3rd Image-Guided Therapy Workshop:
Advances in Multi-Modal Imaging for Intervention
March 8 & 9, 2010
Arlington, VA
History

1st Image-Guided Therapy Workshop: *Challenges in Image Guided Therapy*
October 2006 – Washington, D.C.

- Attended by 75+ people from academia, industry, and the federal government.
- It resulted in a peer-reviewed paper in the journal *Neuroimage*.

2nd Image-Guided Therapy Workshop: *Clinical Image Guided Interventions*
March 10-11, 2008 – Washington, D.C.

- Attended by 120+ people, mostly PIs of recently funded grants from NCI and NIBIB
- Specifically targeted a group of new R21 grantees as invitees and faculty speakers
- The goal was to network and to show reflections and publications, including abstracts of talks, on the NCI website
3rd IGT Workshop Summary
Statistics

Program
• 25 oral presentations
• 43 poster presentations

Attendees
• 102 attendees total from:
  • 32 institutions
  • 12 companies
  • NIH
Statistics

Participants

• Gender
  • Male: 89
  • Female: 15

• Race:
  • Hispanic or Latino: 2
  • Not Hispanic or Latino: 68
  • Unknown: 34

• Ethnicity:
  • Asian: 15
  • Black/African-American: 1
  • White: 41
  • More than One Race: 2
  • Other: 11
  • Unknown: 34
Financial Information

• Registration Fee = $300
• 104 Registered - 24 speakers (waived fee) = 80 paid participants
• Total regular fee collected = $24,000

• Conference Facility & Food = $25,000
• CVENT (registration company) = $1,500

Total Owed = $26,500
Financial Information

NIH R13 Support: $5,000

Distribution Protocol:
• $300 x 8 travel subsidy for out of town oral presenters
• $300 x X travel subsidy for out of town poster presenters
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<tr>
<th>Name</th>
<th>Status</th>
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<tbody>
<tr>
<td>Broadsky, Ethan</td>
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<tr>
<td>Chen, Minghan</td>
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<td>Daly, Mike</td>
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<tr>
<td>Halter, Ryan</td>
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<tr>
<td>Kim, Chunwoo</td>
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<td>Linte, Christian</td>
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<td>Ren, Honglian</td>
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<td>Butts-Pauly, Kim</td>
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<tr>
<td>Song, Sam</td>
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<tr>
<td>Paweena U-Thainual</td>
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<td>Butler, Brian</td>
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<td>Ellis, Randy</td>
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<td>Ferrara, Kathy</td>
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<td>Frangioni, John</td>
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<td>Jaffray, David</td>
<td>Replied</td>
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<tr>
<td>Khuri-Yakub, Butrus</td>
<td>No Response</td>
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<td>Wang, Lihong</td>
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<td>Wright, Graham</td>
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**Posters**

**Presenters**
<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>12:00 PM - 1:00 PM</td>
<td><strong>Lunch</strong>&lt;br&gt;Lunch for all attendees</td>
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<tr>
<td>1:00 PM - 1:30 PM</td>
<td><strong>Keynote:</strong> Ferenc Jolesz, M.D., P.I.-NCIGT, Harvard Medical School and Brigham and Women's Hospital&lt;br&gt;Advanced Multimodality Imaging in the Operating Room</td>
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<tr>
<td>1:30 PM - 2:00 PM</td>
<td><strong>Andreas Melzer, M.D., D.D.S., University of Dundee, Scotland</strong>&lt;br&gt;Advances for Image-Guided Surgery at Dundee, Scotland: MITOS Multimodality Image-Guided Therapy Operating System</td>
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<tr>
<td>2:00 PM - 2:30 PM</td>
<td><strong>Randy Ellis, Ph.D., Queen's University</strong>&lt;br&gt;Intraoperative CT and Cone-Beam CT Imaging</td>
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<tr>
<td>2:30 PM - 3:00 PM</td>
<td><strong>Garnette Sutherland, M.D., University of Calgary</strong>&lt;br&gt;Imaging and Image Guidance in Neurosurgery</td>
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<tr>
<td>3:00 PM - 3:30 PM</td>
<td><strong>John Heiss, M.D., NINDS/NIH</strong>&lt;br&gt;MR-Guided Neurosurgery</td>
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<tr>
<td>3:30 PM - 4:00 PM</td>
<td><strong>Nathan McDannold, Ph.D., Harvard Medical School and Brigham and Women's Hospital</strong>&lt;br&gt;Focused Ultrasound Therapy</td>
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<tr>
<td>4:00 PM - 4:15 PM</td>
<td><strong>Break</strong></td>
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<td>Time</td>
<td>Speaker</td>
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<tr>
<td>4:15 PM - 4:45 PM</td>
<td>David Jaffray, Ph.D., Princess Margaret Hospital</td>
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<td>4:45 PM - 5:15 PM</td>
<td>Alexandra Golby, M.D., Harvard Medical School and Brigham and Women's Hospital</td>
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<tr>
<td>5:15 PM - 5:45 PM</td>
<td>Graham Wright, Ph.D., Sunnybrook Health Sciences Centre</td>
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<tr>
<td>5:45 PM - 7:00 PM</td>
<td>Poster Session and Reception</td>
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Tuesday, March 9, 2010

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<tr>
<th>Time</th>
<th>Speaker</th>
<th>Institution</th>
<th>Topic</th>
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<tr>
<td>7:30 AM - 8:20 AM</td>
<td>Poster Session and Breakfast</td>
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<tr>
<td>8:20 AM - 8:40 AM</td>
<td>Keyvan Farahani, Ph.D., NCI/NIH</td>
<td>NCI Programs and Funding Opportunities in Image-Guided Interventions</td>
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<tr>
<td>8:40 AM - 9:00 AM</td>
<td>Peter Choyke, M.D., NCI/NIH</td>
<td>Image-Guided Prostate Biopsy and Therapy</td>
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<tr>
<td>9:00 AM - 9:20 AM</td>
<td>Brad Wood, M.D., Clinical Center, NIH</td>
<td>Fusion Interventions for Ablation: The Wii Surgeon</td>
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<tr>
<td>9:20 AM - 9:40 AM</td>
<td>Clare Tempany, M.D., P.I. - NCIGT, Brigham and Women's Hospital and Harvard Medical School</td>
<td>Image-Guided Pelvic Intervention</td>
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</table>
Scientific Program:

9:40 AM - 10:00 AM  Russ Taylor, Ph.D., Johns Hopkins University  
Medical Robotics and Computer-Integrated Interventional Medicine

10:00 AM - 10:20 AM  Break

10:20 AM - 10:40 AM  Kevin Cleary, Ph.D., Georgetown University  
EM Tracked Navigation in Cone Beam CT Suite for Abdominal Intervention

10:40 AM - 11:00 AM  Kirby Vosburgh, Ph.D., CIMIT and MGH  
New Approaches for Validating Interventional Procedures

11:00 AM - 11:20 AM  E. Brian Butler, M.D., Methodist Hospital, Weill Cornell Medical College  
Multi-Parametric Visualization in Image-Guided Surgery and Radiation Therapy

11:20 AM - 1:00 PM  Breakout Sessions and Lunch

Session 1: "Multimodal Registration Clinic"  
Moderator: Dominik Meier, Ph.D., Brigham and Women's Hospital

Session 2: "MR-Guided FUS Therapy"  
Moderator: Nathan McDannold, Ph.D., Brigham and Women's Hospital

12:40 PM - 1:00 PM  Anthony Pacifico, Ph.D., Telemedicine and Advanced Technology Research Center (TATRC)  
TATRC Programs in Image-Guided Therapy

1:00 PM - 1:20 PM  William Wells, Ph.D., Harvard Medical School and Brigham and Women's Hospital  
Registration Methods for Image-Guided Therapy
Scientific Program:

1:40 PM - 2:00 PM  Kathy Ferrara, Ph.D., UC Davis
Ultrasound-Guided Drug Delivery

2:00 PM - 2:20 PM  Pierre Khuri-Yakub, Ph.D., Stanford University
Innovations in Ultrasound Instrumentation for Image-Guidance

2:20 PM - 2:40 PM  Lihong Wang, Ph.D. Washington University
Photoacoustic Imaging in Image-Guided Therapy

2:40 PM - 3:00 PM  John V. Frangioni, M.D., Ph.D., Harvard Medical School and Beth Israel Deaconess Medical Center
Image-Guided Surgery using Invisible Near-Infrared Fluorescent Light

3:00 PM - 3:15 PM  Closing Comments
Poster Presentations:

**CARDIAC**


4. Improved Cardiac MRI Gating, Physiological Monitoring and Cardiac-Output Estimation by MRI Compatible 12-Lead ECGs. Z. T. H. Tse, C. L. Dumoulin, G. Clifford, M. Herosch-Herold, D. Kacher, R. Kwong, W. G. Stevenson, and E. J. Schmidt. Radiology, Brigham and Women's Hospital, Boston, MA; University of Cincinnati College of Medicine, Cincinnati, OH; Health Sciences and Technology, Massachusetts Institute of Technology, Boston, MA; Cardiology, Brigham and Women's Hospital, Boston, MA.

**ABDOMEN**

5. Integrated MRI and HIFU Control System: Towards Real Time Treatment of the Liver. A. B. Holbrook, C. L. Dumoulin, J. M. Santos, Y. Medan, and K. Butts Pauly. Bioengineering, Stanford University, Stanford, CA; Radiology, Stanford, University, Stanford, CA; Imaging Research Center, University of Cincinnati College of Medicine, Cincinnati, OH; HeartVista, Los Altos, CA; Electrical Engineering, Stanford University, Stanford, CA; InSightec Ltd, Tirat Carmel, Israel.
Poster Presentations:

ABDOMEN (cont.)


9. **A New System for Image Registered Natural Orifices Transluminal Endoscopy Surgery (IR NOTES).** R. San Jose Estepar¹,², G. Fernandez-Esparrach³, C. Guarner-Argete³, H. Cordova³, A.M. Lacy³, C.C. Thompson⁴, K.G. Vosburgh²,⁵. ¹Laboratory of Mathematics in Imaging, Brigham and Women's Hospital, Boston, MA; ²Surgical Planning Laboratory, Brigham and Women's Hospital, Boston, MA; ³Department of Gastroenterology, Department of Surgery, ICMIM, Hospital Clinic, CIBERehd, Barcelona, Spain; ⁴Division of Gastroenterology, Brigham and Women's Hospital, Boston, MA; ⁵Center for Integration of Medicine & Innovative Technology (CIMIT), Boston, MA.

10. **New Kinematic Metric for Quantifying Surgical Skill for Flexible Instrument Manipulation.** J. Jayender¹,², R. San Jose Estepar¹, K. Obstein³, V. Patil¹,², C. Thompson³, K. Vosburgh¹,²,⁵. ¹Department of Radiology, Harvard Medical School, Brigham and Women's Hospital, Boston, MA; ²CIMIT Image Guidance Laboratory, Boston, MA; ³Division of Gastroenterology, Brigham and Women's Hospital, Boston, MA.

Poster Presentations:

PROSTATE

12. Multiphoton Microscopy of Human Prostate and Periprostatic Tissue for Real-Time Structure Identification During Nerve-Sparing Radical Prostatectomy. A.K. Tewari¹, S. Mukherjee², M. Hermani¹, R. Yadav¹, K. Mudalair¹, J. Sterling², S. Grover³, M. M. Shevchuk³, M.A. Rubin¹, F.R. Maxfield², W.R. Zipfel², C. Xu⁵, W. W. Webb⁵. ¹Department of Urology, Weill Cornell Medical College, New York, NY; ²Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York, NY; ³Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York, NY; ⁴Department of Biochemistry, Weill Cornell Medical College, New York, NY; ⁵School of Applied and Engineering Physics, Cornell University, Ithaca, NY.

13. Online Guidance of Tumor Targeted Prostate Brachytherapy using Histologically Referenced MRI. C. Ménard¹, A. Rink¹, J. Abed¹, A. Simeonov¹, J. Publicover¹, J. Lee¹, A. Beiki¹, K. Brock¹, W. Foltz¹, C. Elliott², G. Morton³, P. Warde¹ and M. Haider¹,³. ¹Princess Margaret Hospital, University of Toronto, Toronto, Ontario, Canada; ²Sentineelle Medical Inc; ³Odette Cancer Center, University of Toronto


16. Shielding Effects on MRI-Compatibility of a Robotic Device for MRI-Guided Transrectal Prostate Intervention. S. Song¹, N. Cho¹, I. Iordachita³, A. Krieger¹,², G. Fichtinger³, L. Whitcomb¹. ¹Department of Mechanical Engineering, Johns Hopkins University, Baltimore, MD; ²Krieger is presently with Sentinelle Medical Inc., Toronto, Canada; ³School of Computing, Queen’s University, Kingston, Canada.

17. MRI Compatibility Study of a Pneumatically Actuated Robotic System for Transperineal Prostate Needle Placement. S. Song¹, N. Cho¹, J. Tokuda², N. Hata², C. Tempany², G. Fichtinger³, I. Iordachita¹. ¹The Johns Hopkins University, ERC/LCSR, Baltimore, MD; ²Harvard Medical School, Brigham and Women’s Hospital, Boston, MA; ³Queen’s University, School of Computing, Kingston, Canada.
18. Improved Prostate MRI with an Integrated Endo-rectal/MR-Tracking Coil Assembly Incorporating Prospective Motion Correction. L. Qin, E. J. Schmidt, K. Butts Paul, C. Afdhal-Tempany. Harvard Medical School and Brigham and Women's Hospital; Stanford University.


20. Real Time MR-Guided Prostate Ablation with Transurethral Multisected Ultrasound Applicators and Multislice Treatment Planning and Control. A. B. Holbrook¹,², P. Prakash³, P. Jones³, C. Planey², J. M. Santos¹,², C. J. Diederich³, K. Butts Pauly², and F. Graham Sommer². ¹Bioengineering, Stanford University, Stanford, CA; ²Radiology, Stanford University, Stanford, CA; ³Radiation Oncology, UCSF, San Francisco, CA; ⁴HeartVista, Los Altos, CA; ⁵Electrical Engineering, Stanford University, Stanford, CA.

BRAIN AND SPINE


24. Visualization-based Feedback for Image-Guided Neurosurgery. A. Joshi¹, X. Papademetris¹,². ¹Department of Diag. Radiology; ²Biomedical Eng, Yale.

Poster Presentations:

BRAIN AND SPINE (cont.)


27. Accuracy of an Electromagnetic Tracking (EM) System for Image-guided Placement of External Ventricular Drain (EVD). V. Patil, R. Shams, J. Stoll, A. Cheung, R. San Jose Estepar, R. Gupta, K. Vosburgh. 1Surgical Planning Laboratory, Brigham and Women’s Hospital, Boston, MA; 2CIMIT Image Guidance Laboratory, Massachusetts General Hospital, Boston, MA; 3College of Engineering and Computer Science, Australian National University, Canberra, ACT, Australia; 4Center for Integration of Medicine and Innovative Technology, Massachusetts General Hospital, Boston, MA; 5Department of Radiology, Massachusetts General Hospital, Boston, MA; 6Laboratory of Mathematics in Imaging, Brigham and Women’s Hospital, Boston, MA.

28. Improved Visualization of the Extra Dural Spinal Nerves for Spine Pain Interventions. G. Danagoulian, E.J.Schmidt, S. Mukundan, A. Shankaranarayanan, K.S.Nayak. 1Radiology Department, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; GE Healthcare Applied Science Lab, Menlo Park, CA; Electrical Engineering Department, University of Southern California, Los Angeles, CA.

BREAST


30. MRI Tools for Focal Spot Visualization During FUS Breast Treatment. E. Kaye, R. Bitton, K. Butts Pauly. Department of Radiology, Stanford University, Stanford, CA.

31. 3D Stereoscopic Vision for MRI Guided Interventions: Technical Feasibility. M. Philip, B. Fetics, Abraham Roth, Amir Roth, E. Nevo, F. Wacker. 1Robin Medical, Inc., Baltimore, MD; 2Department of Radiology and Radiological Science, Johns Hopkins School of Medicine, Baltimore, MD.
Poster Presentations:

BREAST (cont.)


GENERAL IGT

33. Hybrid Referenceless and Multi-Baseline Subtraction MR Thermometry for Monitoring Thermal Therapies in Moving Organs. W. A. Grissom¹, V. Rieke¹, M. Lustig², J. Santos³, M.M. McConnell⁴ and K. Butts Pauly¹.
¹Radiology, Stanford University, Stanford, CA; ²Electrical Engineering and Computer Science, UC Berkely, Berkely, CA; ³Electrical Engineering, Stanford University, Stanford, CA; ⁴Cardiovascular Medicine, Stanford University, Stanford, CA.

34. Minimizing Imaging Dose in X-ray Fluoroscopy Guided Interventions. S. Siddique¹,², E. Fiume², D. A. Jaffray¹,³. ¹Princess Margaret Hospital/Ontario Cancer Research Institute, Toronto Ontario M5G 2M9, Canada; ²Department of Computer Science, University of Toronto, Toronto, Ontario M5S 3G4, Canada; ³Departments of Radiation Oncology and medical Biophysics, University of Toronto, Toronto, Ontario M5S 3E2, Canada.


GENERAL IGT

37. Interventional Device Tracking and Imaging Using RTHawk, an Extensible Real-Time System. E. Brodsky, O. Unal, W. Block. Radiology and Medical Physics, University of Wisconsin, Madison, WI.
38. **Simultaneous MR Image Guidance and Catheter Tracking.** S. Kecskemeti, E. Brodsky, W. Block, O. Unal. Radiology and Medical Physics, University of Wisconsin, Madison, WI.

39. **Wireless Hybrid Tracking System for Image Guided Therapy.** H. Ren, D. Rank, J. Stallkamp, P. Kazanzides. \(^1\)Department of Computer Science, Johns Hopkins University, Baltimore, MD; \(^2\)Fraunhofer Institute for Manufacturing Engineering and Automation, Stuttgart, Germany.

40. **Evaluation of Accuracy and Clinical Feasibility of the MR-Compatible Image Overlay Augmented Reality System for Needle-Based Surgery.** P. U-Thainual, I. Iordachita, Y. Otake, N. Cho, A. Machado, J. Carrino, G. Fichtinger. \(^1\)Queen’s University, Department of Mechanical and Materials Engineering, Kingston, Ontario, Canada; \(^2\)Queen’s University, School of Computing, Kingston, Ontario, Canada; \(^3\)The Johns Hopkins University, ERC/LCSR, Baltimore, MD; \(^4\)Johns Hopkins University School of Medicine, Russell H. Morgan Department of Radiology and Radiological Science, Baltimore, MD.

41. **An Integrated Surgical Guidance System Based on a High-Performance Mobile C-Arm for 3D Imaging.** J. Siewerdsen, G. Hager, D. Mirotta, S. Nithiananthan, Y. Otake, S. Schafer, J. Stayman, R. Taylor, A. Uneri, W. Zbijewski and C. Bulitta. \(^1\)Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD; \(^2\)Department of Computer Science, Johns Hopkins University, Baltimore, MD; \(^3\)Department of Electrical and Computer Engineering, Johns Hopkins University, Baltimore, MD; \(^4\)Department of Mechanical Engineering, Johns Hopkins University, Baltimore, MD; \(^5\)Siemens Healthcare, Workflow & Solutions (SP) Division, Erlangen Germany.


43. **Fusion of Intraoperative Cone-Beam CT and Endoscopic Video for Image-Guided Procedures.** M.J. Daly, H. Chan, E. Prisman, A. Vescan, S. Nithiananthan, J. Qiu, R. Weersink, D. Jaffray, J.C. Irish, J.H. Siewerdsen. \(^1\)Ontario Cancer Institute, Princess Margaret Hospital, Toronto ON; \(^2\)Institute of Medical Science, University of Toronto, Toronto ON; \(^3\)Department of Otolaryngology-Head and Neck Surgery, University of Toronto ON; \(^4\)Department of Biomedical Engineering, Johns Hopkins University, Baltimore MD.
Oral Presentation
Highlights
Image-Guided Therapy is changing the face of Surgery
Integration of advanced imaging technology in the OR

- Enhance the eye with multimodality imaging
- Replace the hand with image controlled robotic devices
- Integrate therapy with intraoperative imaging
- Develop image-guided therapy delivery systems for multiple clinical applications
- Change invasive procedures to minimally invasive or non-invasive ones
Multimodality imaging in the OR-MRI

- Intraoperative MRI
- MRI-guided FUS
- X-MRI
- PET-MRI
New clinical translational infrastructure

Advanced Multimodality Image-Guided OR (AMIGO)
AMIGO
Multimodality Image-guidance

- Use of multiple imaging modalities in the OR
- Image fusion and its advantages
- Integration of MRI with molecular imaging (PET, optical imaging)
- Fully integrated navigation systems
- Image-fusion
- Improved surgical technologies (robots, endoscopes, thermal ablations, FUS)
IMSaT is a joint venture of the Universities Dundee & St Andrews and member of the joint research Institute for medical technologies of the Northern Research Partnership NRP (Universities Dundee, Aberdeen and Robert Gordon). IMSaT’s remit and core research and development activities are along the line of translation of new technologies for the two non invasive imaging modalities MRI, Ultrasound and Biophotonics to life science and clinical applications. The key clinical application is **Integrated multi-modality Imaging Guided Diagnostic and Therapy of Early Cancer and Cardiovascular Diseases.**

**Sonoporation**

Startegic Background: Image-guided interventional oncology has been recognized as the forth column of clinical oncology. The gold standard of x ray guided percutaneous interventions such as biopsies or interstitial tumor ablation is evolving to moresophisticated hybrid image control of delivery of ablative energy, drugs, gene therapy to diseased tissues and organs.
Ultrasound can not only been used for diagnostic imaging but also to influence cell membrane interactions, to release drugs or to destroy tissue. The application of MRI guidance of focused ultrasound and other ablation techniques allow precise navigation to the target lesion and monitoring of temperature responses and tissue destruction. Biophotonics and novel techniques such as Photoporation (see fig) will play major roles for future diagnostic and therapeutic imaging. Novel targeted drug delivery using nanospheres or lysosomes utilizing heat or electromagnetically activated drug release in the target volume of a tumor opens new opportunities for medical device design.

To achieve this goal the University Dundee has invested more than £10m into lab and imaging infrastructure at CRC and IMSaT. The new Clinical Research Center CRC at NHS Tayside Ninewells Hospital and Medical School is associated and complements the technology development pipeline for image guided oncology with the world first installations of 3 Telsa MRI and PET/CT both linked via a multipurpose interventional/surgical suite.
IMSaT at Wilson House comprises labs for ultrasound, biophotonics tissue and cell culture and fully equipped workshop. Since December 2008 a state of the art 1.5 Tesla interventional MRI connected to a surgical suite is operational. GE has awarded IMSaT as their first European Center of Excellence for MRI guided Interventions and Surgery. We are developing new technologies for “one stop” image guided diagnosis of early cancer are MRI guided cardiovascular procedures such as heart valve and stent implantation [4].

Important task is to improve the link of IMSaT with the College of Life Sciences and the Medical School. We are organizing regular translational seminars in the field of life sciences clinical research and medical technologies to foster collaboration and joint projects. International collaborations are very important for medical technology development and thus IMSaT has induced contacts to various leading sites in Europe, USA and Asia. These activities should be coordinated with other collaborations and visible through a centralised listing of of existing Dundee partners. Commercialisation is the prerequisite of a sustained clinical impact of medical technologies as the only successful medical technology is a well selling medical product. IMSaT is adopting the compliance to ISO certification, GMP and GLP.
MRI guided robotic assisted percutaneous interventions

The robotic system Innomotion has been developed in collaboration with Innomedic, GMBH Herxheim as the world’s first MRI and CT compatible robotic system with CE mark. Current clinical studies on MRI guided liver, prostate and bone biopsy, sciatic pain treatment reveal significant improvement of MRI guided percutaneous interventions. INNOMOTION will be further developed at IMSaT for use in 1.5/3 T with specific focus on interventional oncology and neuro interventional procedures and MRI guided surgery. MRI guided breast biopsy, tumor ablation, abscess drainage can be first clinical studies.
Kingston, Canada: IGS Suite
Kingston, Canada: IGS Suite

- Large operating room, ~1000 square feet
- High-flow air curtain (15 changes/hr)
- Floor-mounted operating table
  - Radiolucent
  - Large range of motion
- Two anesthesia arms
- CT acquisition: gantry on rails
- Floor-mounted fluoroscope: Cone-Beam Computed Tomography (CBCT)
Calibration: Results and Future

Mechanical stability of the Innova CBCT:
• 0.1 mm and 0.3 degrees
• Calibration error: **0.3mm**
Overall system error: 0.8mm

Present:
• Underlying general navigation system
• User Interface is task-specific

Future:
• Need to handle real-time 3D images
• Eliminate human image editing
• More volumetric visualization
FUS in the brain: getting through the skull

**Issue 1: Heating**

- Hemisphere array to distribute energy over large area
- Lower frequency
- Active cooling
FUS in the brain: getting through the skull

Issue 2: Distortion

- Phased array
- Acoustic modeling of the skull
Treatment plan: Live MRI, CT, prior contrast MRI

McDannold et al., Neurosurgery 2010
Inoperable recurrent glioblastoma (grade IV on the ASTRO scale) or recurrent metastatic cancer with defined margins on contrast MRI

Eligibility requirements included:
• limitations on tumor number, size and location, patient health

Exclusion criteria included:
• extensive changes to 30% or more of the skull or scalp
• surgical clips or devices in the skull or brain
• evidence of recent (< 2wks) hemorrhage

McDannold et al., Neurosurgery 2010
Maximum power:
- Patient 1: 600 W (conservative power setting)
- Patient 2: 800 W (max available)
- Patient 3: 600 W (pain)

Max temperature achieved during a 20s sonication was approximately 51°C

McDannold et al., *Neurosurgery* 2010
MRTI Artifacts I: Phase instability

Apparent $\Delta T$ in non-heated ROIs:

McDannold et al., *Neurosurgery* 2010
Blood products from biopsy caused signal loss in MRTI

May be limitation of technique in significant # of patients

High grade gliomas, melanoma and renal cell carcinoma metastases

McDannold et al., *Neurosurgery* 2010
Low-frequency TcMRgFUS system

Preclinical tests in phantoms

- Exablate 4000
- 650 kHz → 220 kHz
- Utilizes microbubble-enhanced heating
- Increases treatment envelop
- More patients can be treated without overheating the skull
Events

- Larger than expected focal spot, liquefaction instead of “cooking”
- Secondary damage in basal ganglia
- Hemorrhage at day 4, patient died at day 5
- Currently evaluating data, revising treatment protocol
- Will only treat metastases in future treatments due to bleeding risk
Low-frequency TcMRgFUS: Reflections and standing waves

- Low frequency US $\rightarrow$ Low absorption
- US beam can reflect multiple times in intact skull cavity
- Small “hotspots” could endanger non-targeted regions

Low-frequency TcMRgFUS: Reflections and standing waves

- Hemorrhage was observed with US stroke treatment at 300 kHz
- Device, sonication parameters, patient population were significantly different
- Nevertheless, it is important to rule out large “hotspots” at non-targeted regions

Low-frequency TcMRgFUS: Reflections and standing waves

F#: 0.8
220 kHz

ExAblate 4000 (Hemisphere, 220 kHz)

Intensity beamplots
Contours at 15% and 50%

Focal dimensions:
F# 0.8: 5.4×28 mm
Hemisphere: 3×5.8 mm
Low-frequency TcMRgFUS: Reflections and standing waves

Sonications performed in human skulls filled with tissue mimicking phantom (gelatin/milk powder; proprietary recipe supplied by InSightec)
Low-frequency TcMRgFUS: Reflections and standing waves

2 min sonications performed to avoid cavitation-enhanced heating

Peak temperature achieved + TMAP noise level allowed us to exclude secondary heating at 15% or more of focal value

12 locations, 2 human skulls

Central brain regions selected – where first tumor targets will be

Steering via moving transducer or electronically
Low-frequency TcMRgFUS: Reflections and standing waves

10+ sonications performed per sonications with TMAP planes changed for each sonication

Full 3D coverage achieved

With heating+cooling, each location required 5-6h
Methods - Dose Accumulation via DVFs

Weekly geometry / Planned dose

Planning geometry / Deformed

Deform to planning geometry

Delivered

30 Patients
IGTW'10

Goals of image-guided neurosurgery

**Goal:**
- Complete resection
- No neurologic injury

**Surgeon wants to see:**
- Lesion and define margins
- Critical structures
- Relationship between lesion and eloquent areas

**To accomplish:**
- Pre-operative planning
- Surgical decision-making
White Matter and Neurosurgery

- Preserve functional cortex and white matter tracts
- At surgery tracts are not visible
- Tracts
  - infiltrated, edematous, destroyed
  - displaced
- Tumor mass displaces
  - Gray matter
  - White matter
Case Presentation

• 38 y/o RH WM

• Focal seizures left arm and leg, then secondarily generalized

• MRI: R frontal lobe lesion T2 bright, T1 dark, no enhancement

• Probable low grade glioma
fMRI: Preoperative Mapping

Where are the white matter tracts associated with these activations?

Left toe wiggle

Left hand clenching
Current State of the Art

• Display all DTI tractography
• Selected interactively
  – Anatomical/functional knowledge and scans
• BrainLab (Commercial system)
  – 3D boxes for interactive tract selection
• DTI Studio
  – Multiple ROI select
Interactive DTI exploration

(Golby, Norton et al. submitted)
DTI tractography seeded from hand clenching fMRI
DTI tractography seeded from left cerebral peduncle
Visualizing tracts in regions of crossing fibers: 2 tensor tractography

- Crossing fibers interfere with tract tracing
- Difficulty in visualizing lateral portion of CST
- Two-tensor model improves CST tracing to and/face

(Qazi et al. Neuroimage 2009)
Joint fMRI-DTI atlas for Neurosurgery

- Tumor mass effect displaces
  - Cortex
  - White matter
- More difficult to trace/select tractography
- Cortical and WM displacements expected to track together
- By using fMRI as a frame of reference can locate functionally relevant tracts
Relative Distance Model

- Spatial model of fMRI-fiber distances
  - Rotation and translation invariant
  - Prediction and detection of tracts

O’Donnell et al. MICCAI Workshop 2009
Where is the tract?

(O’donnell et al. MICCAI 2009)
Fiber Detection Method

Atlas AF Model
Mean across 5 subjects

Similarity of fibers
to the atlas AF model
color is 1/(sum sq difference)

Selected fibers
(50 most similar)
Using model to detect fibers in patients with lesions
In OR visualization:
Integrating research and commercial platforms

- BrainLab sends real-time data from its tracking system and/or images to Slicer3
- BrainLab tracker used to manipulate dynamic DTI visualization in Slicer3.
Closed Bore Hybrid X-ray/MRI

- 1.5 T MRI
- Rotating anode x-ray tube
  - Fewer design trade-offs
  - Improved image quality
- Rapid modality switching
- Smooth patient transfer
- No equipment transfer

Sunnybrook Health Sciences Centre, Toronto
Example: In-imager Needle Placement
Example: Information-Enhanced Interactive Surgery
Combining prior knowledge with online images

Prior statistical information (atlas) → Computational process
  • Segmentation
  • Registration
  • Hybrid reconstruction

Prior images & models (mostly 3D) → Patient-specific model

New Images (2D, 3D) → Applications
  • Intervention planning
  • Intervention guidance & visualization
  • Biomechanical analysis

Video: JH Yao, 2002
Deformable 2D/3D Registration to Atlas
Ofri Sadowsky

Prior statistical information (atlas) → Computational process → Patient-specific model

Applications
- Orthopaedic surgery planning
- Biomechanical analysis
- Hybrid reconstruction
Model Completion, Given Partial CT + X-rays

Image-Guided Vertebroplasty Based on Electromagnetic Tracking
Clinical Trial of Electromagnetic Tracking and IGSTK Software in CT for Lung Biopsy
Image Guided Surgical Toolkit (IGSTK) Open Source Software Package

• Basic components for an image-guided system
  – Tracker
  – Registration
  – Visualization
• Available at igstk.org
• Can be used in commercial products
• Compatible with 3D Slicer from BWH
Real time Instrument Tracking & Registration
Metrics: Timed Tasks

• For a fixed time period, give the operator a series of tasks to perform.
• Pro: it’s functionally realistic
• Con: It’s a function of the familiarity with the tasks.
IRGUS vs. EUS in the Localization and Identification of Anatomic Structures

Fraction of correctly identified structures in porcine model: Pancreas body / tail, Spleen, Left kidney, Right kidney, Right lobe of liver, Portal vein, IVC, SMA
Kinematics Analysis:

NOTES in Cadaver Model (BWH)

- Kinematics data are extracted from the position and orientation of the probe as a function of time.
- This plot shows data for Experiment 1, Operator 3, Access 1 (transgastric), Organ 1 (gallbladder).
- Kinematics parameters are computed from those temporal plots.

![Graphs showing kinematics data for gallbladder cystic duct.]
Comparison Per Operator
Novice, Fellow, Expert

Vosburgh
Composite indexes: Global Isotropy Index (GII)

<table>
<thead>
<tr>
<th></th>
<th>Time</th>
<th>Pathlength</th>
<th>Vel.</th>
<th>Accel.</th>
<th>Ang.</th>
<th>Roll</th>
<th>GII</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Yr Res.</td>
<td>715.4</td>
<td>10.92</td>
<td>0.83</td>
<td>0.65</td>
<td>39.7</td>
<td>0.21</td>
<td>3.45</td>
</tr>
<tr>
<td>Second Yr Res.</td>
<td>288.2</td>
<td>7.56</td>
<td>0.98</td>
<td>0.91</td>
<td>44.4</td>
<td>0.26</td>
<td>4.41</td>
</tr>
<tr>
<td>Third Yr Res.</td>
<td>274.9</td>
<td>5.16</td>
<td>1.15</td>
<td>0.63</td>
<td>40.5</td>
<td>0.16</td>
<td>4.60</td>
</tr>
<tr>
<td>Experts Attending</td>
<td>150.1</td>
<td>3.31</td>
<td>1.29</td>
<td>0.99</td>
<td>42.0</td>
<td>0.22</td>
<td>5.01</td>
</tr>
</tbody>
</table>

- Good Metrics but depend on complexity of procedure
- No variation
- Suitable Metric

Jayender, et al., IPCAI 2010
Descriptive Models

Continuum robot model for the colonoscope to relate the forces applied at the proximal end to the distal tip forces.
Operational Multi-Dimensional Visualization: Applications for Improved Treatment

- Visualization and Imaging Are *In-Vivo* Assays

- Compare the “Content Value” of 2D B&W Images to Multi-Dimensional Visualizations, Manipulable in Real Time, Including “Fly Through” Capability, located at the Clinician’s Desktop and portable device.

- **AIM 1**: To Improve Patient Safety and Quality of Care Through More Informed Clinical Decision-making and Treatment Planning, Involving Patients in the Process as Appropriate

- **AIM 2**: To Improve the Knowledge, Education, and Competency of Medical Students, Residents, and Fully-Trained Physicians, including “Flight Simulation” with Real Patients

- **AIM 3**: To Use FDA Cleared “Near Real-Time Clinical Visualization Technology” to Create Multi-Dimensional Detailed Volumetric Versions of Traditional (B&W, 2D Images) from Slices Acquired by DICOM Compatible MRI, CT, US, and PET Instruments

*Plato'sCAVE*  
The Methodist Hospital System  
Weill Cornell Medical College
TATRC: Our Community and its Needs

Tricare (Active, Retired, Beneficiaries)

Healthcare (Cancers, Circulatory Disease)
Soldier Performance (Psychological/Physiological)

Prevention, Detection, Diagnosis and Treatment

Combat Casualty Care “Boots on the ground”

Trauma Care (PTSD/TBI, Bleeding, Amputations,

Pacifico
Conventional Technologies: Detection and Diagnosis

**MRI/S** (soft tissue)
- Nondestructive
- Functional Imaging
- High Resolution
- Penetrates All Tissues
- Ferromagnetic interference
- Not Portable
- Limited to 3T for humans

**CT/XRAY** (bone)
- Functional Imaging (PET)
- High Resolution
- Penetrates All Tissues
- Ionizing Radiation
- PET requires radiotracers
- CT can require contrast agents

**Ultrasound** (combination)
- Nondestructive
- Highly Portable
- Functional Imaging
- Monitor Tissue Properties
- Images can be hard to acquire/interpret
- Sensitive to gas/bone
- Requires Skin Contact
- Poorer Spatial Resolution
Medical Imaging Technologies: Roadblocks for Trauma Care

In the Combat Support Hospital:

• One tool “to do it all”
• Ease of use
• Morbidity of combat-related injuries
• Portability, Maintainability, Reliability

Limitations of Imaging Techniques:

• What more can we do with current technologies using photons, particles and sound waves?
• Where are the standards and models? (acquisition-related, post-processing, instrumentalational,... TISSUE)
• How do we get a tool with sub-millimeter spatial resolution and deep-tissue penetration?
From Symptoms to Classification; Standardization:

- Dr. Vannier of the University of Chicago is focused on developing acquisition and post-processing standards for DTI

- TATRC has worked with the DVBIC, Siemens and the American College of Radiology to develop new visualization software that uses an XIP format for image processing with anatomical data for a telemedicine application (Right: DTI/MRI/Anatomically co-registered image from a thumb tapping experiment)
Medical Imaging Technologies: Cancers
<table>
<thead>
<tr>
<th>PORTABLE IMAGING AND IMAGE GUIDED THERAPIES</th>
<th>HIGH PERFORMANCE RADIOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Portable X-Ray</td>
<td>• Higher sensitivity CT and PET designs</td>
</tr>
<tr>
<td>• Ultrasound</td>
<td>• Higher sensitivity MR Coils/instrumentation</td>
</tr>
<tr>
<td>• Portable EEG</td>
<td>• Radiological and anatomical standards</td>
</tr>
<tr>
<td>• Advanced surgical camera</td>
<td>• Better small molecule tracers</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ADVANCED SURGICAL CAMERA</th>
<th>COMPUTER ASSISTANCE IN DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Incorporate new materials</td>
<td>• Treatment planning and simulation (controls: patient movement, procedure to procedure, patient to patient)</td>
</tr>
<tr>
<td>• Algorithm development (post-processing)</td>
<td>• Development of open software platforms for image registration/segmentation</td>
</tr>
<tr>
<td>• Spectral libraries based on anatomy/pathology</td>
<td>• Novel data visualization schema/image navigation and usability</td>
</tr>
<tr>
<td>• Deep tissue models of targeted pathologies</td>
<td></td>
</tr>
</tbody>
</table>

TATRC Imaging Roadmap 2015: Creating the future for military medicine
A Clinical Case: Overview
Intraoperative Navigation
Image-Based Registration

• early: feature-based, Pellizzari “head in hat”

• later: intensity-based methods
  – 1995: registration by maximization of Mutual Information (MI) Viola, Wells
Image-Based Registration

- early: feature-based, Pellizzari “head in hat”
- later: intensity-based methods
  - 1995: registration by maximization of mutual information (MI) Viola, Wells
- Recent: feature-based
  - Interesting local features in location X scale
  - E.g., SIFT features
  - Entropy based local features
    - Brady et. al. , Oxford
    - Towes, Wells
Medical Image Registration

Medical image data sets

Transform (move around)

Compare with objective function

score

Optimization algorithm

initial value

motion parameters
## Space of transformations

<table>
<thead>
<tr>
<th>Data dimensions</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>2D-2D</td>
<td>cardiac ultrasound, x-ray patient repositioning, histology – MRI, cortical surfaces…</td>
</tr>
<tr>
<td>3D-3D</td>
<td>MR/MR, MR/CT, CT/CT, PET-MR, …</td>
</tr>
<tr>
<td>2D-3D</td>
<td>X-ray/CT, fluoroscopy-CT, surface model/video</td>
</tr>
</tbody>
</table>
Class of transformations

• What motions or distortions are allowed to merge datasets?
  – Rigid Transformations
  – Non-Rigid Transformations:
    • parametric
      – affine
      – piecewise-affine
      – b spline
      – Finite Element
    • non-parametric
      – elastic
      – fluid
Before Registration
After Registration
2D-3D Rigid Registration

Problem: find $T$

Data coordinate system

$T^{-1}$

$T$

$S_1$

$S_2$

Object

Bi-planar imaging coordinate system

Problem: find $T$
Skull: Before Registration


Skull: After Registration
Plastic Pelvis: Before Registration
Plastic Pelvis: After Registration
Before Image-Based Registration
After Image-Based Registration
Registration Evaluation and Validation

• Retrospective Image Registration Evaluation Project (Vanderbilt University, Nashville, TN)
  – West, Fitzpatrick, et al.
  – http://www.vuse.vanderbilt.edu/~image/registration/

• Non-Rigid Image Registration Evaluation Program (NIREP); University of Iowa
  – Gary Christensen
  – http://www.nirep.org
Target Registration Error

• TRE: discrepancy between predicted and actual target location

• In landmark-based registration:
  – Fiducial Localization Error (FLE)
  • easier to estimate
  • MJF: statistical relationships between TRE and FLE
  • Leo Joscowicz, et al., Hebrew U
    – geometric relationships among TRE and FLE
Evolving Role of Registration

• current: registration for determining initial transformation: often Rigid

• future: registration that accommodates changes due to therapy
  – Non-Rigid
    • What are the material properties?
  – surgery
    • brain shift
    • resection
  – radiation treatment
    • weight loss
    • tumor growth / shrinkage
Pre-op / Intra-op MRI Registration

- Petter Risholm
- Resection: tissue goes away
- Retraction: tissue pulled apart
- IPMI 2009: preliminary 2D
- Recent:
  - 3D implementation
  - validation on synthetic data
  - SPIE medical imaging
What is “the answer”?

- single best estimate of transformation
  - maximum likelihood or MAP estimate
  - some info about global accuracy
- posterior distribution on transformation
  - for non rigid registration: uncertainty about localization may vary from place to place
  - how do we present this information to surgeon?
Purpose: Enhance acoustic signal from blood

Why?

• Scattered signal from blood is small (poor SNR)

• Hard to visualize small vessels and slow flows without enhancing the signal from the blood

• Introduce additional signal in the blood by injecting echogenic structures that flow with the blood
Molecular Imaging with Ultrasound:

Target ultrasonic microbubbles with ligands targeting:

- VEGFR2 - angiogenesis biomarker
- P-Selectin - Inflammation biomarker

Percentage of agents that bind to target can be quantified

Facilitates longitudinal monitoring of response to therapy in a single animal

Dual labeling strategies required to monitor controls and release

PET

Optical

J. Seo et al, Bioconjugate Chemistry, 2008
Dec;19(12):2577-84. Qin S Mol Pharm. Epub 2009 Jul 21
Why nanoparticles?

60 to 220 fold improvement over free drug injection

Fold enhancement compared with free dye

“Doxil” Low Chol MPPC DPPC COMB New polymer/loading

Paoli et al, JCR April 2010
Why nanoparticles?

Tumor accumulation

48 Hr average 15% ID/gram

%ID/g

blood  lungs  diaphragm  heart  liver  kidney  duodenum  jejunum  muscle  tumor

Paoli et al, JCR April 2010
Propose two modes of operation and two mechanisms

1. Inject, use particles to find ROI, release drug
   - Mechanism- temperature sensitive release from vehicle

2. Find ROI, insonify then inject
   - Mechanism- mild inflammation induces local increase in endothelial permeability
Demonstrate release and internalization of the accumulated drug

Motivation: application

• Cardiac arrhythmia – atrial fibrillation
  ▪ World’s most common cardiac arrhythmia
  ▪ Over 2.3 million in the US
  ▪ Over 160,000 new cases each year in the US
  ▪ Serious complications
    ▪ Low cardiac output
    ▪ Thrombosis – embolic stroke

• EP guidance method – fluoroscopy
  ▪ Primary means to direct catheter position and movement
  ▪ Long radiation exposure
    ▪ Hazardous for patient and practitioner

Normal vs. Afib

A Philips fluoroscopy system

IGT Workshop March 8-9, 2010
Technology

- Surface Micromachining
  - Sacrificial layer
- Bulk Micromachining
  - Silicon on Insulator (SOI) Bonding
    - Etching defined cavities
    - LOCOS defined cavities
- Through Wafer Via
  - MIS and PN Junctions
  - Trench-Frame Isolation
  - Thick-box process
- Chip-chip bonding (3D integration)
  - Anisotropic Conducting Film (ACF)
  - Solder Bumps
  - Low temperature bonding
- Flexible arrays

(4 French needle tip)
Medical applications

- Imaging
  - Anatomic (1D, 1.5D, 2D, annular, ring, etc...)
  - Photo-acoustic (functional)
    - Endogenous, exogenous, contrast agents (carbon nanotubes, gold nanoparticles, etc.

- Therapy
  - High intensity focused ultrasound (multimodality: imaging+HIFU)

- Hydrophone
  - Pressure field characterization
  - Passive cavitations detection

- Chem/Bio mass loading sensor
  - Airborne
  - Immersion

- Energy transfer

- Array configurations for above applications
  - Linear, phase, annular, ring, 1.5-D, 2-D, etc.
  - Frequency kHz-MHz
Images with ML Catheter
Fluoroscopy

RF Ablation Catheter
ML Catheter
Images with ML Catheter (short range)
Images with ML Catheter (long range)
CMUT Ring Array

- 64-element Ring array
  - ~ 80 μm x 100 μm element
  - Center frequency 10 MHz
  - Outer diameter 2.6 mm
  - Inner diameter 1.6 mm
  - Sacrificial layer process with through-wafer interconnects
  - Silicon-nitride membrane
  - 0.50-μm membrane thickness
  - 0.15-μm gap height
  - Rectangular and circular membranes

- Lumen available for: HIFU, RF ablation, photo-acoustic imaging, etc.
Direct connection to imaging system suffers from poor SNR

- Noise simulation for ring array element
  - 100 pF/m loss-less coaxial cable.
  - Imaging system input impedance:
    - $R_{\text{in}} = 115 \ \Omega$, $C_{\text{in}} = 70 \ \text{pF}$
  - Imaging system noise sources:
    - $I_{n,\text{in}} = 6 \ \text{pA/} \sqrt{\text{Hz}}$
    - $V_{n,\text{in}} = 0.78 \ \text{nV/} \sqrt{\text{Hz}}$

- Direct connection to imaging system has poor noise figure

- Small elements
  - ~ 80 μm x 100 μm
  - Small inherent SNR

- Low SNR and poor image quality

Need nearby LNA to enhance SNR!
Electronics implemented using low-voltage CMOS in a high-voltage process for seamless integration with existing imaging systems.

Switches implemented using diode limiters/expanders
- eliminates the need for explicit control signal
- small area compared to high-voltage transistor switches
Electronics provides ~20dB improvement in SNR over direct connection to imaging system

* One meter long cable assumed between the IC and the load
  - $C = 104 \ \text{pF/m}$, $L = 220 \ \text{nH/m}$, $R = 30 \ \Omega/m$
CMUT Ring Array Provides Wide Bandwidth

- A ring array was wire-bonded to the IC and biased at -45 VDC.
- A single cycle bipolar pulse with an amplitude of $\sim 40 \text{ V}_{pp}$ was applied.
- Device was immersed in oil and pulse-echo signal from the oil-air interface was measured.
CMUT ring array can generate over 1MPa pressure

- A CMUT ring array was wire-bonded to the IC and immersed in oil.
- A 10-cycle, 8-MHz sine wave with an increasing amplitude was applied.
- Pressure was measured using a calibrated hydrophone and then corrected for attenuation and diffraction losses.
Real-time Imaging

- PC-based imaging system from VeraSonics, Inc.
- Data acquisition hardware
  - RF data acquired in front-end is transferred to computer’s memory.
- Software image processing
- Ring array imaging schemes
  - Flash: flat transmit, beamforming on receive
  - Phased array: beam focusing and steering
  - Synthetic phased array: Norton’s weightings for full aperture resolution and cosine apodization

Ring Array

IGT Workshop March 8-9, 2010
Volume image of metal spring using off-line synthetic phased array imaging

30 dB dynamic range
Norton’s weightings and cosine apodization applied
Ring Array Assembly

- One IC is flip-chip bonded to each leg of the flexible PCB
- Ring array is flip-chip bonded to the center of the flexible PCB
- After backing attachment legs are folded under the Ring array
Photoacoustic Computed Tomography

1. Laser pulse (<ANSI limit: e.g., 20 mJ/cm²)

2. Light absorption & heating (~ mK)

3. Ultrasonic emission (~ mbar)

4. Ultrasonic detection (optical scatter/1000)

1 mK $\rightarrow$ 8 mbar $= 800$ Pa

Transcranial Functional Photoacoustic Imaging of Rat Whisker Stimulation In Vivo: Hemodynamics

Left-whisker stimulation  Right-whisker stimulation

Growth of Photoacoustic Tomography: Data from Conference on Photons plus Ultrasound
Chaired by Oraevsky and Wang
#Presentations versus Year
Functional and Molecular Photoacoustic Imaging:
Nude Mouse with a U87 Glioblastoma Xenograft in the Brain

(a) Functional imaging: Tumor hypoxia
- Structural resolution: 60 µm
- Speckle free

(b) Molecular imaging: Tumor over-expression of integrin
- Resolution: 312 µm
- Sensitivity: 4 fmol/voxel (40 nM)

* Contrast agent provided by Chun Li’s Group (MD Anderson)
Reflection-mode Photoacoustic Microscopy: Illustration

Surface

Target

Optical absorption

Photoacoustic signal

Time of arrival or depth

A-scan

B-scan

Wang
Reflection-mode Dark-field Confocal Photoacoustic Microscopy: System

- Tunable laser
- Nd:YAG pump laser
- Photodiode
- Amplifier
- AD
- Computer
- Motor driver
- Translation stages
- Conical lens
- Sample holder
- Base
- Heater & temperature controller
- Optical illumination
- Ultrasonic transducer
- Mirror
- Sample
- Dual foci
- Annular illumination with a dark center

Photoacoustic Imaging Depth and Resolution: 50 MHz System (High Ultrasonic Frequency)

- Imaging depth: ~3 mm
- Axial resolution: ~15 microns
- Depth/resolution: ~200 pixels
- Lateral resolution: ~45 microns
- Acquisition time: 2 µs/A-scan
- Signal averaging: None

Photoacoustic Imaging of a Melanoma Tumor in a Small Animal In Vivo

Composite photoacoustic image with 584 and 764 nm

Contrasts:
Vessel: 13±1
Melanoma: 68±5

Photoacoustic Imaging of Human Palm

Photo

B-Scan @ 584 nm

Max amplitude projection

Epiderm.-derm. junction
Stratum corneum
Epidermis
Dermis
Subpapillary plexus

C. Favazza, unpublished.
Collaboration: L. Cornelius
Photoacoustic Imaging of Extravasated Nanoshells Surrounding a Tumor in a Small Animal In Vivo

Nanoshells provided by Nanospectra

In vivo Molecular Photoacoustic Imaging of B16 Melanoma Using Targeted Gold Nanocages (AuNCs)

\[^{[Nle^4,D-Phe^7]}-\alpha-MSH-AuNCs \rightarrow 38 \pm 3 \text{ (\%)} \text{ at 6 hr}\]

\[^{\text{PEG-AuNCs} \rightarrow 13 \pm 1 \text{ (\%)} \text{ at 6 hr}}\]

Sensitivity: \(~5000\text{ AuNCs / voxel}\)

C. Kim et al., unpublished. Collaboration: Y. Xia
Nature Materials 8, 935 (2009)
Photoacoustic Temperature Sensing

Sensitivity w/ 20X averaging: 0.15°C
Temporal resolution: 2 s

Pramanik, unpublished.
In Vivo Photoacoustic Molecular (Genetic) Imaging:
Gene Expression in Gliosarcoma Tumor in Rat

1. LacZ (gene)
2. Beta-galactosidase (enzyme)
3. X-gal (colorless substrate)
4. Blue product

Image of blood vessels at 584-nm wavelength
Image of expression of LacZ reporter gene at 635-nm wavelength
Composite image

In Vivo Photoacoustic Imaging of Sentinel Lymph Node in Rat at 2.4 cm Depth

Methylene blue (MB): 0.1 mL @ 1%
SD rats: N = 7, 250–390 g
Ultrasound probe: S5-1 (1-5 MHz)
Signal enhancement: 5.4X
Contrast of SLN: 8.3

C. Kim, T. Erpelding, et al., Radiology, accepted.
Collaboration: Philips Research
In Vivo Monitoring of HIF-Mediated Angiogenesis using Optical-Resolution (5 Micron) Photoacoustic Microscopy

S. Hu et al., unpublished (Collaboration: Arbeit).

Wang

Perifollicular microdomain
HIF: hypoxia-inducible factor
In Vivo Optical-Resolution Photoacoustic Microscopy of Mouse Ear: 2.6 Micron Lateral Resolution

S. Hu et al., unpublished.
Multiscale Imaging In Vivo with Consistent Contrast

Depth-resolution ratio = 200

(1) Enable systems biology at multiple length scales
(2) Accelerate translation of microscopic lab discoveries to macroscopic clinical practice

Near-Infrared Light and Biomolecules

Tissue Attenuation as a Function of Wavelength

**Skin** (Rayleigh-Type, i.e., Wavelength-Dependent Scatter)

**Breast** (Mie-Type, i.e., Non-Wavelength-Dependent Scatter)

Frangioni
Sensitivity Curve of the Human Eye under Well-Lit (Photopic) or Poorly-Lit (Scotopic) Conditions

Frangioni
**FLARE™ Imaging System Filter Design**

(Chroma Sputtered Filters, 4-5 logs at boundaries, ≥ 98% transmission)

![Graph showing absorbance and fluorescence emission for different wavelengths.](image)
An Optical Imaging Platform for Image-Guided Surgery

Excitation Light

- **Module**: White
- **Wavelengths**: 400-650 nm
  - 670 nm: 656-678 nm
  - 760 nm: 745-779 nm

800 nm NIR Camera

- **Band-pass**: 794-900 nm

700 nm NIR Camera

- **Band-pass**: 689-725 nm

Fluorinert Cooling Plate

Motors

High-Power White/NIR 1/NIR 2 LED Light Source

Color/NIR or Ratiometric Merge

Surgical Field
Methylene Blue and Indocyanine Green in Swine

Methylene Blue (Single IV Injection, 1 mg/kg, 5 min wait)

Ureters

Bile Ducts

Indocyanine Green (Single IV Injection, 2 mg, 2 hr wait)

Bile Ducts
Two-Channel Assessment of Lymph Nodes and Sentinel Lymph Nodes in Swine

Troyan et al., Ann Surg Onc, 2009
Two-Channel Simultaneous Assessment of Intravascular Thrombi and Blood Flow in Pig using a Stop-Motion Gating System

Tanaka et al., J Thor Cardiovasc Surg, 2009
Gioux et al., J Biomed Optics, 2009
Methylene Blue for Tumor Resection (Insulinoma)