom |
| 10:30a | Session 2: Clinical Indications | Ballroom |
| 12:00p | Lunch | Hearth Room |
| 1:30p | Session 3: Clinical Indications | Ballroom |
| 3:30p | Free time | |
| 7:00p | Dinner | Pavilion |

Tuesday, October 25, 2011

| 6:30a | Breakfast | Mill Room |
| 8:30a | Session 4: Technical Issues | Ballroom |
| 10:30a | Session 5: Technical Issues | Ballroom |
| 12:00p | Lunch | Hearth Room |
| 1:30p | Session 6: Technical Issues | Ballroom |
| 3:30p | Free time | |
| 6:00p | Summation and Closing | Ballroom |
| 7:00p | Dinner | Hearth Room |

Wednesday, October 26, 2011

| 7:00a | Breakfast | Mill Room |
# Detailed Agenda

## Sunday, October 23, 2011

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<thead>
<tr>
<th>Time</th>
<th>Discussion Topics</th>
<th>Location</th>
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<tbody>
<tr>
<td>6:00p – 8:00p</td>
<td>Reception – Cocktails and h’orderves</td>
<td>Hearth Room</td>
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<tr>
<td>8:00p</td>
<td>Dinner on your own</td>
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## Monday, October 24, 2011

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<tr>
<th>Time</th>
<th>Discussion Topics</th>
<th>Location</th>
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<tr>
<td>6:30a – 8:15a</td>
<td>Breakfast</td>
<td>Mill Room</td>
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<td></td>
<td>Breakout Discussion: Movement Disorders Steering Committee I (breakout room TBD)</td>
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<tr>
<td>8:30a</td>
<td>Welcome and Introduction</td>
<td>Ballroom</td>
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<tr>
<td>Session 1: Clinical Indications</td>
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<tr>
<td>8:45a</td>
<td><strong>Essential Tremor</strong></td>
<td>Ballroom</td>
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<td></td>
<td>1) Current Status</td>
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<td></td>
<td>a. UVa – Jeff Elias</td>
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<td>b. Solothurn – Daniel Jeanmonod</td>
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<td>c. Comparative study RF/Gamma Knife/MRgFUS – Mohamad Khaled</td>
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<td>2) Technical Barriers/Clinical Requirements</td>
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<tr>
<td></td>
<td>a. Treatment Planning Software</td>
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<tr>
<td></td>
<td>i. Focal spot localization</td>
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<td>ii. Power/Temperature titration</td>
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<td>b. Transducer positioning system</td>
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<td>c. Stereotactic localization of target</td>
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<td>d. CT scan necessary</td>
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<td>e. Targeting technique and accuracy</td>
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<td>f. Optimal lesion size</td>
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<td>g. Neurophysiologic assessment of target via neuromodulation</td>
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<td>h. RF Head Coil requirements</td>
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<td>3) Next Steps</td>
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<tr>
<td></td>
<td>a. Bilateral lesions, Lesion plus Deep Brain Stimulation</td>
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<td>b. Continued access post pilot trial</td>
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<td>c. Pivotal trial design</td>
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<td>i. Protocol: patients, sites, comparative arm</td>
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<td>ii. Regulatory</td>
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<td>iii. Reimbursement</td>
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<td>iv. Medical Community</td>
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<td>v. Key opinion leaders</td>
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<td>vi. Funding sources</td>
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## Detailed Agenda

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<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Details</th>
<th>Location</th>
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<tr>
<td>9:30a</td>
<td>PD</td>
<td><strong>Parkinson’s Disease</strong>&lt;br&gt;1) Current Status&lt;br&gt;  a. Thalamotomy/Pallidotomy&lt;br&gt;  i. Solothurn Experience – Daniel Jeanninod&lt;br&gt;  ii. Rationale for pilot clinical trial protocol&lt;br&gt;2) Technical Barriers/Clinical Requirements&lt;br&gt;  a. Same as ET&lt;br&gt;3) Next Steps&lt;br&gt;  a. Pilot trial design</td>
<td>Ballroom</td>
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<td>10:00a – 10:20a</td>
<td>Break</td>
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<td>10:30a</td>
<td>Session 2: Clinical Indications</td>
<td><strong>Neuromodulation</strong> (Functional Target Verification &amp; Epilepsy)&lt;br&gt;1) Current Status – Seung-Schik Yoo, Mickael Tanter&lt;br&gt;2) Technical Barriers&lt;br&gt;3) Next Steps</td>
<td>Ballroom</td>
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<td>10:45a</td>
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<td><strong>Brain Tumors</strong>&lt;br&gt;1) Current Status&lt;br&gt;  a. Sunnybrook – Todd Mainprize&lt;br&gt;  b. Zurich – Ernst Martin, Javier Fandino&lt;br&gt;2) Tumor Types&lt;br&gt;3) Technical Barriers/Clinical Requirements&lt;br&gt;  a. Treatment Envelope&lt;br&gt;   i. Whole brain&lt;br&gt;   ii. High value targets: location, volume, treatment time&lt;br&gt;  b. Treatment Time&lt;br&gt;  c. Skull heating and Cranial Nerves&lt;br&gt;  d. Cavitation detection, characterization and control&lt;br&gt;   i. Enhanced ablation&lt;br&gt;   ii. Microbubbles&lt;br&gt;   iii. Histotripsy&lt;br&gt;   iv. Sonodynamic therapy&lt;br&gt;4) Next steps&lt;br&gt;  a. Treatment envelope evaluation on current devices&lt;br&gt;   i. Simulation&lt;br&gt;   ii. Hydrophone measurement&lt;br&gt;   iii. Thermal measurement&lt;br&gt;  b. BBB Opening + Drug Delivery</td>
<td>Ballroom</td>
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<tr>
<td>11:15a</td>
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<td><strong>Temporal Lobe Epilepsy</strong>&lt;br&gt;1) Current Status&lt;br&gt;  a. Preclinical feasibility – Stephen Monteith&lt;br&gt;2) Technical Barriers/Clinical Requirements</td>
<td>Ballroom</td>
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<td>11:30a</td>
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<td>Ballroom</td>
<td><strong>Neuropathic and Cancer Pain</strong></td>
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<td>1) Current Status</td>
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<td>a. Zurich: Long term follow-up – Daniel Jeanmonod</td>
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<td>2) Technical Barriers/Clinical Requirements</td>
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<td>a. Same as ET</td>
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<td>3) Next Steps</td>
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<td>a. Pivotal trial design</td>
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<td>b. Physician acceptance</td>
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<td>c. Regulatory</td>
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<td>d. Reimbursement</td>
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<tr>
<td>12:00p – 1:15p</td>
<td>Lunch</td>
<td>Hearth Room</td>
<td><strong>Breakout Discussion:</strong> Movement Disorders Steering Committee II (breakout room TBD)</td>
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<td>1:30p</td>
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<td>Ballroom</td>
<td><strong>Blood Brain Barrier Opening + Drug Delivery</strong></td>
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<td>1) Current Status</td>
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<td></td>
<td>– Todd Mainprize, Kullervo Hynynen, Fabrice Marquet, Nathan McDannold</td>
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<td>a. GBM pilot trial</td>
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<td>b. Parkinson’s Disease</td>
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<td>c. Alzheimer’s Disease</td>
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<td>2) Technical Barriers/Clinical Requirements</td>
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<td>a. Non-thermal focal spot verification</td>
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<td>b. Treatment Envelope</td>
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<td>c. Cavitation Detection and Control</td>
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<td>d. Pharmacokinetics</td>
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<td>3) Next Steps</td>
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<td>a. GBM BBB pilot trial</td>
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<td>2:00p</td>
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<td>Ballroom</td>
<td><strong>Intracerebral Hemorrhage</strong></td>
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<td>1) Current Status</td>
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<td></td>
<td>– Stephen Monteith</td>
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<td></td>
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<td>a. In vitro/in vivo parameter selection</td>
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<td>b. Preclinical safety and feasibility</td>
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<td>2) Technical Barriers/Clinical Requirements</td>
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<td>a. Non-thermal focal spot verification</td>
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<td>c. Cavitation localization</td>
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<td>3) Next Steps</td>
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<td>a. Pilot clinical trial design</td>
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**Focused Ultrasound Surgery Foundation | Brain Workshop 3, 2011**
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<tr>
<th>Time</th>
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<tbody>
<tr>
<td>2:30p</td>
<td>Ischemic Stroke</td>
<td>1) Current Status – Thilo Hoelscher, Stephen Monteith, Kullervo Hynynen</td>
<td>Ballroom</td>
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<td>2) Technical Barriers/Clinical Requirements</td>
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<td></td>
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<td>a. Treatment Time, Patient and system preparation time</td>
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<td>3) Next Steps</td>
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<td>a. Pilot trial design</td>
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<td>2:45p</td>
<td>Obsessive Compulsive Disorder</td>
<td>1) Current Status – Jin Woo Chang</td>
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<td>2) Technical Barriers/Clinical Requirements</td>
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<td>a. Treatment envelope</td>
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<td>3) Next steps</td>
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<td>a. Pilot trial design</td>
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<tr>
<td>3:00p</td>
<td>Trigeminal Neuralgia</td>
<td>1) Current Status</td>
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<td></td>
<td>a. Preclinical safety and feasibility – Stephen Monteith</td>
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<td>2) Technical Barriers/Clinical Requirements</td>
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<td></td>
<td></td>
<td>a. Skull base heating</td>
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<td>3) Next Steps</td>
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<td>3:15p</td>
<td>Future Indications</td>
<td>1) Aneurysm – Daniel Coluccia</td>
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<td>2) Vasospasm</td>
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<td>3) Epilepsy (other than TLE)</td>
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<td>4) Others from the floor time permitting</td>
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<td>3:30p</td>
<td>Unstructured Meeting/Discussion Time</td>
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<td>-Breakout Discussion: Intracerebral Hemorrhage (Breakout room TBD)</td>
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<td>7:00p</td>
<td>Dinner</td>
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<td>Pavilion</td>
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## Detailed Agenda

**Tuesday, October 25, 2011**

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<tr>
<th>Time</th>
<th>Discussion Topic</th>
<th>Location</th>
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<tbody>
<tr>
<td>6:30a – 8:15a</td>
<td>Breakfast</td>
<td>Mill Room</td>
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<tr>
<td><strong>Session 4: Technical Issues</strong></td>
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<td>8:30a</td>
<td>What is the treatment envelope and how can it be extended (220 kHz, 650 kHz, 1MHz)</td>
<td>Ballroom</td>
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<td>1) How should we define the treatment envelope? Definitions/criteria?</td>
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<td>2) Simulations – 220kHz, 650kHz, 1MHz</td>
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<td></td>
<td>- Kullervo Hynynen, Jean-Francois Aubry, Doug Christensen</td>
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<td>3) Hydrophone Measurements – 220 kHz – Arne Voie</td>
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<td>4) Thermal Measurements 220/650 kHz – Matt Eames</td>
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<td>5) Trigeminal Neuralgia/Temporal Lobe Epilepsy targets – Stephen Monteiith</td>
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<td>6) What is the treatment time for targets of different sizes and locations for each</td>
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<td>transducer frequency? – Matt Eames, Eyal Zadicario, Jean-François Aubry</td>
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<td></td>
<td>Cavitation: Can it be detected, characterized and controlled?</td>
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<td>- Thilo Hoelscher, Arne Voie, Nathan McDannold, Jean-François Aubry</td>
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<td></td>
<td>1) Detection &amp; Characterization</td>
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<td>2) Closed loop cavitation in vivo</td>
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<td></td>
<td>Are remote effects a significant issue?</td>
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<td></td>
<td>1) Measurement – Kullervo Hynynen</td>
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<td>2) Simulation – Jean-François Aubry</td>
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<td>How do skull size, shape and thickness affect the focus?</td>
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<td>1) Skull Database – Thilo Hoelscher</td>
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<td><strong>10:00 – 10:20 Break</strong></td>
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<td><strong>Session 5: Technical Issues</strong></td>
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<tr>
<td>10:30a</td>
<td>Can the need for a CT exam be eliminated?</td>
<td>Ballroom</td>
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<td>1) MR-ARFI, MR-based Focusing – Mickael Tanter, Kim Butts-Pauly</td>
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<td>2) Can skull correction be accomplished with MR bone imaging?</td>
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<td></td>
<td>- Max Wintermark</td>
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<td>3) How do we detect and handle calcifications? – Kim Butts-Pauly</td>
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<td>4) Are cysts an issue?</td>
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<td>5) Neurosurgical debris: shunt catheters, clips, screws, etc?</td>
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## Detailed Agenda

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<tr>
<th>Time</th>
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<tbody>
<tr>
<td>12:00p – 1:15pm</td>
<td>Lunch</td>
<td>Hearth Room</td>
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<tr>
<td>12:00p – 1:15pm</td>
<td>Lunch - Breakout Discussion: Brain Tumor Steering Committee (breakout room TBD)</td>
<td>Hearth Room</td>
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<tr>
<td>1:30p</td>
<td>Remote Monitoring – Eyal Zadicario, Nadir Alikacem, John Snell</td>
<td>Ballroom</td>
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<tr>
<td>1:30p</td>
<td>What does the optimal treatment planning system look like?</td>
<td>Ballroom</td>
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<tr>
<td>1:30p</td>
<td>Panel: Jeff Elias, Ernst Martin, Daniel Jeanmonod, Jean-François Aubry, Mickael Tanter, John Snell, Kim Butts-Pauly, Eyal Zadicario, Stephen Monteith, Beat Werner</td>
<td>Ballroom</td>
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<tr>
<td>1:30p</td>
<td>Can we treat without a stereotactic frame?: Head Motion Tracking/Frameless Stereotaxy - Eyal Zadicario, Jean-François Aubry</td>
<td>Ballroom</td>
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<tr>
<td>1:30p</td>
<td>Phantoms – Matt Eames, Arne Voie</td>
<td>Ballroom</td>
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<tr>
<td>1:30p</td>
<td>Cadaver Models – Stephen Monteith, Jean-François Aubry, Sandy Cochran</td>
<td>Ballroom</td>
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<tr>
<td>1:30p</td>
<td>Animal Models – Stephen Monteith, Nathan McDannold, Thilo Hoelscher</td>
<td>Ballroom</td>
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<tr>
<td>3:30p – 5:30p</td>
<td>Unstructured Meeting/Discussion Time</td>
<td>Ballroom</td>
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<tr>
<td>3:30p – 5:30p</td>
<td>- Breakout Discussion: Training, Credentialing, Staffing and Logistics for Neurological Indications (Room TBD)</td>
<td>Ballroom</td>
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Detailed Agenda

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<thead>
<tr>
<th>Time</th>
<th>Discussion Topics</th>
<th>Location</th>
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<tr>
<td>6:00p</td>
<td>Summation and Closing</td>
<td>Ballroom</td>
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<td>Deliverables:</td>
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<td>1) White Paper by December 1, 2011</td>
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<td></td>
<td>2) Action Plan (1-2 Year): Tasks/Assignment/Metrics</td>
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<tr>
<td></td>
<td>a. Essential Tremor</td>
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<td>b. Parkinson's Disease</td>
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<td>c. Brain Tumors – Expanded Envelope</td>
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<td>d. Temporal Lobe Epilepsy</td>
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<td>e. Intracerebral Hemorrhage</td>
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<td>f. Pain</td>
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<td>g. Others</td>
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<td>3) Collaborative Environment – FUSF CRN</td>
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<tr>
<td>7:00p</td>
<td>Dinner</td>
<td>Hearth Room</td>
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**Wednesday, October 26, 2011**

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<tr>
<th>Time</th>
<th>Discussion Topics</th>
<th>Location</th>
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<tbody>
<tr>
<td>7:00a</td>
<td>Breakfast</td>
<td>Mill Room</td>
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Brain Program Overview

Program Rationale:
Brain disorders represent a highly crucial treatment area for MR-guided FUS. Key reasons are: 1) these conditions are the most devastating and debilitating ailments afflicting humanity and are increasing in prevalence; 2) clinically, the brain is the most difficult organ to treat safely and effectively, and success of MR guided FUS in this segment will be viewed as proof of its ability to treat other organs; 3) from a societal perspective, the brain is a high-profile topic—there is widespread fascination with its workings and fear of its disorders. Successful, new treatments of brain disorders are likely to attract public interest and increase investment in other MR-guided FUS applications.

Workshops:
The Focused Ultrasound Surgery Foundation assisted in defining a comprehensive R&D roadmap for brain applications by organizing an invitation-only workshop in March 2009. Attended by thought leaders from industry, academia and the NIH, the workshop produced a roadmap of technical, preclinical, and clinical studies needed to escalate development of neurological applications. It also laid the groundwork for collaborations between manufacturers and academic research laboratories. A follow on workshop was held March 2010 at the request of the first workshop participants and was central to further refinement of the brain program’s clinical and technical research roadmaps.

The Brain Program has gotten off to a strong start and now encompasses a robust infrastructure. Components include:

- Brain Advisory Committee
- Data Safety Monitoring Board
- Clinical Trial Steering Committees for Brain Tumors and Movement Disorders (such as Essential Tremor and Parkinson's Disease)
- Core Imaging Laboratory
- Research Working Groups for Intracerebral Hemorrhage, Ischemic Stroke, and Neuromodulation
Brain Program Overview

Brain Advisory Committee
The Brain Program Advisory Committee provides advice and counsel to the Focused Ultrasound Surgery Foundation (FUSF) Brain Program team on both research and development (R&D) and program activities.

Membership
- Neal F. Kassell, MD, **Chairman**, Professor of Neurosurgery, University of Virginia, Charlottesville, VA
- Ferenc Jolesz, MD, B. Leonard Holman Professor of Radiology & Vice Chairman for Research, Brigham & Women’s Hospital, Harvard Medical School, Boston, MA
- Dade Lunsford, MD, Lars Leksell Professor & Distinguished Professor of Neurological Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA
- Edward Oldfield, MD, Professor of Neurosurgery and Internal Medicine, University of Virginia Medical Center, Charlottesville, VA
- Jacques Souquet, PhD, CEO, Supersonic Imagine, Aix-en-Provence, France
- Mickael Tanter, PhD, Laboratoire Ondes et Acoustique, E.S.P.C.I, Paris, France
- Eyal Zadicario, BSc, MSc, Director of Neurological Programs, Insightec, Tirat Carmel, Israel

Data Safety Monitoring Board
The DSMB is charged with monitoring adverse event (AE) data from the pilot clinical trials for MR-guided FUS for brain disorders sponsored by industry leaders. The DSMB will conduct an independent, objective review of all AEs to assess their relationship to MR-guided FUS or the procedure. Based on this review the DSMB will advise the sponsor on the appropriateness of continuing the clinical trials as designed.

Membership
- Howard M. Eisenberg, MD, **Chairman**, R.K. Thompson Professor and Chairman, Department of Neurosurgery, University of Maryland School of Medicine and Medical Systems, Baltimore, MD
- William G. Bradley, MD, PhD, FACR, Chairman and Professor of Radiology, University of California at San Diego, San Diego, CA
- Robert Grossman, MD, Chair of Neurosurgery, The Methodist Hospital, Houston, TX

Steering Committees
The Foundation brings together investigators and other key individuals in a collaborative setting that crosses medical disciplines in order to provide oversight and direction to pilot clinical studies for the Brain Program. The goal of these clinical trials is to demonstrate the feasibility and safety of MR-guided FUS for the treatment of various indications in the brain. The resulting data from these early clinical trials will be used to support the development of definitive safety and efficacy trials for submission and approval to the appropriate regulatory agencies and ministries of health as well as to support the needs of the medical and scientific community.
Brain Program Overview

Brain Tumor Steering Committee

- Edward H. Oldfield, MD, **Chairman**, Professor of Neurosurgery and Internal Medicine, University of Virginia Medical Center, Charlottesville, VA
- Jason Sheehan, MD, PhD, **Principal Investigator**, Associate Professor of Neurological Surgery, University of Virginia, Charlottesville, VA
- Javier Fandino, MD, Associate Professor, Department of Neurosurgery, Universities of Berne and Zurich, Switzerland; Vice-Chairman, Department of Neurosurgery Kantonsspital Aarau, Aarau, Switzerland
- Ferenc Jolesz, MD, B. Leonard Holman Professor of Radiology & Vice Chairman for Research, Brigham & Women’s Hospital, Harvard Medical School, Boston, MA
- Todd Mainprize, MD, Assistant Professor, Division of Neurosurgery, University of Toronto, Toronto, Ontario, Canada
- David Schiff, MD, Professor of Neurology, University of Virginia Medical Center, Charlottesville, VA
- James C. Torner PhD, Professor and Chairman, Department of Epidemiology, University of Iowa, Iowa City, IA
- J. Pablo Villablanca, MD, Associate Professor of Radiology, Section Chief, Diagnostic Neuroradiology, David Geffen School of Medicine at UCLA, Los Angeles, CA

Movement Disorders Steering Committee

- G. Frederick Wooten Jr., MD, **Chairman**, Professor of Neurology, UVA Medical Center, Charlottesville, VA
- William Jeffrey Elias, MD, **Principal Investigator**, Associate Professor of Neurological Surgery and Neurology, UVA Medical Center, Charlottesville, VA
- Antonio DeSalles, MD, PhD, Director of Functional Neurosurgery, UCLA Medical Center, Los Angeles, CA
- Daniel Jeanmonod, MD, Professor of Neurosurgery, University Hospital, Zurich, Switzerland
- Andres Lozano, MD, PhD, Professor of Surgery (Neurosurgery), Ron Tasker Chair of Stereotactic and Functional Neurosurgery, University of Toronto, Ontario, Canada
- James C. Torner PhD, Professor and Chairman, Department of Epidemiology, University of Iowa, Iowa City, IA
- J. Pablo Villablanca, MD, Associate Professor of Radiology, Section Chief, Diagnostic Neuroradiology, David Geffen School of Medicine at UCLA, Los Angeles, CA
Workshop Attendees

Nadir Alikacem, PhD
InSightec, Ltd., Dallas, Texas
nadira@insightec.com

Nadir Alikacem is VP Global Regulatory Affairs and CRO for InSightec, and was previously North America Pole Manager, Mr. Alikacem is responsible for regulatory strategy, clinical research planning to support the regulatory strategy, research protocols coordinated with the VP Clinical R&D, working with all relevant regulatory bodies, and managing the CRO activities.

Prior to joining InSightec in 2001, Dr. Alikacem was an Assistant Professor at UT Southwestern Medical Center in Dallas, Texas. Previously, he was a Scientist at Saint Francois’ D’Assise Hospital in Quebec-City, Canada. Dr. Alikacem received his Postdoctoral fellowship in Physics from the University of Massachusetts at Amherst, Massachusetts. He received a Ph,D & M.Sc in Physics from the University of the University of California, Berkeley.

Marie Armbruster, MS
University of Virginia, Charlottesville, Virginia
ma6ua@virginia.edu

Jean-Frcois Aubry, PhD
Institut Langevin, Paris, France
jean-francois.aubry@espci.fr

Jean-Francois Aubry was born in Marseille, France, in May 1973. He graduated in Physics from Ecole Normale Superieure de Cachan and University Paris XI in 1998. In 2002, he received the PhD degree in Physics (acoustics) from the University of Paris VII. Since 2002, he has a permanent position as a researcher for the National French Center of Science (CNRS). He is currently working at the Institut Langevin, Paris, France. He has mainly working on adaptive focusing through bones (transcostal and transcranial focusing), including three clinical applications: ultrasonic brain imaging, and brain and liver therapy with High Intensity Focused Ultrasound. He holds 3 patents on these applications. He published 27 peer reviewed articles, gave 20 invited talks in international conferences. He received the bronze medal of the CNRS (2011 CNRS awards, in Paris, France) and the Frederic Lizzi Early career award (11th ISTU symposium, New York, USA).

Stanley Benedict, PhD
University of Virginia, Charlottesville, Virginia
shb4x@virginia.edu

Dr. Benedict received a PhD in Biomedical Physics from UCLA, and an M.S. in Radiological Health Physics from San Diego State University. He is Professor and Director of Biomedical Physics in the Department of Radiation Oncology at the University of Virginia, which recently installed the first dedicated MRIgFUS Center in the USA. He is a Diplomat from the ABR in Therapeutic Radiologic Physics, and is a Fellow of the ACMP and the AAPM. He is currently a Co-Chair of AAPM Task Group No. 193 on Image Guided Focused Ultrasound.

S. Morry Blumenfeld, PhD
MediTech Advisors, Ltd., Jerusalem, Israel
morry@meditechadvisors.com

Dr. Blumenfeld is a Founding Partner of Meditech Advisors Management, a General Partner in Ziegler Meditech Equity Partners, LP. He was an executive with General Electric for nearly 35 years and served GE in many roles including Managing Director of GE Medical Systems Israel. Dr. Blumenfeld holds five patents and has served on an Institute of Electrical and Electronics Engineers Standards Committee, a National Cancer Institute Advisory Board, the Ontario R&D
**Workshop Attendees**

Challenge Fund Imaging Advisory Committee, a Scientific Advisory Board of the Ontario Consortium for Image-Guided Therapy and Surgery, and the Imaging Research Centre for Cardiac Intervention at the University of Toronto. He is on the Advisory Board of the Advanced Multimodality Image Guided Operating Suite at Harvard and is on the boards of the Hebrew University and a number of medical device and technology companies including Insightec, MAKO, Dune Medical, Oridion and others. Dr. Blumenfeld received his undergraduate degree and Ph.D. from the University of Toronto.

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**William Bradley, MD, PhD, FACR**  
*University of California San Diego, San Diego, California*  
[wgbradley@ucsd.edu](mailto:wgbradley@ucsd.edu)

William G. Bradley, Jr, is Professor and Chairman, Department of Radiology, at UCSD. He received his BS at Caltech and his PhD at Princeton, both in Chemical Engineering. He received his MD and did his Radiology residency at UCSF where he first became involved in MRI in 1979. He has published over 190 papers, 52 chapters, and 21 textbooks, including Magnetic Resonance Imaging (3rd Edition), co-edited with David Stark. He was President of the SMRI (now ISMRM) 1988-89. He was honored with the Gold Medal of the SMRM (now ISMRM) in 1989 and that of the RSNA in 2003 for “pioneering research in MRI”. He served on the Board of the Research and Education Foundation of the RSNA 1995-2001 and was Chairman of the RSNA Fund Development Committee from 1996-2007. He was on the Board of Chancellors of the American College of Radiology where he chaired the Commission on Neuroradiology and MRI from 1999 to 2005 and served as Vice President 2005-2006. He is currently on the Boards of the Association of University Radiologists, the Clinical MRI Society, and the International Society for Strategic Studies in Radiology.

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**Falko Busse, PhD**  
*Philips Healthcare, Vanta, Finland*  
[falko.busse@philips.com](mailto:falko.busse@philips.com)

Falko Busse studied Physics at the ‘Rheinische Friedrich-Wilhelms-Universität’ Bonn. He performed a PostDoc period in Jena (Germany) and Copenhagen. He started his career as Project manager at Philips Research Aachen and continued as Project manager at Philips Medical Systems. After having returned to Philips Research, he headed the Department ‘Imaging Systems’ in Aachen. Since 2004 he has been Vice President of Philips Research, responsible for the global research program on medical imaging.

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**Kim Butts Pauly, PhD**  
*Stanford University School of Medicine, Stanford, California*  
[kbpauly@stanford.edu](mailto:kbpauly@stanford.edu)

Kim Butts Pauly received a BS degree in physics from Duke University, Durham, NC. She received her PhD in biophysical sciences from the Mayo Graduate School in Rochester, MN. In 1996, she joined the faculty at Stanford University’s Department of Radiology, where she has been working on MR-guided high intensity focused ultrasound, cryoablation, RF ablation, and biopsy. She has also been involved with the development of a truly integrated X-Ray and MRI system.
Workshop Attendees

Alexander Bystritsky, MD, PhD
University of California Los Angeles, Los Angeles, California
abystritsky@mednet.ucla.edu

Professor Alexander Bystritsky graduated from Pavlov Medical Institute (currently Pavlov Medical University) in St. Petersburg, Russia (former Soviet Union) with MD in 1977 and then his PhD in Pharmacology in 1979. In 1976 his paper won the Gold Medal for the Best Student Scientific Paper and Maria Petrova National Award in Neuroscience. After he arrived to New York, he worked for one year as an Associate Researcher in the NYU Department of Psychiatry prior his admission to the NYU-Bellevue residency program in Psychiatry. He completed his residency in 1985 and moved to UCLA as a Robert Wood Johnson Clinical Scholar. Dr. Bystritsky has been on the UCLA Faculty since 1987. He is currently a Professor of Psychiatry and Biobehavioral Sciences in Jane and Terry Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles where he directs the Anxiety Disorders Program and Brainstimulation Laboratory. Dr. Bystritsky published over 150 peer-reviewed papers and has served as the PI and Co-PI on several NIH, foundations and industry sponsored grants. Over the years he earned several honors and awards including OCD Foundation Research Award and Brain and Behavior Distinguished Investigator Award. He is also listed in the Best Doctors in America for the last 12 years. For the past few years he has been a collaborator with Brigham and Women's Hospital Harvard Medical School Boston, Massachusetts working with Professor Ferenc Jolesz, Professor McDannold and Professor Seung-Schik Yoo investigating Focused Ultrasound Pulsation effects on brain using fMRI. He has authored several patents on image-guided neuromodulation of brain neurons using Low Intensity Focused Ultrasound Pulsation. His current area of interest is neuroimaging guided brain stimulation. He the director of collaborative clinical and research program on image-guided DBS with the department of Neurosurgery at UCLA with Professor Antonio DeSalles.

Bob Carter, MD, PhD
University of California San Diego, San Diego, California
bobcarter@ucsd.edu

Jin Woo Chang, MD, PhD
YUCM Severance Hospital, Seoul, Korea
jchang@yuhs.ac

Dr. Jin Woo Chang is a professor of neurosurgery at Yonsei University College of Medicine in Seoul, Korea. He is currently interested in clinical applications of MR-guided focused ultrasound to functional neurosurgery.

Pin-Yuan Chen, MD
Chang University, Taiwan
pinyuanc@gmail.com

Dr. Chen received his MD from the Chang-Gung University in 1998. Subsequently, he completed his medical residency in the Chang-Gung Memorial Hospital in 2006, and now serve as Attending Physician in the Department of Neurosurgery. He is also Director of the Intensive Care Unit in the same hospital. He has received board certifications from the Taiwan Department of Health, Taiwan Surgical Association, Taiwan Neurosurgical Society, Taiwan Society of Critical Care Medicine, and Taiwan Atomic Energy Council. In addition to his medical service and hospital work, Dr. Chen also devotes time to translational and preclinical research and has published several peer-reviewed papers, especially in the area of enhancing drug delivery into brain tumors.
David Chen, MBA
University of Virginia, Charlottesville, Virginia
dc9rk@virginia.edu

Douglas Christensen, PhD
University of Utah, Salt Lake City, Utah
christen@ee.utah.edu

Douglas A. Christensen received the BSEE degree from Brigham Young University in 1962, the MS degree from Stanford University in 1963, and the PhD degree from the University of Utah in 1967. During 1972-74, he held a Special NIH postdoctorate position in biomedical engineering at the University of Washington. He has been a faculty member at the University of Utah since 1971. He currently holds a joint appointment as Professor of Bioengineering and Professor of Electrical and Computer Engineering. His major research interests are in the area of waves in medical diagnosis and therapy, including therapeutic ultrasound, ultrasonic bioinstrumentation, optical biosensors, and numerical modeling of acoustic fields. He is the author of the books Ultrasonic Bioinstrumentation in 1988 and Introduction to Biomedical Engineering: Biomechanics and Bioelectricity in 2010, and co-author of Basic Introduction to Bioelectromagnetics, 2nd edition in 2010.

Gregory Clement, PhD
Surgical Planning Laboratory, Boston, Massachusetts
gclement@hms.harvard.edu

Greg Clement's research concentrates on the propagation of ultrasound for both the detection and treatment of cancerous and benign tumors. He received his BS (Ohio State 92), MS, and PhD (Rhode Island, 96, 99) degrees, all in physics. While a postdoctoral fellow at Brigham and Women's Hospital, Boston (1998-2000) he developed a method for noninvasive focusing of ultrasound through the human skull for treatment of brain tumors. Dr. Clement is presently the Technical Director of the Brigham Focused Ultrasound Laboratory, which participates in simulation, experimental and clinical studies of ultrasound for novel therapeutic or diagnostic use. His present research interests include noninvasive transskull focusing of ultrasound in the brain for cancer treatment, shear-mode brain imaging, perfusion imaging, high-resolution (super-resolution) methods, ultrasound coded excitation, phase-contrast ultrasound imaging, and automated diagnosis of ischemia and perfusion.

Sandy Cochran, MBA, PhD
University of Dundee, Dundee, United Kingdom
s.coehran@dundee.ac.uk

Sandy Cochran has been working in ultrasound for more than 25 years. The core of his activity is the ultrasonic transducer and array, and he has complemented this with many other related topics, both upstream, in materials and fabrication techniques, and downstream, in instrumentation and applications. He is presently with the Institute for Medical Science and Technology (IMSaT) at the University of Dundee, Scotland, where he leads the Ultrasound Team as well as holding the role of Deputy Director. Ultrasound has three faculty, two research staff, and twelve PhD students. Its research includes new piezoelectric materials, imaging devices, and therapeutic ultrasound. In the latter, both focused ultrasound surgery and focal drug delivery are covered. A particular topic of interest is the use of the Thiel cadaver for ex vivo testing of human anatomy. This type of cadaver maintains flexibility and colour, in turn translating into the possibility for use in MRI and ultrasound imagining and therapy, as well as extensive use for training. Both breathing motion and pulsatile vascular flow have been demonstrated empirically, and a program of elastographic imaging and monitoring has begun.
Workshop Attendees

Daniel Coluccia, MD  
Kantonsspital Aarau (KSA), Zurich, Switzerland  
daniel.coluccia@ksa.ch

Jacques Coumans, PhD  
GE Healthcare, Waukesha, Wisconsin  
jacobs.coumans@ge.com

Matt Eames, PhD  
Focused Ultrasound Surgery Foundation, Charlottesville, Virginia  
meames@fusfoundation.org  

Matt Eames is the Brain Program Senior Project Engineer and joined the Focused Ultrasound Surgery Foundation in December 2009. Dr. Eames earned his PhD in Biomedical Engineering at the University of Virginia performing research in the design, modeling, fabrication, and characterization of combined diagnostic/therapeutic ultrasound transducers. In conjunction with John Snell PhD, he supports the technical component of the Brain R&D Program and establishes and maintains collaborative relationships with members of the ultrasound industry and research communities who share a common interest in advancing the Foundation's Research Programs.

W. Jeffrey Elias, MD  
University of Virginia, Charlottesville, Virginia  
wje4r@hscmail.mcc.virginia.edu  

Dr. Elias was born in Durham, NC. He graduated Phi Beta Kappa from Wake Forest University. He attended the University of Virginia for Medical School and Neurosurgical training. He completed intramural fellowships in neuropathology and spinal surgery before spending a year in Plymouth England as a senior registrar. Following his neurosurgical residency, he pursued additional training in stereotactic and functional neurosurgery at the Oregon Health Sciences University. Dr. Elias returned to the University of Virginia where he is currently the Director of Stereotactic and Functional Neurosurgery with a large multidisciplinary program in the surgical treatment of movement disorders and epilepsy. For this, he was awarded the School of Medicine's Excellence in Clinical Medicine Award. He has been named to Best Doctors in America by Best Doctors, Inc. His clinical practice also includes minimally-invasive spine surgery, peripheral nerve surgery, spasticity, and neuropsychiatric procedures. His clinical research interests are in the fields of movement disorder and intracranial monitoring for epilepsy. His laboratory research is focused upon thalamic physiology in epilepsy. He is currently the principal investigator of the first clinical trial for the treatment of essential tremor using MR-guided focused ultrasound.

Javier Fandino, MD  
University Children's Hospital, Zurich, Switzerland  
javier.fandino@ksa.ch  

Javier Fandino is Chairman at the Department of Neurosurgery, Kantonsspital Aarau, Switzerland. After his neurosurgical residency at the Universities of Bern and Zurich, Switzerland, Dr. Fandino completed his training at the Universities of Virginia, VA, and Cincinnati, OH. Before moving to Aarau, Dr. Fandino was on the faculty at the Department of Neurosurgery, University Hospital Bern. He has an active clinical practice specializing in patients with cerebral vascular disease, including aneurysms and arteriovenous malformations, and spine surgery. His research interests focus on intracranial aneurysms, experimental SAH models, aneurysms models for the research of
endovascular technologies, and new therapeutic method for brain tumors. In addition, Dr. Fandino concentrate his effort in the development and optimization of intraoperative imaging technologies in cerebrovascular and brain tumor surgery, such as the setup of hybrid Ors and intraoperative MRI. Dr. Fandino is member of numerous national and international societies and serves actively in the training or neurosurgeons in Switzerland.

**Keyvan Farahani, PhD**  
National Cancer Institute, Rockville, Maryland  
farahani@nih.gov

Dr. Farahani is a Program Director in the Image-Guided Interventions (IGI) Branch, Cancer Imaging Program, National Cancer Institute. In this capacity he is responsible for the development of NCI initiatives that address diagnosis and treatment of cancer through integration of advanced imaging and minimally invasive technologies. Since 2002 Dr. Farahani has lead the NCI initiatives in Oncologic IGI with programs focused on industrial developments, early phase clinical trials, and image-guided drug delivery using nanotechnologies. He has led a series of NCI workshops that promote an open science model to develop, optimize and validate platforms for IGI. These initiatives have engaged other agencies of the federal government namely other institutes of the NIH, FDA, NIST and CMS. Prior to joining NCI in fall of 2001, Dr. Farahani was a faculty of the department of Radiological Sciences at the University of California, Los Angeles, where he obtained his MS (89) and PhD (93) degrees in Biomedical Physics.  

Dr. Farahani is a member of the American Association of Physicists in Medicine, the Scientific Program Committee of the Radiological Society of North America, and a past president of the Interventional MR study group of the International Society of Magnetic Resonance in Medicine.

**Jessica Foley, PhD**  
AAAS Science & Technology Policy Fellowships  
jifoley8@gmail.com

Jessica Foley is currently serving as a 2011-2012 Science & Technology Policy Fellow through the American Association for the Advancement of Science. During this year she will be based at the National Science Foundation, in the Division of Chemical, Bioengineering, Environmental, and Transport Systems. Prior to the fellowship, Jessica worked at InSightec as the Neuro Projects Manager for North America. She received her BSE in Biomedical Engineering from Duke University and her PhD in Bioengineering from the University of Washington. Her doctoral dissertation research investigated the biological and physiological effects of focused ultrasound on peripheral nerves.

**Robert Frysinger, PhD**  
University of Virginia, Charlottesville, Virginia  
rfsy@virginia.edu

Robert C. Frysinger is an electrophysiologist with a 20 year history of helping neurosurgeons treat movement disorders, beginning with radio-frequency lesions, moving to deep brain stimulation, and currently excited at the prospects of FUS thalamotomy. Dr. Frysinger is a Research Professor of Neurological Surgery at the University of Virginia.

**Rock Hadley, PhD**  
University of Utah, Salt Lake City, Utah  
rock@ucair.med.utah.edu
Workshop Attendees

Arik Hananel, MD, MBA
Focused Ultrasound Surgery Foundation, Charlottesville, Virginia
ahananel@fusfoundation.org

Arik Hananel is the Scientific and Medical Director of the Focused Ultrasound Surgery Foundation. Prior to joining the Foundation, Dr. Hananel worked at InSightec for more than 12 years, doing research and development in multiple applications of MR-guided focused ultrasound. Dr. Hananel has numerous publications, presentations at academic conferences, and patents in the field of MR-guided focused ultrasound.

Sagi Harnof, MD
Sheba Medical Center, Ramat Gan, Israel
sagi.harnof@sheba.health.gov.il

Dr. Harnof graduated the Tel-Aviv University School of Medicine in 1997 (including an internship in Wolfson Medical Center). He completed his Neurosurgery residency in Sheba Medical Center in Israel, including a short rotation at the Cerebro-Vascular service with Dr. M. Lowton in UCSF. He was involved in the research of ICH – by developing MR guided minimal invasive approach for the treatment of ICH. His basic research focused on the utilizing of PN-277 for the treatment of stroke – animal models. Dr. Harnof spent two years with Dr. Neal Kassell in the University of Virginia, performing Cerebro-Vascular clinical fellowship along with vasospasm research and developing the MR Guided Focus Ultrasound research included performing preclinical experiments. Dr. Harnof is an attending Vascular Neurosurgeon at Sheba Medical Center department of Neurosurgery, running the Cerebro-vascular service; as well as the Deputy Director of the Department of Neurosurgery at Chaim Sheba Medical Center. He also serves on the Board of EURONICH. His clinical interests are focused on Vascular Neurosurgery of the brain and spine, benign tumors of the brain and spinal cord and minimal approach techniques. His research projects include: MR Guided focus Ultrasound for the treatment of ICH, Stroke, and for the treatment of Facet related pain. Immune-modulation of CNS repair – in vitro studies with Monocysts after stroke and spinal cord injury; image analysis of anti brain edema treatment and response to treatment by novel MRI methods – animal studies and feasibly human clinical stud; and more.

Thilo Hoelscher, MD
University of California San Diego, San Diego, California
thoelscher@ucsd.edu

Thilo Hoelscher Assistant Professor UCSD Departments of Radiology, Neurosciences, Mechanical and Aerospace Engineering, UCSD faculty since 08/2002 leading scientists in the field of contrast-enhanced ultrasound imaging of the human brain. Research (last 3 years mainly) on therapeutic ultrasound (sonothrombolysis, drug carrier systems). Research activities in Engineering: flow mechanics (bubble tracking, echoPIV), transcranial sound field characterization, effects of primary/secondary radiation force on acoustically active drug carriers. Since June ’08 main research focus on transcranial sonothrombolysis using High Intensity Focused Ultrasound. M.D. degree in 1995 at the University of Esseen/Germany. Stroke fellowship training under Prof. H.-C. Diener, Department of Neurology, University of Essen. Specialization in clinical neurology and neurosonology under Prof. U. Bogdahn, Department of Neurology, University of Regensburg/Germany. Published: 25 peer reviewed articles, 5 book chapters, 20 abstracts for scientific meetings, holds 5 U.S. patents (assignee: University of California, San Diego)
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Thomas Huerta
University of Virginia, Charlottesville, Virginia
teh6@virginia.edu

Thomas E. Huerta is an MRI tech at the University of Virginia. He does clinical MR at the UVA Medical Center and, clinical and research MR at the MRgFU center. He has 18 years experience as an MRI tech and has experience in both private practice and academic settings. He can perform MR scans in all disciplines, Cardiac, MR angiography, MR, MR Spec. He’s a member of the ISMRM/SMRT organization. He has presented lectures, written abstracts, presented posters and co-authored MR related articles in major radiology journals.

Diane Huss, PT, DPT, NCS
University of Virginia, Charlottesville, Virginia
dsh6z@virginia.edu

Diane Huss is a Board Certified, Neurologic Physical Therapist Clinical Specialist. Dr. Huss serves as the physical therapist consultant with the functional neurosurgery team with Dr. Jeffery Elias at the University of Virginia. She developed and conducts the intra-procedure monitoring protocol and the pre and post procedure assessments that are in use with the FDA Clinical Trial for MRgFUS Thalamotomy for treatment of Essential Tremor. Dr. Huss has extensive expertise in the evaluation and treatment of individuals with Essential Tremor, Parkinson’s Disease, Dystonia, Spasticity and other neurological impairments. She determined the functional outcome measures in use for the functional neurosurgery procedures at UVA for movement disorders, conducts these assessments, and maintains these outcomes in an on-line database. She is interested in the development of uniform assessment protocols across centers to facilitate communication and the advancement of these clinical applications.

Kullervo Hynynen, PhD
Sunnybrook Health Sciences Centre, Toronto, Canada
khynynen@sri.utoronto.ca

Dr. Hynynen received his Ph.D. from the University of Aberdeen, United Kingdom. After completing his postdoctoral training in biomedical ultrasound also at the University of Aberdeen, he accepted a faculty position at the University of Arizona in 1984. He joined the faculty at the Harvard Medical School, and Brigham and Women’s Hospital in Boston, MA 1993. There he reached the rank of full Professor, and founded and directed the Focused Ultrasound Laboratory. In 2006 he moved to University of Toronto. He is currently the Director of Imaging Research at the Sunnybrook Research Institute and a Professor in the Department of Medical Biophysics at University of Toronto, Toronto, Ontario, Canada. He holds a Canada Research Chair in Imaging Systems and Image-Guided Therapy awarded by the Government of Canada. Dr. Hynynen served as the General Chairman for the 5th International Symposium on Therapeutic Ultrasound in Boston, MA, USA in October 2005 and served as the president of the International Society of the Therapeutic Ultrasound in 2006-9.

Daniel Jeannmonod, MD
Center of Ultrasound Functional Neurosurgery, Solothurn, Switzerland
daniel.jeannmonod@gmail.com

Dr. Daniel Jeannmonod graduated from the faculty of medicine at the University of Lausanne in 1978. His doctoral thesis in 1982 was in the field of neuroplasticity. He trained in neurosurgery in Lausanne, then in Queen’s Square (London) and Lyon, obtaining his swiss title in neurosurgery in 1989. He was head of the Department of Functional Neurosurgery at the University Hospital Zürich between 1989 and 2009, and holds the titular professorial chair for functional neurosurgery at the University of Zürich since 1993. He holds since 1998 an adjunct assistant professorship in the Department of Physiology and Neurosciences at New York University.
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School of Medicine (Dr. R. Llinas). His interest and expertise are focused on the field of functional neurosurgery, with research accents on neuroanatomy and neurophysiology, and covering the treatment of chronic and therapy-resistant functional brain disorders including movement disorders, neuropathic pain and tinnitus, epilepsy and neuropsychiatric disorders. He received in 1998 the Pfizer Research Prize in the domain of neurosciences and diseases of the nervous system. He has described together with Dr. Llinas the mechanisms, at thalamic and cortical levels, of the thalamocortical dysrhythmia. He developed the concept of selective regulatory symptom control, centering therapeutic action on dysfunctional regulators of the thalamocortical system. He performed in 2008 and 2009, together with his colleague Prof. Ernst Martin, the first series of focused ultrasound interventions against neuropathic pain. He is now head of the Center for Ultrasound Functional Neurosurgery (Solothurn, Switzerland), where he leads the project, Transcranial MR-guided Functional Ultrasound Neurosurgery“ against neuropathic pain, Parkinson’s disease and essential tremor.

Soren Johansson, MSc
Elekt, Stockholm, Sweden
soren.johansson@elekta.com

Ferenc Jolesz, MD
Brigham and Women’s Hospital, Boston, Massachusetts
jolesz@bwh.harvard.edu

Ferenc Jolesz has achieved international recognition as one of the great innovators and leaders in radiological research. He continues to distinguish himself with ongoing cutting edge research in magnetic resonance imaging and image-guided therapy. In 1998, Dr. Jolesz was appointed B. Leonard Holman Professor of Radiology at Harvard Medical School and Vice Chairman for Research at the Department of Radiology of Brigham and Women's Hospital in 2000; he has been Director of the Division of Magnetic Resonance Imaging since 1988. In 1993, Dr. Jolesz established the Image-Guided Therapy Program at the Brigham and Women's Hospital, which includes an internationally recognized intraoperative MRI facility, the Surgical Planning Laboratory, and the Therapeutic Ultrasound Laboratory-the center of ground breaking therapeutic technology development. In 2002, Dr. Jolesz was appointed Director of the Neuroimaging Core of the Harvard Center for Neurodegeneration and Repair. Dr. Jolesz maintains a research focus in basic and clinical neurosciences, magnetic resonance imaging, and image guided therapy. Along with a highly trained and dedicated research staff of over 100, Dr. Jolesz spearheads the development and implementation of innovative image processing methods and has brought several minimally invasive therapies into successful clinical application. Dr. Jolesz is also credited with developing, refining, and introducing into clinical practice the idea of direct, real time MR image-guided surgical interventions. In collaboration with key industrial partners, Dr. Jolesz has driven the development of various image-guided therapy delivery systems in current use in several sites around the world. Among these, interventional an interoperative MRI, MRI-guided laser, cryoablation, and MRI-guided brachytherapy are the most significant. Dr. Jolesz is further recognized for perfecting the use of high in intensity-focused ultrasound as a tissue ablation tool and integrating it with MR imaging guidance systems. Dr. Jolesz' pioneering research in image-guided brain surgery in particular has had an enormous impact on the fields of modern Radiology and Neurosurgery. His contributions are widely acknowledged in the literature and in medical curricula throughout the world. Dr. Jolesz' substantial research support comes from a variety of public and private sources, including several NIH grants of which he is principle Investigator, corporate-sponsored clinical trials, and industry supported research efforts. He belongs to several professional societies and serves on the editorial boards of prestigious peer review journals. Commensurate with his prolific research, Dr. Jolesz has published over 300 articles in scholarly, peer reviewed journals and has contributed many chapters and review articles in the fields of surgery, computer science, neurology, and radiology.
**Workshop Attendees**

**Neal Kassell, MD**  
University of Virginia, Charlottesville, Virginia  
nfk8g@hscmail.mcc.virginia.edu

Dr. Neal Kassell is a Distinguished Professor of Neurosurgery at the University of Virginia, and the Founder and Chairman of the Focused Ultrasound Surgery Foundation. Prior to UVA, Dr. Kassell served on the faculty at the University of Iowa. Dr. Kassell is a founder of numerous private ventures including Interax, Inc, the Virginia Neurological Institute, Multimedia Medical Systems, the Neuroclinical Trials Center, Neuroventure Fund, and MedSpecialist. He currently serves as a director of the Virginia National Bank and the La Gesse Foundation, and is on the editorial board of Neurosurgery and Stroke. Dr. Kassell has been a recipient of the McKenzie Memorial Award of the Canadian Neurosurgical Society and the Grass Award of the Society of Neurological Surgeons. He has published over 450 scientific papers. Dr. Kassell received his undergraduate and medical education at the University of Pennsylvania.

**Mohamad Khaled, MD**  
University of Virginia, Charlottesville, Virginia  
mak6i@virginia.edu

**Hyungmin Kim, PhD**  
Harvard Medical School, Boston, Massachusetts  
Hkim34@rics.bwh.harvard.edu

Dr. Kim is currently a Research Fellow in Radiology Department at Harvard Medical School, Brigham and Women's Hospital. He received his M.S. degree from the School of Mechanical and Aerospace Engineering at Seoul National University in 2001. After that, he entered himself into the medical industry for developing various medical imaging softwares (Vworks, Vceph, Vimplant, OnDemand3D) and surgical navigation system (In2Vision) at Cybermed, Inc., Korea. Then, he continued his academic career in biomedical engineering at the University of Bern, Switzerland, and completed his Ph.D. degree on soft-tissue simulation for cranio-maxillofacial surgery in 2011. His research focus lies on developing planning and image-guided navigation systems for various surgical environments.

**Manabu Kinoshita, MD, PhD**  
Osaka University Graduate School of Medicine, Osaka, Japan  
m-kinoshita@nsurgmed.osaka-u.ac.jp

**Walter Koroshetz, MD**  
National Institute of Health, Bethesda, Maryland  
koroshetzw@ninds.nih.gov

Walter J. Koroshetz is the Deputy Director of NINDS. Working with Dr. Story Landis, the NINDS Director, he oversees extramural and intramural research programs of the Institute. At the NIH, he led the trans-NIH Task Force on Research in the Emergency setting and was instrumental in the establishment of the joint intramural NIH-Unifomed Services University program in Traumatic Brain Injury research (The Center for Neuroscience and Regenerative Medicine). He is a member of the trans-NIH comparative effectiveness committee, Global Health Committee, Health Economics Committee, Alzheimer’s disease Neuroimaging Initiative proteomics workgroup, and the Foundation for NIH neuroscience biomarkers consortium. Before joining NINDS, Dr. Koroshetz served as vice chair of the neurology service and director of stroke and neurointensive care services at Massachusetts General Hospital (MGH). He was also a professor of neurology at Harvard Medical School and led neurology resident training at
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Nir Lipsman, MD, PhD
Sunnybrook Health Sciences Centre, Toronto, Canada
nir.lipsman@utoronto.com

Nir Lipsman is a neurosurgery resident and PhD graduate student at the University of Toronto. He completed his medical training at Queen's University and his undergraduate work at the University of Toronto. He is currently the Toronto study-coordinator for the FUS Essential Tremor Trial at Sunnybrook Health Sciences Center, with Principle Investigator, Dr. Michael Schwartz and supervisor Dr. Andres Lozano. He has an interest in minimally invasive and functional neurosurgery, including deep brain stimulation, radiosurgery and focused ultrasound, and how these techniques can be applied to disorders of motor, mood and behaviour.

Johanna Loomba
University of Virginia, Charlottesville, Virginia
jil4d@virginia.edu

Todd Mainprize, MD
Sunnybrook Health Sciences Centre, Toronto, Canada
todd.mainprize@sunnybrook.ca

Dr. Todd Mainprize is an Arthur and Sonia Labatt Brain Tumour Research Centre Associate Scientist at Sunnybrook Health Centre in Toronto. His clinical and academic focus is Neuro-Oncology. Currently, he is focusing on the translational applications of MRI-guided focused ultrasound in the treatment of both primary and metastatic brain tumours. He is also looking at the role of blood brain barrier disruption for the delivery of novel therapeutic agents in recurrent glioblastoma.

Fabrice Marquet, PhD
Columbia University, New York, New York
Fm2364@columbia.edu

Fabrice Marquet received an BS/MS engineering degree in physics from Ecole Superieure de Physique et de Chimie Industrielles de Paris (ESPCI-ParisTech) in 2005. He then received his MS and his PhD degrees from University Paris VII for his work on transcranial and transcostal HIFU at the Langevin Institute in 2005 and 2009 respectively. Fabrice has been a postdoctoral research scientist at the Ultrasound and Elasticity Imaging Laboratory at Columbia University, New York, NY since 2009. His current research interests include drug delivery using ultrasound induced blood-brain barrier opening and biomechanical tissue characterization, cancer therapy, and therapy monitoring.
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**Ernst Martin, MD**  
University Children’s Hospital, Zürich, Switzerland  
ernst.martin@kispi.uzh.ch

Dr. Ernst Martin became a professor in Pediatrics and Pediatric Neuroradiology in 1996. In addition, he managed several research projects on higher cognitive brain functions in children using multimodal imaging techniques, e.g. EEG and functional MRI. His current experimental and clinical research interests include BBB opening and targeted drug delivery, and neurosurgical interventions for brain tumors and for various functional brain disorders, such as neuropathic pain, movement disorders, epilepsy and neuro-psychiatric disorders, in children and adults using transcranial MR-guided FUS.

**Jaime Mata, PhD**  
University of Virginia, Charlottesville, Virginia  
jfm4q@virginia.edu

Jaime F. Mata is an Assistant Professor of Radiology & Medical Imaging and the Assistant Director of the Center for In-Vivo HPG MRI at the University of Virginia. He has been an active researcher in the development of magnetic resonance imaging (MRI) techniques for over 13 years and holds two patents in MR pulse sequence design. Dr. Mata has been the lead researcher in developing animal models for his Center, which has made numerous pioneering contributions to the development and application of MRI techniques, including in neuroimaging. In the past two years, his work in neuroimaging and respective collaborations with the local division of neuroradiology, have contributed for his 2011 Research Scientist Award from the American Society of Neuroradiology (ASNR) and for his grant from the Neuroradiology Education & Research Foundation (NERF), in the area of non-invasive targeted delivery of brain therapy using MRgFUS.

**Nathan McDannold, PhD**  
Brigham & Women’s Hospital, Harvard Medical School, Boston, Massachusetts  
njm@bwh.harvard.edu

Dr. Nathan McDannold received his BS in Physics from the University of Virginia in Charlottesville and his PhD in Physics from Tufts University in Boston. He is currently an Associate Professor in Radiology at Harvard University. He has been working in the Focused Ultrasound Laboratory at Brigham & Women’s Hospital since June 1996. His work has been primarily concerned with the development and implementation of MRI-based thermometry methods, animal experiments testing MRI and ultrasound related work, and clinical focused ultrasound treatments of breast tumors, uterine fibroids, and brain tumors. In recent years, a main focus of his work has been studying the use of ultrasound for temporary disruption of the blood-brain barrier, which may allow for targeted drug delivery in the brain.

**Stephen Meairs, MD**  
University of Heidelberg, Mannheim, Germany  
meairs@neuro.ma.uni-heidelberg.de

Stephen Meairs is an American citizen and currently Professor of Neurology at the University of Heidelberg in Mannheim. He graduated from Stanford University and studied medicine at Stanford and Heidelberg. He received training in internal medicine at the German Diagnostic Center and in neurology at the University of Heidelberg in Mannheim. His research interests center around ultrasound applications for diagnosis and therapy of stroke. Stephen Meairs has carried out studies on sonothrombolysis, perfusion imaging, drug delivery through the blood-brain-barrier, molecular imaging, ultrasound-enhanced viral gene therapy to the brain, and recently, angiogenesis using a novel human BBB model. He worked on the German government
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Ricky Medel, MD
University of Virginia, Charlottesville, Virginia
rm5qk@hscmail.mcc.virginia.edu

Ricky Medel is a fifth year neurosurgery resident who has worked on focused ultrasound projects for the last two years with a focus on sonothrombolysis.

Stephen Monteith, MD
University of Virginia, Charlottesville, Virginia
sjm9n@virginia.edu

Stephen Monteith was born in the United Kingdom and completed his undergraduate and Medical School training at the University of Auckland, New Zealand. After internship and initial neurosurgery training in Auckland, he joined the residency program at the University of Virginia in 2007. His clinical and research interests are in the area of cerebrovascular neurosurgery. Dr Monteith has begun basic training in endovascular neurosurgery and intends on completing an endovascular fellowship post residency. He will begin his chief residency in July 2010 after completion of his dedicated laboratory time. His current research in FUS is in sonothrombolysis for intracerebral hemorrhage and he is conducting experiments with the team at the University of Virginia Focused Ultrasound Surgery Center in Charlottesville, Virginia.

David Moser
SoniModul AG, Solothurn, Switzerland
david.moser@sonimodul.ch

David Moser was born in August 1980 in Nyon, near Geneva (CH). He studied electrical engineering at the High School of Engineering in Yverdon-les-Bains (CH) where he obtained his Electrical Engineer's Degree in January 2007 with a specialization in power electronics. From February 2007 to December 2010, he worked at the Institute of Electrical Systems and Energy (IESE) of the High School of Engineering, for applied research and development in the field of power converters. His developments included realization (electronic boards: power and microprocessor control) and programming of power converters ranging from 3 to 30kW. Since January 2011, he works for the Center for Ultrasound Functional Neurosurgery in Solothurn as chief engineer, involved in MR-guided focused ultrasound neurosurgery. He is also responsible for quantitative EEG recordings and analysis.
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Edward Oldfield, MD  
University of Virginia, Charlottesville, Virginia  
eho4u@virginia.edu

Dr. Oldfield received his MD from the University of Kentucky Medical School, training in general surgery and neurosurgery at Vanderbilt University and in neurology at the National Hospital for Nervous Disease, London, England. Until 2007, when he joined the Department of Neurosurgery at the University of Virginia, he lead a laboratory and clinical research effort in neurosurgery at the National Institutes of Health, where he was chief of the Surgical Neurology Branch, National Institutes of Neurological Disorders and Stroke. His interests include brain and pituitary tumors, syringomyelia, the development of new drug delivery techniques for the central nervous system, neural transplantation and regeneration, Von Hippel-Lindau disease, and certain types of vascular disorders of the central nervous system, particularly arteriovenous malformations affecting the spinal cord, dural arteriovenous fistulas, and the pathophysiology and treatment of cerebral vasospasm. In addition to his clinical interests, he has sought to use new information and techniques of basic science to develop new treatment approaches for disorders of the brain and spinal cord. Dr. Oldfield is former chairman of the Editorial Board of the Journal of Neurosurgery. In 1995 he was awarded the Grass Medal from the Society of Neurological Surgeons and in 1999 he received the Farber Award of the American Association of Neurology Surgeons. He is currently president of the Society of Neurological Surgeons.

Dennis Parker, PhD  
University of Utah, Salt Lake City, Utah  
parker@ucair.med.utah.edu

Dr. Parker a medical physicist with over 30 years experience in research in physics applied to medical imaging. In about 1979, while developing a CT scanner for radiation therapy planning, he performed early experiments to test whether MRI could be used to measure temperature and published the first papers showing that MRI could be used to create images of temperature in the early 1980's. Dr. Parker came to the University of Utah in 1982, and has ever since been involved in developing medical imaging research programs, with an emphasis on MRI research. He has supervised a large number of students who have obtained PhD’s and have taken productive careers in academics and industry. He has worked with several other faculty and the Chairs of Radiology to develop the Utah Center for Advanced Imaging Research (UCAIR), which functions to provide imaging infrastructure to support research throughout the campus. We have established several interdisciplinary research programs in conjunction with UCAIR, including the collaboration between Radiology, Mechanical, Electrical, and Bio-Engineering, Oncology and Surgery, to develop our program in MRI guided High Intensity Focused Ultrasound (HIFU). In this program he has been able to continue to work with students and post docs in developing improved MRI temperature measurement methods. Their research has received support from Siemens Medical Solutions, and three R01 grants from the NIH. The two active grants include an academic / industrial collaboration (R01 CA 134599) to develop a system for MRI guided focused ultrasound treatment of breast lesions. The second active MRgHIFU NIH grant (R01 EB013433) is a collaboration with centers in the US, Toronto, and Paris, France to develop rapid, high spatial resolution, temperature imaging throughout the brain for monitoring the safety and efficacy of transcranial MRgHIFU.

Joy Polefrone, PhD  
Focused Ultrasound Surgery Foundation, Charlottesville, Virginia  
jpolefrone@fusfoundation.org

Dr. Joy Polefrone is the Program Director for the Foundations internally driven research initiative in focal drug delivery, which was launched in early 2010. Prior to filling this role, Dr. Polefrone served as the Director of Patient Support Organizations at the FUS Foundation, a
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position she held from May 2008 to January 2010. While in this role, Dr. Polefrone founded the Foundation’s first patient support organization, Fibroid Relief, and served as its Executive Director from October 2008 - February 2010. Prior to joining the Foundation, Dr. Polefrone worked as a biotech equity analyst at CRT Capital Group in Stamford, Connecticut. She earned her PhD in Chemistry at the University of Virginia in the fall of 2006 in the Laboratory of Donald F. Hunt, PhD. The focus of her doctoral dissertation was the use of mass spectrometry to interrogate research questions related to cancer immunology and immunotherapy.

Nader Pouratian, MD, PhD
UCLA Ronald Reagan Medical Center, Los Angeles, California
npouratian@mednet.ucla.edu

Paul Prentice, PhD
University of Dundee, Dundee, United Kingdom
p.a.prentice@dundee.ac.uk

Dr. Paul Prentice’s research is largely focused on optical approaches to predetermine the location and instant of acoustic cavitation occurrence associated with therapeutic ultrasound. This permits the incorporation of high speed cameras for direct imaging, critically, at the temporal and spatial resolutions required to characterize inception and evolution, with parallel monitoring via acoustical detection techniques. The overall aim is to develop a fundamental understanding of the phenomenon, and associated effects, ultimately for control and manipulation techniques.

Rich Price, PhD
University of Virginia, Charlottesville, Virginia
rjp2z@virginia.edu

Dr. Richard Price is an Associate Professor of Biomedical Engineering at the University of Virginia and the Research Director of the UVa Focused Ultrasound Center. His primary research interests are in the regulation of microvascular growth and remodeling by hemodynamics and bone marrow-derived cells and in the development of therapeutic approaches based on interactions between focused ultrasound and microbubbles. Within the ultrasound-microbubble field, Dr. Price has studied the molecular mechanisms through which ultrasonic microbubble destruction stimulates skeletal muscle angiogenesis. He has also developed methods that use ultrasound and microbubbles for stimulating therapeutic arteriogenesis through growth factor-bearing nanoparticle delivery. More recent work has focused on using ultrasound and microbubbles for brain tumor therapy, including targeted drug-bearing nanoparticle delivery and mechanical tumor ablation.

Mark Quigg, MD
University of Virginia, Charlottesville, Virginia
msg6g@unix.mail.virginia.edu

Mark Quigg is an Associate Professor of Neurology Director of Clinical EEG, EP, and Neurological Sleep Labs at University of Virginia. Trained in medicine and engineering, he is the Director of Clinical EEG, EP, and Neurological Sleep Labs. Research interests include the hormonal regulation of epilepsy, EEG monitoring techniques, and epilepsy surgery.
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Viola Rieke, PhD
Stanford University, Stanford, California
vrieke@stanford.edu

Viola Rieke received her PhD in Electrical Engineering in 2005 from Stanford University. She currently is Senior Research Associate in the Department of Radiology at Stanford University. Viola Rieke has research experience in interventional MRI and MR-guided focused ultrasound therapy. Her research interests include the technical development of magnetic resonance imaging methods and advanced image processing algorithms. In particular, her research focuses on pulse sequence development and reconstruction methods for guiding and monitoring focused ultrasound therapy in real-time.

David Schlesinger, PhD
University of Virginia, Charlottesville, Virginia
djs9c@virginia.edu

David Schlesinger is an Assistant Professor and Medical Physicist in the Departments of Radiation Oncology and Neurological Surgery at the University of Virginia. He serves as the chief physicist for the University of Virginia Gamma Knife center and helps to oversee treatment quality assurance at the UVA Focused Ultrasound Center. Dr. Schlesinger is board-certified in Therapeutic Medical Physics by the American Board of Radiology.

Michael Schwartz, FRCSC, MD
Sunnybrook Health Sciences Centre, Toronto, Canada
m.schwartz@utoronto.ca

Jason Sheehan, MD, PhD
University of Virginia, Charlottesville, Virginia
jps2f@hscmail.mcc.virginia.edu

Jason Sheehan is an alumni professor of neurosurgery and radiation oncology at the University of Virginia. He also serves as one of the directors of the UVA FUS Center. He has completed neurosurgical training at the University of Virginia with a fellowship in stereotactic and functional neurosurgery at the University of Pittsburgh. He also completed graduate training in the fields of biomedical engineering and biological physics. Dr. Sheehan's clinical interests include image guided neurosurgical procedures. He has active research in the areas of radiosurgery of the brain and spine.

John Snell, PhD
Focused Ultrasound Surgery Foundation, Charlottesville, Virginia
jsnell@fusfoundation.org

Dr. John Snell is the Technical Director of the FUS Foundation's Brain Program, having joined the Foundation in October 2009. He received a PhD in Biomedical Engineering from the University of Virginia in 1994 and brings a depth of academic and commercial experience in the areas of medical image analysis, neurosurgical planning, surgical navigation, radiation therapy and radiosurgery planning. He has served on the faculty of the University of Virginia Neurological Surgery Department and has made contributions to commercial medical device development with several companies including Multimedia Medical Systems, Medical Numerics and Varian Medical Systems. Dr. Snell is responsible for the definition and coordination of Brain Program technical research projects as well as providing engineering support to participating research sites.
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Sham Sokka, PhD
Philips Healthcare, Andover, Massachusetts
sham.sokka@philips.com

Dr. Sham Sokka is currently the CTO & Director of Research & Clinical Science for the Philips Healthcare MR-HIFU group. In this role, he has responsibility for all research, clinical activities, and business development in the MR-guided HIFU area. He received his masters in Electrical Engineering from the Massachusetts Institute of Technology (MIT) in 1999 and then his PhD in 2004 in Electrical & Medical Engineering from the Harvard-MIT Health Sciences & Technology Program. His dissertation topic was in the area of MR-guided HIFU, specifically on cavitation and heating mechanism critical to thermal ablation and HIFU-mediated drug delivery. In 2003, he joined Philips Research as a Senior Scientist in the area of ultrasound-mediated drug delivery. This work focused more specifically on ultrasound methods with bubble and nanoparticle agents for drug delivery. While at Philips Research, he also managed projects in the area of multi-modality imaging for clinical electrophysiology interventions. Dr. Sokka has over 20 publications and pending patents in the area of HIFU, ultrasound imaging, and multi-modality image guidance for interventions.

Jacques Souquet, PhD
Supersonic Imagine, Aix-en-Provence, France
jacques.souquet@supersonicimagine.fr

From 2000 to 2005 Dr. Souquet served as Chief Scientific and Technology Officer (CTO) and Senior Vice President of Philips Medical Systems. From 1993 to 2000 he was CTO and Senior Vice President for Product Generation at ATL Ultrasound. From 1989 to 1993, Dr. Souquet served as Director of Strategic Marketing and Product Planning and Vice President for Product Generation of ATL Ultrasound. He joined ATL Ultrasound in August 1981 as a principal scientist in the cardiology division. Dr. Souquet holds a Higher Engineering Degree from the Ecole Superieure d'Electricite of Paris, France, a PhD in the field of optical memory, from Orsay University, France, and a PhD in the field of new acoustic imaging techniques for medical ultrasound applications and nondestructive testing from Stanford University. Dr. Souquet is a member of the board of Directors of SonoSite, Inc., an ultrasound imaging company and world leader in the field of hand-carried ultrasound systems. He is also on the board of Directors of Median Technologies, a French company in medical computer aided detection systems. He is the inventor of the multiplane transesophageal echo probe, which is now used in 30% of all ultrasound echocardiography examinations. Dr. Souquet is the owner of 10 patents in the field of ultrasound imaging. He is also the author of more than 50 technical papers and is a keynote speaker at major technical and clinical meetings worldwide.

Mickael Tanter, PhD
Institut Langevin, Paris, France
mickael.tanter@espci.fr

Mickaël Tanter is a Research Professor of the French Institute for Medical Research (INSERM). He is currently heading the team Inserm U979 “Wave Physics for Medicine” at Institut Langevin, from Ecole Superieure de Physique et Chimie Industrielles (ESPCI ParisTech), France. He received a Diplôme d'Ingénieur (High Engineering Degree) from Ecole Supérieure d'Electricité in 1994 and was awarded in 1999 a PhD degree from Paris VII University in Physics. His main activities are centered around the development of new approaches in wave physics for medical imaging and therapy. His current research interests a wide range of topics: transcranial ultrasonic therapy, elasticity imaging of organs using ultrafast ultrasound scanners, adaptive focusing, functional brain imaging. In 2009, he received the Frederic Lizzi Early Career Award of the International Society of Therapeutic Ultrasound and the Montgolfier Prize of the National Society for Industry valorization (S.E.I.N.). In 2010, he received the Leon Brillouin Prize of the
Workshop Attendees

Institute of Electrical and Electronics Engineers (IEEE) and SEE society. In 2011, he received the Yves Rocard Prize from the french Society of Physics. M. Tanter is the recipient of 17 patents in the field of ultrasound imaging. He is the author of more than 100 technical peer reviewed papers. In 2005, along with M. Fink, J. Soquet and C. Cohen-Bacrie, he founded Supersonic Imagine, an innovative French company (72 M€ capital venture) positioned in the field of medical ultrasound imaging and therapy. This company launched in 2009 a revolutionary Ultrasound imaging platform called Aixplorer™ with a unique shear wave imaging modality. Recently, his team published the first article on functional imaging of brain activity with ultrasonic waves.

Nicholas Tustison, PhD
University of Virginia, Charlottesville, Virginia
nj4rn@virginia.edu

Nick Tustison is currently an assistant professor in the radiology department at the University of Virginia. Theoretical interests include image analysis (including registration and segmentation), and the dissemination of robust, open source tools which includes development of the Insight Toolkit (http://www.itk.org) and the Advanced Normalization Tools package.

Arne Voie, PhD
University of California San Diego, San Diego, California
avvie@ucsd.edu

Dr. Voie earned his PhD in Bioengineering at the University of Washington in 1996, where the focus of his work was quantitative 3D reconstruction and measurement of anatomical structures. He was the director of research at Spencer Technologies in Seattle for 12 years, conducting research to use ultrasound to measure cochlear blood flow, characterize otitis media, enhance thrombolysis, and detect changes in the brain during and after ischemic events. In 2010 he left private industry to join Dr. Thilo Hoelscher at the Brain Ultrasound Research Laboratory at UCSD in San Diego, where he is now the director of research. Current research efforts, supported by NIH and FUSF, include sonothrombolysis, detection and characterization of cavitation, transcranial focused ultrasound, and measurement of acoustic fields. He has published several peer-reviewed articles, with more either in submission or in preparation.

Kobi Vortman, PhD
InSightec, Ltd., Haifa, Israel
kobiv@insightec.com

Dr. Vortman is Founder, President, and Chief Executive Officer InSightec Ltd. He is the former president and CEO of Diasonics Vingmed Ultrasound. Dr. Vortman has also held research and development management positions at Elscint Ultrasound Imaging and RAFAEL (the Israeli Armament Development Authority). Dr. Vortman received his undergraduate degree from Hebrew University and his Ph.D. from Technion, the Israeli Institute of Technology.

Tiffani Voss, MD
University of Virginia, Charlottesville, Virginia
tv4e@virginia.edu

Dr. Voss is Assistant Professor of Neurology at the University of Virginia. She completed medical school and residency training in Neurology at the University of Pennsylvania and completed her fellowship in Movement Disorders and Experimental Therapeutics at the University of Rochester. Current research interests include the development of outcome measures in movement disorders, clinical trials and trial methodology, and fall reduction in Parkinson's disease.
Workshop Attendees

Urvi Vyas, PhD
Stanford University School of Medicine, Stanford, California
urivyas@gmail.com

Urvi Vyas is a postdoctoral fellow at Stanford University. She earned her PhD working with Professors Douglas Christenson, Robert Roemer, and Dennis Parker at the University of Utah. Her work entailed developing rapid techniques for modeling ultrasound beam propagation in 3D inhomogeneous tissue geometries. She also developed a parameter estimation technique using optimization routines to probe changes in acoustic properties of tissues after MRgFUS treatments and demonstrated this non-invasive technique for the first time in-vivo. She was the recipient of the Young Investigator Award at the 2nd International Symposium on MR-guided Focused Ultrasound and the New Investigator Award at the Society of Thermal Medicine for this work.

Natalia Vykhodtseva, PhD
Focus Ultrasound Laboratory, Boston, Massachusetts
natalia@bwh.harvard.edu

Natalia Vykhodtseva received her MS in Physics and Electrical Engineering at Moscow State Pedagogical Institute and her PhD in Biological Sciences at the Institute of Higher Nervous Activity and Neurophysiology, All-Union Academy of Sciences in Moscow. She began studies on HIFU in the brain in late 1960s at the Moscow Brain Research Institute, where she developed a technique to produce sharply defined lesions in the brain using a hemispherical transducer. Following this, Dr Vykhodtseva became a PI of numerous studies and head of the Bioacoustic Group at Brain Research Institute in Moscow. In 1989 she became a permanent researcher in Focused Ultrasound Laboratory at Brigham and Women's Hospital and Harvard Medical School. Throughout her career her studies have concentrated on non-invasive interventions for treating brain disorders, such as tumors, neurodegenerative diseases, and vascular malformations using FUS methods.

Beat Werner, PhD
University Children's Hospital, Zürich, Switzerland
beat.werner@kispi.uzh.ch

Beat Werner graduated from the faculty of physics of ETH Zurich, Switzerland in 1988 and started working at University Children's Hospital Zurich on C-13 MR-spectroscopy. He left MR-research in 1990 and worked for several years in software development and marketing communication with new media. In 2002 he joined again the MR-Center at University Children's Hospital. Since 2005 he has been involved in the brain project for technical and physical aspects of the related research activities. Research Focus: Physical and technical aspects of clinical application of tMRgFUS in brain for ablation and drug delivery.

Max Wintermark, MD
University of Virginia, Charlottesville, Virginia
mw4vh@virginia.edu

Dr. Max Wintermark is a graduate of medicine from Lausanne University in Switzerland. He received his professional training in radiology from Lausanne University Hospital, as well as from the University of California San Francisco. A pioneer in the development of Perfusion-CT and CT-Angiography with patented work pertaining to the technique, Dr. Wintermark is a published author of numerous articles and text chapters in the field of cerebrovascular imaging. He has been involved in a number of clinical trials of image-guided stroke therapy. Dr. Wintermark is currently the Chief of Neuroradiology at the University of Virginia.
Workshop Attendees

Seug-Schik Yoo, MBA, PhD
Brigham and Women’s Hospital, Brookline, Massachusetts
yoo@bwh.harvard.edu

Dr. Yoo graduated from the Johns Hopkins University in 1994 majoring in Biomedical Engineering. He later completed his Ph.D. in 2000 for the development of adaptive real-time functional magnetic resonance imaging method at Harvard-MIT Division of Health Science and Technology and Nuclear Engineering department at MIT. While he was pursuing his Ph.D., Dr. Yoo also received MBA degree in Marketing from the University of Massachusetts Boston in 1999. He continued his research at Brigham and Women’s Hospital (BWH) in Boston as postdoctoral fellow, and joined faculty at Harvard Medical School in 2004. He is currently an associate professor in Radiology, and serves as director of Functional MRI Service at BWH. Dr. Yoo has pioneered the real-time functional MRI method for the neurofeedback and brain-computer-interface through multi-modal imaging approaches. His recent research also extends to the development of robot-driven three-dimensional cell printing technology for the application in tissue engineering and regenerative medicine using stem cells. His laboratory, with the collaboration of Focused Ultrasound Laboratory at Brigham and Women’s Hospital and UVA, investigates the mechanism of focused ultrasound-mediated non-invasive modulation of the brain function and its clinical applications. Research Focus: Multi-modal real-time functional brain mapping; Focused ultrasound; Non-invasive neuromodulation; Neurofeedback; Medical imaging processing; Brain tumor; Epilepsy; Tissue engineering; Stem cell engineering; Cell tracking and homing.

Eyal Zadicario, MSc
InSightec, Ltd., Haifa, Israel
eyalz@insightec.com

Eyal Zadicario is VP R&D and Director of Neuro Programs in InSightec. InSightec is the leader in MRgFUS technology and has developed the first and only clinical MRgFUS system. Eyal has been with InSightec since it has been founded in 1999 and held various positions in its research and development team. As Director of Neuro Programs in InSightec, Eyal has been leading the program from its early design, development and preclinical phase throughout its initial clinical trials to date. Recently Eyal has been assigned the role of VP R&D. In his responsibilities he manages the R&D team and oversees the technological and product development programs in InSightec.
## Intracerebral Hemorrhage Roadmap

### Research Questions:
- Can focused ultrasound lyse intracerebral hemorrhage transcranially?
- What is the speed of clot lysis? Can microbubbles accelerate lysis?
- Does sonothrombolysis precipitate rebleeding?
- What is the nature of the hemolysate produced by focused ultrasound compared to the naturally occurring hemolysate and the hemolysate resulting from tissue plasminogen activator?
- What are the optimal parameters for sonothrombolysis of intracerebral hemorrhage?
- Are these parameters safe in terms of normal brain?

### Parameters

1. Develop in vitro clot model
2. Determine provisional sonothrombolytic parameters
3. Lyse in vitro clots
4. Can MR be used to visualize clot lysis?
5. Develop transcranial in vitro clot model
6. Lyse in vitro clots transcranially
7. Develop in vivo clot model
8. Lyse in vivo clots
9. Optimize sonothrombolytic parameters

### Safety

1. Develop animal safety model
2. Determine safety of sonothrombolytic parameters in normal brain

### Clinical Research

- Pilot/Feasibility Clinical Trial
Acute Ischemic Stroke Roadmap

Parameters

- Develop/Select In Vitro Transcranial Clot Model
- Develop/Select In Vivo Transcranial Vessel Model
- Develop/Select In Vivo Transcranial Clot Model
- Lyse In Vitro clots
- Determine Provisional Parameters
- In Vivo Transcranial Lysis of Clots
- Optimize sonothrombolytic parameters

Safety

- Arterial Wall Safety
- Normal Brain Safety
- Ischemic Brain Safety

Clinical Research

- Pilot/Feasibility Clinical Trial

Visualization

- MR Visualization of Clot
- Target verification of Clot

Research Questions:

- Can focused ultrasound lyse intravascular clots transcranially?
- What is the speed of clot lysis?
- What are the optimal parameters for sonothrombolysis of intravascular clots?
- Are these parameters safe in terms of normal brain, ischemic brain and arterial wall?
- Can the clot be visualized and targeted?
- Can focused ultrasound be used to lyse intravascular clots in humans in a timely manner?
### FUS NM for neurophysiologic assessment roadmap

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Safety</th>
<th>Clinical Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Determine the appropriate large animal (sheep and pigs)</td>
<td>Consult FDA on permissible parameters and number of animal</td>
<td>Pilot/Feasibility in clinical trials</td>
</tr>
<tr>
<td>Determine provisional neuromodulation parameters (Aim for excitation and suppression of neural activity separately)</td>
<td>Successful reversible neuromodulation</td>
<td></td>
</tr>
<tr>
<td>Determine the FUS set up (phased array or single US transducer)</td>
<td>Determine the safety of NM parameters in normal animal brain</td>
<td></td>
</tr>
<tr>
<td>Determine the physiological monitoring methods (EEG, MEG, fMRI, PET, SPECT, etc)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conduct neuromodulation experiments</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimize parameters</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Research Questions and:

<Parameters>

- **Fundamental FUS frequency: 350 or 700KHz? Higher or lower?** – Currently lower frequency seems to favor the successful neuro-modulation at lower acoustic intensities. However, one should be careful that lower frequency tends to increase the risk of mechanical damage, i.e. consideration of MI.
- **Type of FUS transducer, multi-array or single transducer?** Both multi-array or single FUS transducer system can be used. However, the single-FUS transducer may suffer from typical problems with acoustic distortion by the skull. The tolerance of the study will depend on frequency, treatment area and depth, imaging-guidance method etc. Multi-array system is advantageous is proposed deep brain stimulation and subsequent ablation.
- **Tone burst duration (TDB), pulse repetition frequency (PRF; determining the duty cycle), acoustic intensity in terms of SPPA (SPTA can be calculated from the duty cycle), sonication duration (SD)**
- **Excitation or suppression/ both?** For stimulation, 0.5ms-1ms TBD, 0.5-1Khz PRF, SD 100-300msec, Ispta < 3 W/cm² (adjust Isppa according to the Duty factor). For suppression, apply only 30-50% of the acoustic intensity that elicited the activation, give lower PRF such as 100Hz, increase the SD to > 20 secs and more. Make sure that you will not heat the tissue by applying low Ispta.
- **Dimension of the focus?** Few millimeters in diameters would be sufficient as most of the FUS equipments can reasonably achieve this.
- **Dimension of the treatment area (Thalamic area? Anywhere else):** examine the sonication parameters that results in the modulation of electrophysiological signals (the amplitude and latencies in VEP, MEP,
and SSEP) by sonicating lateral geniculate nucleus (LGN: for VEP), internal capsule (IC: for MEP), and ventral posterolateral nucleus (VPN: for SSEP).

- Intra operative MRI guidance: Slight increase of the temperature (1°C) and subsequent detection of the temperature profile using temperature-sensitive MR sequence can be used. Optionally, ARFI type of technique as well as less accurate separate extra-operative image-guidance can be used.

- Accuracy/reliable of the guidance: ARFI would provide the best performance in accuracy, however, the method is still in development..

**<Safety>**

- MI and Ispta considerations: MI less than M<0.9; Ispta < 3 w/cm²
- FDA limitation on clinical systems? the upper regulatory limit for non-obstetric ultrasound imaging (720 mW/cm²; AIUM Clinical Standards Committee, 2004) guidelines (i.e., 1.9 for all applications except ophthalmic (maximum 0.23); FDA, 2008). Cavitation-related brain tissue damage, in the absence of air bubbles, is rare at pressures less than 40 MPa (Dalecki, 2004)
- Short and long-term biological effects (acute, intermediate and long term: what is the period that are favored by FDA?) Upto 2-3 months post survival
- BBB disruption (via Gad injection or Trypan/Evan’s blue injection); Gad injection and MR exam right after the sonication or Trypan/Evan’s blue injection right before at the short-term effect sacrifice. Cavitation-related brain tissue damage, in the absence of air bubbles, is rare at pressures less than 40 MPa (Dalecki, 2004), and the neuromodulation can typically occur less than 1MPa.
- Record Behavioral changes: As needed according to the species.
- Over excitation needs to be monitored by EEG: VEP measuring can be also used to EEG. However, long-term monitoring may be indicated.
- Temperature consideration: MR thermometry? See above. 1 C increase for the targeting purpose. MR thermometry will be needed.
- Types of histological study: Caspase3 for apoptosis, DNA defragmentation kit, glial infiltration). Electron microscopy
- Different animal species (larger animal or even human application?) Would FUS be applied to the species of choice? (pigs has more difficult cranial structure) Sheep at BWH and Pig at UVA
- In addition to evaluations of neuronal damage, assessment of glia may be needed due to its high population. Oxidative stress in glial cultures: Detection by DAF-2 fluorescence
- Number of animal species? 10 minimum
- Acoustic Radiation Force imaging (ARFI)? On-going.. maybe collaboration with Stanford group?

**<Clinical Research>**

- Optimization of the FUS application and its modulatory effects on In vivo fMRI mapping (PET mapping?)
- Use anatomical as well as functional information from the brain? fMRI and DTI mapping in separate sessions, Imaging registration would be necessary.
- EEG monitoring: Yes. A pair of thin (~200 µm in diameter) Ag/AgCl electrodes (SWE Ives EEG Solution, Canada) will be subdermally introduced into skin to enable single-montage EEG recordings.
- EMG monitoring (for motor task?) A pair of thin (~200 µm in diameter) Ag/AgCl electrodes (SWE Ives EEG Solution, Canada) will be subdermally introduced into skin to enable single-montage EMG recordings. The signal will be amplified (PowerLab 8/30, AD Instrument, CO) and recorded (LabChart 7, AD Instrument, CO) at a sampling rate of 1000 Hz. The data acquisition system will be situated outside of the 5 guass line in MRI suite (in case of intra MR guidance)
- PET imaging to examine the functional metabolism: On going on rats, using FDG PET (at BWH)
- Application in human study as a part of functional neurosurgery in motion/pain disorder? While FUS-mediated functional neurosurgery emerged as potential non-invasive treatment modalities for neurological disorders such as essential tremor and pain, the on-site validation of the brain function of the targeted sonication prior to thermal ablation would greatly increase the accuracy of the treatment.
- Would sonication in non-thalamic area be sufficient for thalamic modulation? We will modulate the thalamic area.
- Would be need to include animal model? such as MPTP model of Parkinson’s Disease or essential tremor model (or… does such thing exist?) Further collaboration may be needed.

**<references>**


# Brain Cancer Draft Roadmap

**Project Leads:** Kullervo Hynynen, Nathan McDannold & Todd Mainprize

## Parameters

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Identify the appropriate preclinical animal model of brain cancer for studying BBB opening &amp; drug delivery*</td>
</tr>
<tr>
<td>2.</td>
<td>Identify candidate chemotherapeutic agent(s) and microbubble(s) Doxil + Definity/Optison</td>
</tr>
<tr>
<td>3.</td>
<td>Determine ultrasound parameters to perform initial in vivo studies</td>
</tr>
<tr>
<td>4.</td>
<td>Optimize ultrasound parameters in small animal model</td>
</tr>
<tr>
<td>5.</td>
<td>Determine FUS targeting and monitoring parameters without thermometry (not a requirement for “this” trial)</td>
</tr>
<tr>
<td>6.</td>
<td>Determine drug delivery and monitoring parameters</td>
</tr>
</tbody>
</table>

### Completed Experiments and Supporting Citations
- Rabbit model and delivery
- Rat model and Glioma
- Primate Studies - NJM

### Research Questions
- What is the cavitation threshold in FUS system with chosen microbubbles?
- What is the behavior of bubble mediated cavitation below safety threshold?
- How large a volume can be practically treated? In what time?
- How will dose delivery be monitored? Quantitatively? In preclinical models as well as in clinical applications (ex. drug and contrast within same drug delivery system?)

### Additional questions
- Does treatment planning go in here – seems critical part of the roadmap if our goal is patient treatment?
- Would survival studies be necessary?
Literature searches were performed through September 2011 with the qualifiers “focused ultrasound” and “brain.” The output of these searches can be found on the following pages as well as on the FUSF Website. We greatly appreciate your assistance in pointing out any missing references and aiding us in providing the most up-to-date bibliographic content.

Search output has been segmented by the topics listed below:

- Brain Tumors 43
- Functional Neurosurgery 52
- Epilepsy 54
- Intracerebral Hemorrhage 57
- Ischemic Stroke 59
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- Drug Delivery 78
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**Ischemic Stroke**


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Cavitation


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**Drug Delivery**


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