IMAGE-GUIDED INTERVENTIONS WORKSHOP

March 10-11, 2008

Hilton Washington, DC / Rockville, MD
Executive Meeting Center

Welcome!

On behalf of the National Cancer Institute (NCI), National Institute of Biomedical Imaging and Bioengineering (NIBIB), National Center for Research Resources (NCRR), and the National Center for Image-Guided Therapy (NCIGT) at the Brigham & Women's Hospital we welcome you to this workshop on advanced clinical methods in image-guided therapies.

The overall goal of this workshop is to asses the current needs and opportunities in the field of image-guided interventions and NCIGT's role as a national center in relation to the greater IGT community. Critical IGT issues of translational research opportunities, clinical applications, and adherence to standard approaches are all important. Most importantly for all of us is to ensure the safe, effective and reproducible adoption by our clinical colleagues around the world.

This workshop is held in conjunction with the first annual meeting of the investigators funded under RFA-EB-06-003 initiative: Technology Development of Image-Guided Interventions. We hope that the joint meeting will provide an extraordinary opportunity to share and exchange ideas among clinical and scientific investigators. It should also provide a unique opportunity to all investigators to seek out new collaborative relationships that can help move the field of advanced clinical IGT further along the path to clinical translation.

Workshop Co-Chairs,

Keyvan Farahani, PhD Clare Tempany, MD Ferenc Jolesz, MD

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Acknowledgments:

The workshop organizers wish to thank the following individuals for their invaluable help:

- Barbara Croft, Marc Foltz, Paula Jacobs, Phil Lowery, Dorothy Sanders
  National Cancer Institute

- Maren Laughlin
  National Institute of Diabetes and Digestive and Kidney Diseases

- Tina Kapur, Kim Lawson, Kathryn Moody, Debbie O'Shea
  Brigham & Women's Hospital

- Lisa Gail, Jill Vanderweit
  BL Seamon, Inc.

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Program

NIH Workshop on
Clinical Image-Guided Therapy: Opportunities and Needs
March 10-11, 2008
Rockville, Maryland

Monday, March 10

8:00-8:15am *Introduction:* K. Farahani, PhD (NCI/NIH)

8:15-8:45am **Day 1 Keynote Address:** *National Center for Image-Guided Therapy* - F. Jolesz, MD (BWH)

Session 1: Prostate

Moderator: K. Farahani (NCI/NIH)

8:45-9:05am Session Keynote: *Image-Guided Interventions in Prostate Cancer* -P. Choyke, MD (NIH)

9:05-9:20am *Prostate Image-Guided Intervention: The NCIGT Core and Beyond* -C. Tempany, MD (NCIGT/BWH)

9:20-9:35am Image-Guidance during Radiotherapeutic Interventions for Prostate Cancer - Cynthia Ménard, MD (U Toronto)

9:35-10:05am Speakers Panel

10:05-10:20am Break

Session 2: Body

Moderator: P. Tandon (NCI/NIH)

10:20-10:40am Session Keynote: *RFA of Hepatic Tumors: Where Do We Go From Here?* – G. Dodd, III, MD (UTHSC, San Antonio)

10:40-10:55am *Planning, Targeting, Monitoring, Control, and Assessment of Image-Guided Percutaneous Ablations: Need for a 3-Dimensional Volumetric Approach* -K. Tuncali, MD (NCIGT/BWH)

10:55-11:10am MRI-Mediated Radiofrequency Ablation-E. Nevo, MD, DSc (Robin Medical Inc.)

11:10-11:25am *Image-Guided Osteoporotic Bone Augmentation with Intraoperative Biomechanical Guidance* -M. Armand, PhD (Johns Hopkins)

11:25-11:55am Speakers Panel

11:55am-1pm Lunch

Session 3: Neurosurgery

Moderator: J. Haller (NIBIB/NIH)

1:00-1:20pm Session Keynote: *Intraoperative MR-Guided Neurosurgery* – W. Hall, MD, MBA (SUNY Upstate, NY)

1:20-1:35pm *Image-Guided Neurosurgery* -F. Jolesz, MD (NCIGT/BWH)

1:35-1:50pm *Research Interfaces for Image Guided Neurosurgery* - X. Papademetris, PhD (Yale)

1:50-2:05pm *Mechanical Clot Obliteration for the Treatment of Stroke*- M. Gounis, PhD (UMASS, Worcester)

2:05-2:35pm Speakers Panel

2:35-3:35pm **Poster Presentations**

Session 4: Computation and Visualization

Moderator: A. Levy (NCRR/NIH)

3:35-4:05pm Session Keynote: *Computational and Visualization Challenges in 4-Dimensional Radiotherapy*- G. Chen, PhD (MGH)

4:05-4:20pm *The NCIGT Computation Core: A Technological Resource for Surgical Navigation Projects* -W. Wells, PhD (NCIGT/BWH)

4:20-4:35pm *The Changing Roles for Soft-Tissue Modeling: Therapy Guidance* - M. Miga, PhD (Vanderbilt)

4:35-4:50pm *In-Situ Image Guidance: Recent Advances in Design, Implementation, and Psychophysics* –G. Stetten, PhD (U Pittsburgh)

4:50-5:05pm *MRI Guided Radiation Therapy: Brachytherapy* --R. Cormack, PhD (Rad Onc, BWH)

5:05-5:35pm Speakers Panel

5:45-6:45pm: Parallel Breakout Sessions

- Breakout Session 1:
  Preoperative Functional MRI and Diffusion Tensor Imaging; Acquisition and Visualization for Neurosurgery
  Steve Whalen, Lauren O'Donnell (NCIGT/BWH)

- Breakout Session 2:
  Slicer Prostate Module
  Steve Haker, Noby Hata (NCIGT/BWH)

- Breakout Session 3:
  Liver Visualization: Application of Slicer 3.0 for Non-Rigid, Multi-Modality Image Registration for Thermal Ablation: Pre-procedural MRI on Intra-Procedural CT for Tumor Targeting
  Nicu Archip, Paul Morrison (NCIGT/BWH)

Tuesday, March 11

8:00-8:10am Introduction

8:10-8:40am **Day 2 Keynote Address:** *Image-Guided Local Drug and Gene Delivery* -C. Moonen, PhD (U Bordeaux, France)

Session 5: Focused Ultrasound & Endoscopy

Moderator: H. Lopez (NIBIB/NIH)

8:40-9:00am *Session Keynote: Image-Guided Focused Ultrasound Therapy* -K. Hynynen (U Toronto)

9:00-9:15am *Focused Ultrasound Treatment Planning* - G. Clement, PhD (NCIGT/BWH)

9:15-9:30am *Guiding Cardiac Ablation Therapy with ARFI Imaging* -P. Wolf, PhD (Duke)

9:30-9:45am *Spectrally Encoded Endoscopy for Image-Guided Therapy of Twin-Twin Transfusion Syndrome* - G. Tearney, MD, PhD (MGH)

9:45-10:15am Speakers Panel

10:15-10:30am Break

Session 6: Imaging

Moderator: A. Levy (NCRR/NIH)

10:30-10:50am Session Keynote: *MR Imaging for Image-Guided Interventions* – J. Pauly, PhD (Stanford)

10:50-11:05am *Building a Toolbox to Support Enhanced MR Imaging in Image-Guided Therapy* -L. Panych, PhD (NCIGT/BWH)

11:05-11:20am *Body Imaging – A Role for Light Based Imaging?* -D. Fowler, MD (Columbia)

11:20-11:35am *An Integrated MRI-Guided Electrophysiology Diagnosis/Therapy system: Lessons Learned for Closed-Bore Interventional Procedures* -E. Schmidt, PhD (BWH)

11:35-12:00pm Speakers Panel

12:00pm-1pm Lunch

Session 7: Targeted Drug and Cell Delivery

Moderator: K. Farahani (NCI/NIH)

1:00-1:20pm Session Keynote: *Image-Guided Therapy in Cancer* - Z. Bhujwalla, PhD (Johns Hopkins)

1:20-1:35pm *Targeted drug delivery in the brain via ultrasound-induced blood-brain barrier disruption* --N. McDannold, PhD (NCIGT/BWH)

1:35-1:50pm *Microbubbles as a Tool for Targeted Ultrasound Imaging and Drug Delivery*- A. Klibanov, Ph.D. (U Virginia)

1:50-2:05pm *Cell Tracking and Cell Delivery: From Imaging to Intervention* - J. Bulte, PhD (Johns Hopkins)

2:05-2:35pm Speakers Panel

2:35-2:45pm Concluding Remarks

Adjournment

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Day 1 -

Keynote Address

National Center for Image-Guided Therapy

Ferenc Jolesz, M.D.

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Brigham and Women's Hospital Harvard Medical School
75 Francis Street, Boston MA

On behalf of the National Center for Image-Guided Therapy (NCIGT) at the Brigham & Women's Hospital, we welcome all participants in this workshop on "Clinical Image-Guided Therapy: Opportunities and Needs".

The National Center for Image Guided Therapy (NCIGT) is an NIH-funded Biomedical Technology Resource Center. Through support from three NIH Institutes (NCRR, NCI and NIBIB) the NCIGT serves as a national resource for most aspects of image-guided therapy research. The center provides extensive translational and clinical research programs, training, and service-oriented resources for scientists and clinicians in the field. We believe that multidisciplinary development of innovative image-guided intervention technologies will enable effective, less invasive or non invasive treatments that are not only more economical, but also produce better outcomes. **As a national center, we have the responsibility to advance the field of image-guided therapy (IGT) and to develop the necessary advanced technology and multidisciplinary clinical applications. At the same time, we have to disseminate the newly acquired knowledge and train researchers and clinicians in this emerging field.**

A major goal of this workshop is to asses the current needs and opportunities in the field of image-guided clinical interventions and demonstrate NCIGT's role as a national center in relation to the greater IGT community. The workshop is composed of scientific sessions in areas of brain-, prostate, and body interventions, thermal ablations, focused ultrasound, and targeted drug-delivery, as well as imaging, computation and visualization technologies in support of image-guided therapies (IGT). There will also be parallel hands-on breakout sessions focused on various applications of the Slicer visualization modules.

As a national center we have developed relationships with most of the other IGT centers nationally and worldwide at the level of partnership, collaboration, cooperation or

exchange of relevant research information. In this workshop we will use all possible interactive methods for the dissemination of our technologies and clinical applications. We make our research data available, providing our research products as downloadable open source software and clinical protocols that can be easily implemented. We also help and facilitate initiation of new IGT centers as advisors, collaborators and/ or consultants.

The operating philosophy of the IGT program has been to apply the best available technical solutions and by the teamwork of world class scientists, engineers, and procedural clinicians to demonstrate and validate new procedures up to the point of enabling full scale clinical trials. For each procedure, pathways are identified to "strip out" the technology and personnel not required for ongoing clinical care, so the procedure may then be more widely adopted. Key to these efforts is long term collaborations with other academic centers and leading industry teams.

Session 1: Prostate

Moderator: Keyvan Farahani, PhD

Image Guided Intervention in Prostate Cancer

Peter L. Choyke, M.D.
National Cancer Institute, Bethesda, MD

Improvements in imaging of prostate cancer and the pressing need to develop minimally invasive and gland sparing methods of prostate cancer therapy have led to renewed interest in image guided intervention. MRI provides the best anatomic depiction of the prostate but it is more cumbersome to perform image guided interventions in the MR environment. It is possible to direct needles into the prostate under MR guidance, however, the techniques are usually time intensive and require several operators. Moreover, it is more difficult to achieve real time feedback with MR except at the expense of image quality. By transferring MR data to real time ultrasound via a co-registration process, it is possible to perform real time interventions under ultrasound with the MR data superimposed. Moreover, it is possible to document the location of acquired biopsies in 3 dimensions. Although there is inevitably some mis-registration between the MRI (obtained with the endorectal coil) and the US (obtained with a transrectal probe), this method has proven remarkably accurate in patients undergoing biopsy of suspicious lesions. MR guided real time ultrasound procedures may soon enable focal ablation procedures of the prostate. Early work in the canine model is promising.

Prostate image-guided interventions- the NCIGT core and beyond

Clare Tempany, MD
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Overall aims: To improve current diagnostic and minimally invasive techniques for Prostate cancer.

Background: Prostate cancer is a significant healthcare problem, 1:6 men in the US are diagnosed with Prostate cancer and 1:34 will die of this disease. With widespread use of PSA, here is thought to be overdiagnosis and over treatment of early localized prostate cancer in the US. The role of imaging is expanding and new techniques with MRI (Hyperpolarized C13, diffusion imaging, DCE & MRSI) and molecular imaging appear very promising. Current treatments for localized prostate cancer (T2 or less) are generally whole gland/global treatments, with either radical prostatectomy or radiation (External or Brachytherapy).

Current research: For over 10 years we have pioneered a MR guided approach to both diagnosis and treatment. These programs will be discussed. As we demonstrated in the Brachytherapy program, sub-total treatments of the prostate can lead to very successful cancer control with excellent quality of life post treatment. The morbidities of all prostate cancer treatments today remain a very significant source of concern for men when discussing treatment options and choosing how to manage their disease. Many men are currently choosing “active surveillance” or watchful waiting. The role of imaging in this group is becoming important.

Future needs: New treatment options with focal, sub-total gland targets are being aggressively pursued by many groups and centers worldwide. Examples are cyrotherapy, HIFU and photodynamic therapy. The critical role of imaging in these approaches will require new efforts and challenges which will be discussed. These future needs for prostate IGT will be outlined for discussion at the panel session.

Image-Guidance during Radiotherapeutic Interventions for Prostate Cancer

Cynthia Ménard, MD
Princess Margaret Hospital and University of Toronto, Canada

Gains in the therapeutic ratio are largely accomplished with spatial selection of target tissues for high-dose radiation exposure. While modern techniques can achieve precision in delivery, improvements in accuracy hinge on image-guidance strategies. Mounting clinical evidence now point to the essential role of image-guided radiotherapy (IGRT) in improving prostate cancer control through judicious management and reduction of targeting uncertainties.

The entire prostate gland has traditionally been considered the target for prostate radiotherapy for two reasons: 1) prostate cancer is inherently multifocal, placing the entire gland at risk, and 2) direct imaging of foci of cancer within the gland has historically been elusive. In reality, the local extent of prostate cancer is neither confined nor defined by the boundaries of the prostate gland. MR Images depicting prostatic sub-sites of tumor burden can now be integrated in radiotherapy for selective modulation of dose intensity.

Given unparalleled precision in delivery by virtue of the exponential decline in dose intensity with distance from the source, brachytherapy poses the highest requirement for accuracy in targeting. The real-rime 2D feedback of TRUS, the geometric integrity and brachytherapy device resolution of x-ray, and soft-tissue resolution of the anatomy and biology on MRI are highly complementary in image-guided brachytherapy (IGBT). Since no single imaging modality embodies all the optimal characteristics for image-guidance of brachytherapy for prostate cancer, multi-modality guidance models will likely predominate for the foreseeable future. The potential role of interventional MRI in this context will be reviewed.

Session 2: Body

Moderator: Pushpa Tandon, PhD

RFA of Hepatic Tumors: Where Do We Go From Here?

Gerald D. Dodd, III, M.D.
Professor and Chair
Department of Radiology
University of Texas Health Science Center at San Antonio
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Radiofrequency ablation (RFA) of hepatic tumors has emerged as a clinically relevant therapeutic technique for the treatment of primary and metastatic hepatic tumors. Local tumor eradication rates and 5-year survival rates for patients with a few small tumors treated by RFA rival the success achieved with hepatic resection. However, the efficacy of RFA of larger hepatic tumors is disappointing. This presentation will review the success of RFA of hepatic tumors, its limitations, identify technologic improvements that could improve its efficacy, and explore its future use with combinational therapies.

Planning, Targeting, Monitoring, Control, and Assessment of Image-guided Percutaneous Ablations: Need for a 3-Dimensional Volumetric Approach

Kemal Tuncali, MD
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Image-guided percutaneous ablation of a tumor involves the basic steps of pre-procedural planning of the procedure, intra-procedural targeting of the tumor, intra-procedural monitoring and control of the ablation, and post-procedural assessment. Unlike surgical resection, all steps of percutaneous ablation rely on cross-sectional imaging, mainly CT, ultrasound, and MRI. Today, in clinical practice multiplanar but 2-dimensional images with very few metrics are utilized. This has limitations during all steps of an ablation. Whereas a volumetric modeled approach lends itself to advanced metrics and may improve precision.

To demonstrate the advantages of 3-dimensional volumetric approach, we present our preliminary work in:

1. A software tool for pre-procedural volumetric planning of image-guided percutaneous ablations.
2. A software package for intraprocedural volumetric targeting, monitoring, and control during ablations utilizing automatic segmentation, and optical flow.
3. A software segmentation tool for post-procedural volumetric assessment of ablations.

The advantages of these techniques include assessment and 3-dimensional display of all margins of ablation at the same time, and instantaneous calculation of advanced ablation metrics such as percent tumor coverage, Dice similarity coefficient, minimal ablative margin, and proximity to surrounding critical structure.

Main limitation is that the techniques are preliminary and further advances in segmentation, registration, and thermal calculation packages will have to be applied. Also the techniques have to be validated for accuracy and robustness at multiple preclinical and clinical levels before it can be used routinely for clinical applications of image-guided percutaneous ablations.

References:

1. Butz T, Warfield SK, Tuncali K, Silverman SG, vanSonnenberg E, Jolesz FA, Kikinis R. Pre- and intra-operative planning and simulation of percutaneous tumor ablation. In: DiGioia AM, Delp S. MICCAI 2000: Third International Conference on Medical Robotics, Imaging and Computer Assisted Surgery; 2000 Oct 11-14; Pittsburgh, PA, USA. Heidelberg, Germany: Springer-Verlag;2000. p. 317-326.

2. Tuncali K, Zientara GP, Nakamura R, Morrison PR, Warfield SK, Silverman SG. 3D Computerized Monitoring of MRI-guided Percutaneous Cryoablations: Validation of the System in an Animal Model and Retrospective Clinical Case Applications. Presented at RSNA Meeting, Chicago, IL, 2005
3. Silverman SG, Sun MR, Tuncali K, Morrison PR, vanSonnenberg E, Shankar S, Zou KH, Warfield SK. Three-dimensional assessment of MRI-guided percutaneous cryotherapy of liver metastases. AJR Am J Roentgenol. 2004;183(3):707-12.h

MRI-Mediated Radiofrequency Ablation

Erez Nevo, MD, DSc; Robin Medical, Inc., Baltimore, MD
Jerome L. Ackerman, PhD; Harvard Medical School, MGH, Boston, MA

Purpose: The objective of the project is to develop an RF ablation technique for use with MRI scanners. In addition to providing image guidance to the procedure, the scanner will also provide the ablation mechanism through the use of its own radio-frequency (RF) transmission to mediate tissue heating and coagulation. The specific aims of the project are: to demonstrate the feasibility of using energy deposition from native RF transmission of the MRI scanner during a scan to create sufficient heat for tissue ablation; to conduct numerical and experimental studies to define the optimal solution for MRI-guided ablation by the use of RF transmission by the scanner; to develop a self-contained prototype for RF ablation and imaging with controllable heat generation; and to conduct technical experiments and animal studies to demonstrate the ability of the probe to ablate tissues simultaneously with local MR imaging.

Background and Significance: A well known risk in diagnostic and interventional MRI is heat injury due to RF energy deposition by the high intensity RF transmission during scan. Examples include guide-wires, pacemaker leads, and lead wires for spinal fusion stimulators. Extensive empirical measurements by several groups have shown that RF heating occurs primarily at the tip of wire-shaped conductive structures and is a function of the total length of the wire, the immersed length of the wire, and the position of the wire in the magnet. There is also large evidence of focal heating and patient skin burns sustained while undergoing diagnostic MRI scans. The majority of these thermal injuries occurred when the patient was connected to some form of physiological monitoring device, and the burn usually occurred where the skin was in contact with the monitoring sensor or cable. The comprehensive literature on heating of elongated objects during MRI, the physical basis of the heating phenomena, and the many experimental studies and clinical events that demonstrate the extent of heating due to RF energy deposition all provide sound evidence for our basic hypothesis that RF energy deposition into imaging coils and cables can be applied to generate sufficient heating for tissue ablation.

The envisioned clinical product will be a disposable, self-contained, ablation probe that can be used on any MRI scanner for various clinical applications. Using the large installed base of close to 10,000 scanners in the USA, the new technology will provide a nation-wide public access to an advanced, minimally invasive technology for various clinical procedures, including ablation of various tumors (liver, lung, breast, prostate, kidney). The technology will be developed through collaboration between Robin Medical, Inc., that will develop the new ablation device, and a team at the Massachusetts General Hospital that will support the initial analysis of the different potential embodiments of the concept and the experimental work with the device prototypes.

Methods: Various configurations of heating elements were either positioned in air or inserted into a small chamber filled with agar gel. A fiber optic thermometer was used to monitor the temperature increase during imaging close to the tip of the device. Initial

experiments were conducted on 1.5T and 3.0T closed-bore MRI scanners. The cable of the heating element was routed along the patient bed, close to the inner surface of the bore to achieve maximal level of exposure to the RF field of the scanner. The heating element was not connected to the scanner and received RF energy transmitted from the body coil during the scan. The body coil was used for transmit and receive. Scan prescriptions with mid to high RF utilization were applied with peak specific absorption rate (SAR) below the upper limit of 4 W/kg.

Initial results: We experimented with many different heating element configurations and for some setups we achieved substantial heating to the levels of tissue burning temperature (50 degrees Celsius). We have noticed the great dependency of heating on the physical properties of the setup, including parameters like the type, dimensions and location within the scanner of the conducting wires of the heating element. We have noticed a dramatic effect on the level of heating when the user touched the conducting wires with exposed hands. While these initial findings generate opportunities to achieve the goals of the project, they also raise major concerns on the safety of using catheters containing long conducting wires, like catheters with embedded RF coils.

Image-Guided Osteoporotic Bone Augmentation with Intraoperative Biomechanical Guidance

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The rate of mortality after hip fracture in elderly patients with osteoporosis is reported to be catastrophic and as high as 30%. There is a need for a therapeutic intervention routine for patients with osteoporosis who are at highest risk of motality and morbidity if they were to sustain a fall. We are looking at femoral augmentation as a possible countermeasure to reduce the risk of fracture in the highly susceptible hip. The technique would be especially valuable for those patients with extremely high risk of falls and fractures. Clinical case studies, however, suggest that the success of bone augmentation requires detailed planning, biomechanical analysis, and precise control of the augmentation procedure to avoid generation of areas of high stress due to augmentation.

We present an overview of our proposed image-guided surgical execution system with biomechanical planning and intraoperative updates for osteoporotic bone augmentation. We also report our ongoing efforts in the following areas:

1) The development of a geometrical and biomechanical planning module for patient-specific optimization of the bone augmentation procedures using preoperative CT scans.

2) The development of an integrated surgical execution system that will involve co-registration of the preoperative model and surgical tools with a fluoroscope and a navigation system specifically developed for this project.

Session 3: Neurosurgery

Moderator: John Haller, PhD

Intraoperative MR-Guided Neurosurgery

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For more than a decade, neurosurgeons have become increasingly dependent on image-guidance to perform safe, efficient, and cost-effective surgery. Neuronavigation is frame-based or frameless and requires obtaining computed tomography or magnetic resonance imaging (MRI) scans several days or immediately before surgery. Unfortunately, these systems do not allow the neurosurgeon to adjust for the brain shift that occurs once the cranium is open. This technical inability has led to the development of intraoperative magnetic resonance imaging (ioMRI) systems ranging from 0.12- to 3.0-Tesla (T) in strength. The advantages of ioMRI are the excellent soft tissue discrimination and the ability to view the operative site in three dimensions. Enhanced visualization of the intracranial lesion enables the neurosurgeon to choose a safe surgical trajectory that avoids critical structures, to maximize the extent of the tumor resection, and to exclude an intraoperative hemorrhage. All ioMRI systems provide basic T1- and T2-weighted imaging capabilities but high-field (1.5-T) systems can also perform magnetic resonance (MR) spectroscopy, MR venography (MRV), MR angiography (MRA), brain activation studies, chemical shift imaging, and diffusion weighted imaging. Identifying vascular structures by MRA or MRV may prevent injury during surgery. Demonstrating elevated phosphocholine within a tumor may improve the diagnostic yield of brain biopsy. Mapping out neurologic function may influence the surgical approach to a tumor. The optimal strength for MR-guided neurosurgery is currently under investigation.

Image-Guided Neurosurgery

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The fundamental principle of image-guided neurosurgery is to target, access, and remove intracranial lesions without injuring normal and functioning brain tissue or blood vessels. The preservation of neurological function, requires precise delineation of functional anatomy and correct definition of tumor margins. Because of the difficulty in recognizing exact tumor margins, complete resection in malignant brain tumor is problematic. Using advanced computing technologies, multimodality, multiparametric lesion characterization, and 3D image fusions represent an enrichment of the information. They do not change the diagnosis, but can contribute substantially to surgical planning. The most novel aspect of neurosurgical planning is the *intraoperative* use of the 3D model for interactive surgical simulation such as trajectory optimization, access route selection, and in the case of thermal therapy, 3D thermal dosimetry.

To enable the use of preoperatively acquired multimodal images for surgical guidance, a mechanism capable of compensating for brain shift must be put in place. Development and implementation of non-rigid registration algorithms for this purpose has continued to be a central research focus. Modern neurosurgery requires ever more comprehensive integration of sophisticated morphologic and functional imaging techniques into the surgical flow. This integration process includes the incorporation of interactive dynamic imaging, high performance computing and real-time image processing in the operating room. The evolution of novel intraoperative imaging techniques, including local probes (nuclear, optical, mass spectrometric) can result in the development of several revolutionary image-guided therapy methods currently in the process of implementation into the neurosurgical practice.

Intraoperative MRI has become the method of choice for achieving the safest and most accurate resection of glial neoplasms. Visual inspection is often unreliable in distinguishing tumor from normal brain tissue. However, the usefulness of preoperatively acquired MR images for surgical guidance is limited by changes in brain configuration, which inevitably occur during surgery. The local probes may reveal more about the relationship between intra-axial infi ltrative brain tumors, such as low- and high-grade glial neoplasm and the functionally active neural tissue has not been entirely elucidated. Local probes also can refine the integration of neuronavigation tools. After registering the multimodal preoperative images with the intraoperative scans, the composite volume can be immediately used for surgical navigation (‘virtual intraoperative scan’).

With the introduction of MRI as a monitoring method for thermal therapies, a novel mechanism for controlling energy deposition became available. Since the original

description of MRI monitoring and control of laser–tissue interactions, MRI-guided interstitial laser (ILT) has become a clinically tested and accepted minimally invasive treatment option. Among currently developed thermal therapy methods, focused ultrasound (FUS) appears to be the most promising, since its use does not require any invasive intervention. There is no more convincing example for the FUS benefits than in the brain, where deep lesions can be induced without any associated damage along the path of the acoustic beam. This necessitates the use of an imaging technique for localization, targeting and real-time intraoperative monitoring, and to control the spatial extent of heat deposition.

Research Interfaces for Image Guided Neurosurgery

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http://bioimaging.yale.edu/faculty/papademetris.html

In the main part of the talk, I will discuss issues pertaining to the interaction between image-guided neurosurgery and image analysis research. In particular the presentation will focus on the development of network interfaces between research systems and commercial image-guided surgical navigation systems and describe the development of the VectorVision link interface. This is a key tool in bringing new methodology within the operating room environment. I will present applications of this work in the domain of epilepsy neurosurgery, including guidance of intracranial electrode implantation and tissue resection. In addition, I will briefly describe some newer, ongoing, work on the development image-guided deep brain multiphoton microscopy for optical biopsy.

Mechanical Clot Obliteration for the Treatment of Stroke

M. Gounis
UMASS, Worcester

Purpose: Develop representative in vitro and in vivo methodology for testing and refinement of an ultrasound-based endovascular ultra-thin thrombectomy device that mechanically breaks down intracranial blood clot for the treatment of ischemic stroke.

Methods: Data of human cerebrovascular anatomy was acquired with magnetic resonance angiography and three-dimensional x-ray angiography from adult patients and converted into computer models. Representative life-size optically clear vascular replicas were built by a rapid prototyping system and inserted in mock circulation flow loop. Various prototypes of the thrombectomy device were assessed for their maneuverability, efficacy in recanalizing bovine clot in the middle cerebral artery segment of the models, and particulate generation. Concurrently a canine middle cerebral artery stroke model is being developed reflective of the tortuosities encountered in the in vitro models.

Results: Methodology has been solidified to provide produce accurate silicone vascular replicas from medical imaging, circulation flow loops operating within the hemodynamic parameters found in the human cerebral circulation, embolic occlusions of the main trunk of the middle cerebral artery with bovine clot, and access for manipulations of device prototypes. A concurrently developed canine stroke model has been shown to be operational angiographically and is ready to be validated with MR perfusion/diffusion imaging.

Conclusions: Reliable in vitro methodology has now been established to permit optimization of the device design and operating parameters to safely deliver maximum efficacy. A foundation has been laid for subsequent in vivo assessment in a canine middle cerebral artery stroke model.

Session 4: Computation &Visualization

Moderator: Abraham Levy, PhD

Computational and Visualization Challenges in 4-Dimensional Radiotherapy

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4D CT is routinely used in radiation therapy planning of moving targets. Its current role is often limited to assessing the extent of target motion, and designing an aperture that encompasses this motion. However, much more information can be extracted from 4D imaging, if computational and visualization tools were available. Examples include: 1) regional ventilation analysis in lung irradiation; 2) analysis of serial 4D CT to quantify tumor trajectory variations 3) identification of corresponding airway bifurcations to provide validation of deformable registration algorithms 4) interactive 4D volume rendering to permit visualization of structures within the radiation field. While the core tools of image processing remain the same (segmentation, image registration, change detection, visualization), extrapolation to 4D requires new and powerful implementations.

The NCIGT Computation Core:
A Technological Resource for Surgical Navigation Projects

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The NCIGT Computation Core serves primarily as an infrastructure resource for application projects in IGT. Its major activities are software infrastructure for IGT projects, the development image registration facilitated by high performance computation, a recent effort in navigation for endoscopy, and a component that is focused on technological support for neurosurgical navigation with fMRI.

I will discuss the 3D Slicer software environment as a general purpose platform for medical image processing, including its architectural evolution, with an emphasis on the support for surgical navigation that has been enabled by the NCIGT, along with several application examples.

Subsequently I will summarize our recent project in endoscopic navigation, as well as some recent local examples of non-rigid registration for IGT.

Finally I will describe recent results that we have obtained in the area of distortion correction of echo-planar MRI as is used for fMRI scanning.

The Changing Roles for Soft-Tissue Modeling: Therapy Guidance

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Challenges in soft-tissue modeling include understanding the nature of physiological processes, developing mathematical descriptions and/or constitutive relationships that reflect physical behavior, and developing measurement methods to produce model-validating frameworks. These challenges have been the predominant concerns within the soft-tissue modeling community. However, with the recent breakthroughs in CPU power and medical image processing, the role of soft-tissue modeling is changing such that computer models are being extended from their predictive roles to that of a more integrated one within therapy guidance, novel forms of medical imaging, and disease characterization. In this seminar, the changing roles of soft-tissue modeling will be explored within the context of image-guided interventions.

In-Situ Image Guidance:
Recent Advances in Design, Implementation, and Psychophysics

George Stetten, Roberta Klatzky, John Galeotti, Bing Wu, Gaurav Shukla, Mel Siegel

The *sonic flashlight* (SF) is a device that merges ultrasound (US) with a direct view of the patient using a half-silvered mirror to facilitate guidance of interventional procedures. We call this *in-situ* viewing, in contrast to the *ex-situ* viewing of conventional US on a screen displaced from the patient. A series of prototype SF devices has been developed and tested, including four based on portable 2D ultrasound scanners and one based on a real-time 3D scanner. The clinical model of the SF has been tested in clinical trials involving more than 70 patients, placing catheters in the deep veins of the arm. Preliminary tests of clinical feasibility have been conducted for jugular line placement and breast biopsy. The concept of in-situ display has been extended to holographic and tele-robotic systems with working prototypes of each. The holographic system permits larger in-situ images to be created from a smaller display and is intended for deeper procedures such as amniocentesis and liver biopsy. The robotic system is intended for catheter based procedures and microsurgery. A series of psychophysical studies has been conducted under controlled laboratory conditions to understand the perceptual/cognitive processing that underlies use of both in-situ and ex-situ displays. Collectively, this research has unequivocally demonstrated several advantages for in-situ displays: in localizing and accessing targets under rigid and deformable surfaces, ease of learning, transfer of training to new targets, and visualization of hidden structures exposed by a sequence of US slices. These advances could have important implications for image-guided therapy.

MRI Guided Radiation Therapy: Brachytherapy

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Permanent brachytherapy (BRT) of the prostate probably is the most widely practiced and studied image guided procedure in the field of radiation oncology. Due to the nature of brachytherapy, the imaging challenges are significantly different from external beam treatments (XRT). The use of imaging in BRT and XRT is contrasted. Experience with MR guided intraoperative planning of permanent prostate implants with adaptive dosimetry is reviewed with particular emphasis on the computational and visualization needs. Recent work to generalize the techniques for use in the management of cervical cancer is discussed to highlight the challenges that remain.

Parallel Breakout Sessions

Breakout Session 1

Preoperative Functional MRI and Diffusion Tensor Imaging; Acquisition and Visualization for Neurosurgery
Steve Whalen, Lauren O'Donnell (NCIGT/BWH)

Breakout Session 2

Slicer Prostate Module
Steve Haker, Noby Hata (NCIGT/BWH)

Breakout Session 3

Liver Visualization: Application of Slicer 3.0 for Non-Rigid, Multi-Modality Image Registration for Thermal Ablation: Pre-procedural MRI on Intra-Procedural CT for Tumor Targeting
Nicu Archip, Paul Morrison (NCIGT/BWH)

fMRI/DTI Acquisition and Visualization for Neurosurgery

Stephen Whalen, Lauren O'Donnell
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Harvard Medical School
75 Francis Street, Boston MA

The goal of surgical treatment for cerebral neoplasms is to maximize the extent of tumor resection while preventing or minimizing postoperative neurologic deficits. Preoperative functional MRI (fMRI) and diffusion tensor imaging (DTI) are highly effective, non-invasive methods of mapping eloquent cortical areas and critical white matter structures, so as to assess their relationship with a tumor or other pathological neural manifestations. We describe these two preoperative imaging methods as they are used in the Golby Surgical Brain Mapping Laboratory at Brigham and Women's Hospital. The discussion of fMRI will show how we can clearly identify language, motor, and visual cortical areas preoperatively. DTI analysis will include novel whole-brain tractography segmentation by clustering. And we will also include an overview of the new Slicer3 DTI visualization software.

Application of Slicer in Prostate Intervention

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The goal of this breakout session is to learn the state-of-art in computer assisted prostate intervention using open-source software for navigation, registration, and visualization. We will highlight 3D Slicer (www.slicer.org) that has been essential to enable the MR-guided prostate biopsy and brachytherapy in Brigham and Women's Hospital. The coordinates of suspicious tumor foci are specified in 3D Slicer and corresponding holes in the needle guiding template grid are computed, which effectively shortens surgery time and reduces the potential for computational errors. A key feature of the system is volumetric data fusion, allowing for target planning on high- resolution preoperative T2-weighted images mapped onto intraoperative 0.5T images. The prostate biopsy module also provides methods to control real-time image MR imaging and on-line image transfer of acquired real-time images, using Open IGT Link, a new open standard for inter-device communication in Image Guided Therapy. Development is underway to apply the Open IGT Link to control robot in prostate therapies inside a close-bore 3-tesla MRI scanner. In conclusion, the participants of this session will learn how 3D Slicer enables MRI guided prostate interventions by providing advanced image processing and computing. The participant will also learn the benefit of using open-source and open-standard in IGT research. Recommended for further reading: Tempany C, et al. J Magn Reson Imaging. 2008 Feb;27(2):356-67.

Application of Slicer 3.0 for Non-Rigid, Multi-Modality Image Registration for Thermal Ablation: Pre-procedural MRI on Intra-Procedural CT for Tumor Targeting

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The goal of this break-out session is to provide the participants with a brief overview of contemporary image-guided thermal therapies for percutaneous tumor ablation. The overview is then focused down to CT-guided RF ablation in the liver. Sample images from recent clinical cases contrast the information-rich pre-procedural MRI scan against the information-poor un-enhanced CT scan available at the time of the procedure. This clarifies for the participant, one area of need which image registration can address – targeting the lesion.

The session will also provide an introduction to Slicer 3.0 and will demonstrate in this environment the registration of pre-procedural MRI scan with intra-procedural CT scan for lesion targeting with an RF electrode.

Participants will appreciate how such registration techniques in moving organs can improve the depiction of tumor margins intra-procedurally to make for a more efficient and effective procedure. The same techniques have the potential of improving the treatment planning and acute assessment of treatment success.

Day 2 -

Keynote Address

Image-Guided Local Drug and Gene Delivery

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Local drug delivery has the potential of increasing the local therapeutic effect while limiting systemic toxic effects. Either targeted or non-targeted drug-carrying nanoparticles may be used for local drug delivery. The objectives of image guidance may be summarized as: 1) target identification and characterization; 2) temporo-spatial guidance of actions to release or activate the drugs and/or permeabilize membranes; 3) Evaluation of pharmacodistribution; 4) Physiological read-outs to evaluate the therapeutic efficacy. Whereas the value of imaging, in particular MRI, is well known in the first and fourth objective, the emphasis of this review is on the second and third objective. Special attention is paid to the potential of MRI guided focused ultrasound.

Research in the field of nanoparticles for local drug/gene delivery is very active. Local release may be triggered by natural processes, such as membrane fusion, phagocytosis, pinocytosis, but also by external physical means such as ultrasound. Nanoparticles may be designed specifically to enhance ultrasound induced bio-effects, notably cavitation. Most microbubbles consist of air- or perfluorocarbon-filled microsphere stabilized by an albumin or lipid shell with a size in the range of 1-10 μm. Drugs can be attached to the membrane surrounding the microbubble, they can be imbedded within the membrane itself, they can be bound non-covalently to the surface of the microbubble and can be loaded to the interior of the microbubble, either in an oil or aqueous phase. These microbubbles can be targeted to specific (pathologic) sites using different targeting ligands incorporated into bioconjugates.

The concept of using thermosensitive liposomes in combination with local hyperthermia for local drug release was proposed more than 25 years ago by Weinstein et al. Liposomes remain relatively stable in the circulation at temperatures well below the phase transition temperature (T_c) of the liposome membrane. At T_c distinctive structural changes occur in the lipid bilayer resulting in increased membrane permeability and the accompanying release of the liposomes' content. Liposomes may carry both hydrophilic and hydrophobic drugs in their aqueous interior and lipid bilayer membrane, respectively. The circulation half-life may be increased by incorporating polyethylene glycol (PEG)-

lipids in the bilayer. The recent developments of measuring and controlling temperature with MRI guided Focused Ultrasound should lead to improved control of locally release drugs with temperature sensitive nanocarriers.

Viral-mediated gene transfer is efficient but safety aspects have limited therapeutic applications. Stem cells and immune cells have a particular advantage as gene delivery systems since they home in to lesions by the action of chemokines. They can be labeled and tracked using imaging methods.

A thorough analysis of pharmacodistribution is a mandatory aspect of local drug/gene delivery. Using most of the methods described above, genes are delivered within the vascular system, and the local distribution and its temporal evolution are a function of the local perfusion, uptake by surrounding cells, metabolism, and release. Therefore, such local delivery must be accompanied by evaluation of pharmacodistribution and pharmacokinetics, in order to predict outcome. Imaging may provide a non-invasive assessment of such parameters. Similar to the encapsulation of drugs in nanocarriers, contrast agents can be included that report on the local release of drugs and subsequent tissue distribution. Ideally, such agents would be directly linked with the drugs. However, in many cases co-released MR contrast agents may provide useful data related to pharmacodistribution even when they are not linked.

Among the key challenges in gene therapy are the method of gene delivery and the spatial and temporal control of therapeutic (trans)gene expression in the targeted tissue. The ability of High Intensity Focused Ultrasound (HIFU) to heat tissue deep inside the body can be used to control transgene expression when the gene is placed under control of a heat-sensitive promoter.

Several studies have convincingly demonstrated the large potential of image guided drug and gene delivery, in particular with respect to the use of (focused) ultrasound. However, there is a clear need for better quantification of the results, development of suitable (mult-modality) contrast agents for pharmacodistribution, optimization of ultrasound procedures, and of drug/gene nanocarriers.

Session 5: Focused Ultrasound
&
Endoscopy

Moderator: Hector Lopez, PhD

Image-Guided Focused Ultrasound Therapy

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Focused ultrasound allows noninvasive focal delivery of energy deep in to soft tissues. The focused energy can be used to modify and eliminate tissue for therapeutic purposes. This talk will review the current clinical status of image-guided focused ultrasound therapy and discuss the future opportunities of this method.

Focused Ultrasound Treatment Planning

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Treatment planning in radiation therapy refers to the stages before clinical operation in which the beam strength, distribution, target windows, and predicted doses are calculated on a per-patient basis. Such planning has become a standard part of radiation oncology and is the primary role of medical physicists. Although MR-guided Focused ultrasound surgery (MRgFUS) is rapidly gaining worldwide clinical acceptance for procedures throughout the body, standardized treatment guidelines have yet to be established. Presently, new treatment planning methods are examined that correct for beam distortion by modeling ultrasound with the aid of diagnostic pre-imaging. It will be shown that a number of aspects of traditional radiation planning stages can potentially be expedited in MRgFUS, allowing relaxed requirements for immobilization and altogether eliminating the need for certain steps such as marking. Procedures include an imaging and registration stage, followed by tissue identification and segmentation, modeling of the acoustic and thermal fields within the relevant region, identification of sensitive areas, beam modification, and finally, quantitative prediction of the optimized ultrasound beam. With this information it is possible to restore a distorted ultrasound focus by means of aberration correction methods. Several competing proposed methods for planning will be compared, including the use of spatial projection, time-reversal, and time-domain techniques.

Guiding Cardiac Ablation Therapy with Acoustic Radiation Force Impulse Imaging

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Cardiac ablation therapy is commonly used to treat arterial and ventricular tachyarrhythmias. Complex ablations rely on the creation of transmural and contiguous aggregate lesions to block reentrant conduction. Incomplete lesions result in extended procedure times and frequent repeat procedures (30%). Excess energy delivery leads to significant morbidity causing collateral tissue damage with potentially fatal complications (1%). There is a vital need for an imaging technology to titrate energy delivery and guide ablation tachyarrhythmia therapy.

Acoustic radiation force impulse (ARFI) imaging uses an ultrasound impulse to apply a small directional force to tissue. The elastic response to the force is measured using standard ultrasound imaging techniques. Parameters related to these elastic properties are then displayed in image form. ARFI imaging from the body surface has been shown previously to differentiate normal and ablated tissue in liver and kidney. Our goal is to implement ARFI imaging on an intra-cardiac echo (ICE) platform and use it as an imaging tool to guide cardiac ablation therapy.

The multimodal system we are building will enable 1) real time evaluation of lesion growth, 2) visual evaluation of lesion continuity, and 3) guidance and placement of catheters based on ARFI images. The successful implementation of this system will shorten procedure times, reduce the incidence of repeat procedures and limit complications due to collateral damage.

Spectrally Encoded Endoscopy for Image-Guided Therapy of Twin-Twin Transfusion Syndrome

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Twin-twin transfusion syndrome (TTTS) is a severe complication of twin pregnancies that carries a high fetal mortality rate. TTTS can be successfully treated by laser coagulation of communicating vessels that shunt blood from one fetus to the other. However current operative fetoscopes are too large, causing undue membrane damage when introduced into the amniotic cavity. Consequently, placental laser therapy is associated with unacceptable rates of iatrogenic preterm premature rupture of membranes (iPPROM) and *in utero* fetal demise (IUFD). In this talk we describe a new form of endoscopy, termed spectrally encoded endoscopy (SEE), that uses wavelength division multiplexing to obtain high-resolution two- and three-dimensional endoscopic images and coagulate vessels through a single optical fiber. Since SEE devices can be an order of magnitude smaller than current fetal surgery instrumentation, this new technique enables the safe treatment of TTTS and other procedures conducted *in utero*.

Session 6: Imaging

Moderator: Abraham Levy, PhD

MR Imaging for Image Guided Interventions

John Pauly
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Introduction Image guided interventions provides a number of unique challenges for MR imaging systems. These include the need for real-time interactive imaging, the need to visualize and track devices, the issues of device heating and MR compatibility, and the requirements for unique contrasts to visualize the results of the intervention. This talk will provide an overview of these issues, and describe work to address each of these points. We are concerned with three major applications. The first is vascular procedures, particularly the revascularization of total chronic occlusions. The second is the MRI guided RF ablations of liver lesions. The third is MRI guided electrophysiology ablations to treat cardiac arrythmias.

Real-Time Interactive Imaging One of challenges for image guided interventions is the need for real-time information. In addition, the acquisition parameters must be adjustable in real time. Beyond this, the MR system may need to simultaneously acquire different types of information. This requires a new perspective on how MR systems are implemented. We have been developing an approach based on a time-sharing model, where all of the different acquisitions that might be needed in a procedure are initiated, and then paused. Then, during the procedure, any of these can immediately be activated (given magnet time), either individually, or interleaved with other acquisitions. Complex acquisitions involving imaging while tracking devices, navigated motion correction, or interleaved real-time and high resolution scans can then be accomplished simply by scheduling the component acquisitions.

Device Visualization and Tracking Another challenge is the need to visualize and track devices. Other investigators have developed a wide range of mechanisms have been devised to visualize devices both passively and actively. We have been focusing on positive contrast passive visualization, as well as active device tracking. The passive visualization methods must be available interactively as needed. The active tracking information must be available for controlling the scan geometry.

Device Safety A major concern for imaging guided interventions is the safety of devices during the MR procedures. This is particularly true as the field strengths used have gone to 1.5T and 3T. The problem is that devices such as guidewires act as antennas. The transmit RF field can interact with these devices, and produce significant heating. We have been looking at several aspects of this problem. One is that if the currents induced on the device are enough to produce measurable heating (1 degree C), there is enough current in the divice to perturb the RF field. They are then easily detectable by RF transmit field mapping. This will allow dangerous device interactions to be identified well before significant heating is produced.

We are working on actively driving devices to null out interactions using current sensors, and active feedback. We are also working on using transmit arrays to eliminate the

interaction between the devices and the transmit field. We have developed a parallel transmit system that will allow highly parallel systems to be built up very inexpensively (about $2000/channel, including RF power amps). The transmit amplitudes and phases are then set to optimize field uniformity, subject to a constraint on the maximum current induced in the devices. We believe this will be one of the major motivations for parallel transmit array technology.

Image Contrast Mechanisms A central issue with image guided interventions is how to provide visualization of the tissue that has been treated. There are many tissue changes that evolve over time, and are visible after the procedure. However, it is often difficult to assess therapeutic lesions acutely. Some of the more promising approaches, such as diffusion weighted imaging, are difficult to apply in rapidly moving organs like the heart. A major part of our effort has been to identify which contrast mechanisms will allow lesions to be predicted, and to be visualized acutely.

Conclusion Image guided interventions is one of the most interesting applications of MRI. It is the most demanding in terms if imaging speed, interactivity, and flexibility. The need to image in the presence of devices raises many technical issues. A better understanding of the physiological changes that occur when tissue is treated will help guide how to image lesions acutely.

Building a Toolbox to Support Enhanced MR Imaging in Image-Guided Therapy

Lawrence P Panych
Brigham & Women's Hospital, Boston, MA

MR Image-guided therapy (IGT) applications often involve requirements that are difficult to achieve using the standard imaging approaches and tools. For example, to achieve high temporal resolution, it is often necessary to compromise on volume coverage. Enhanced imaging methods such as parallel imaging can help to achieve imaging goals such as high temporal resolution while minimizing compromises elsewhere.

Specialized tools such as real-time imaging controls are also of importance for MR image-guided therapy. To some extent, capabilities such as parallel imaging and real-time control have been implemented on commercial MR systems. However, such implementations are limited and are rarely ideal for IGT applications. A principal goal of the Imaging Core within the National Center for Image-Guided Therapy is to develop freely available libraries of functions to support enhanced imaging in IGT. To this end, three separate but compatible libraries have been built containing: (1) functions to support real-time data acquisition, reconstruction and scanner control, (2) functions to support enhanced imaging including the principal parallel imaging methods, temporal sampling methods such as UNFOLD and other fast imaging approaches, and (3) functions to enable 2D RF selective excitation for reduced field-of-view imaging. In addition to the development of these libraries, we have worked to apply them synergistically in a series of IGT applications such as thermal monitoring during focused ultra-sound treatments and tracking of devices during IGT procedures. As a core of a National Resource Center, a central component of our mission is to enable the dissemination of our toolbox of enhanced imaging libraries to the broader IGT community and to provide expertise in its use to support IGT applications. Through this workshop we aim to broaden the network of users and developers who can benefit from our work as well as to join with us in tailoring these libraries to best address the needs of the IGT community.

Body Imaging – A Role for Light Based Imaging?

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Light based imaging was the original imaging used to guide therapy. For centuries, surgeons could obtain an "image" to guide intervention only by making an incision large enough to use direct visualization to guide therapy. In the 20th century, scientists and clinicians developed imaging modalities not perceivable in their native form by humans. By converting the data from these imaging modalities into an image perceivable by humans, information not formerly available could be used by surgeons and other interventionalists to treat patients. This has led to a remarkable improvement in many types of therapy.

Enabling these improvements in therapy with other imaging modalities raises a fundamental question: Is there still a role for light based imaging? Clearly various applications of magnetic resonance imaging, computerized tomography using X-rays, and ultrasound provide critical information about various organs and images not provided by light based imaging, and many therapies are best guided by these imaging modalities. Yet, many interventions may still be best completed using light based imaging.

We believe that there are several essential improvements to light based imaging that may make it more useful. Further, combining light based imaging with other forms of imaging may provide the best possible information for safely and effectively completing an image guided therapy. Our project is to build an insertable, remotely controlled platform for delivering cameras, other sensors, and tools close to the target organ. The following are potential developments that may enhance light based imaging or otherwise be useful to improve imaging by any other modality.

- Develop new imaging modalities (spectral analysis, sensors for pH, temperature, pressure, linear measurement, etc.), particularly those in which the sensor might require close proximity to the internal target

- Registration of intraoperative light based imaging with preoperative imaging
- Enhancement of intraoperative imaging by integration of preoperative information/images with intraoperative imaging – augmented reality
- Develop sensors and displays for reporting and interpreting response data

The use of an insertable hardware platform to deliver both imaging technology and tools for intervention has the potential to improve image guided therapy.

An Integrated MRI-Guided Electrophysiology Diagnosis/Therapy system: Lessons learned for closed-bore interventional procedures

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An MRI-guided EP system, capable of measurement of Voltage potentials in the heart, as well as of RF Ablation of cardiac chambers, was constructed at MGH between 2003 and 2007. The system was intended for diagnosis and treatment of Ventricular Tachycardia and Atrial Fibrillation, entirely within the MRI environment. Via a successful collaboration with St. Jude Medical, clinical-grade MRI-compatible EP catheters and sheathes were built and utilized successfully in a variety of animal procedures. The advantages and disadvantages of the system architecture will be discussed, in order to improve the design of IGT systems for minimally invasive interventions in closed-bore MRI systems.

Session 7: Targeted Drug & Cell Delivery

Moderator: Keyvan Farahani, PhD

Image-Guided Therapy in Cancer

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Current advances in multi-modality imaging, contrast development, and molecular biology, are revolutionizing the applications of imaging in cancer therapy. In our program the identification of specific targets in cancer is driving advances in novel image-guided platforms such as liposomes and microencapsulation devices to deliver siRNA to down regulate specific targets and pathways. Another exciting development is in the development, synthesis and application of a novel prototype agent for image-guided prodrug therapy. This prodrug enzyme platform can be combined with siRNA targeting. Damage to normal tissue is a major limiting factor in chemotherapy as well as radiation therapy and numerous strategies to protect normal tissue while maximizing damage to cancer cells have been actively pursued. Prodrug enzyme activation systems, where enzymes delivered to the tumor convert a nontoxic prodrug to a cytotoxic drug are one of the most attractive of these strategies but to date have resulted in limited success. Imaging the delivery of the enzyme so that the prodrug is administered when enzyme levels are highest in the tumor and lowest in systemic circulation and normal tissues would be of significant importance for optimizing such a therapeutic strategy. We have synthesized a prototype agent consisting of a cancer therapeutic prodrug enzyme labeled with multimodal magnetic resonance (MR) and optical imaging reporters. The prodrug enzyme, cytosine deaminase, converts a non toxic prodrug 5-fluorocytosine (5-FC) to 5-fluorouracil (5-FU). The prodrug 5-FC and its conversion to 5-FU can be detected noninvasively by 19F magnetic resonance spectroscopy. The conjugate demonstrates high relaxivity, low cytotoxicity, improved enzymatic specificity to prodrug, efficient cell uptake, and high enzymatic stability in serum as well as in breast cancer cell culture. This prototype agent has been used to demonstrate the feasibility of image-guided prodrug enzyme therapy using magnetic resonance imaging (MRI); imaging can be used to time the administration of the prodrug when the enzyme has cleared from normal tissue but is still present in the tumor. Such an approach minimizes cytotoxic side-effects. We are expanding this platform to targeted delivery of the prodrug enzyme using targeting peptides. We are also using this prototype platform to combine prodrug enzyme delivery, and the delivery of siRNA to target, for instance, choline kinase. The optical reporter is especially useful to track the conjugate in cells and tissue using microscopy, while the MR reporter provides potential clinical translatability of this approach. These advances can be used to target specific pathways, microenvironments, and cell types within tumors.

Targeted drug delivery in the brain
via ultrasound-induced blood-brain barrier disruption

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The blood-brain barrier (BBB) severely limits the delivery of drugs to the central nervous system. This barrier restricts the passage of most small molecules and all large molecules from being delivered to the brain tissue from the blood stream. We have developed a method where the BBB is temporarily disrupted in the focal zone of a focused ultrasound transducer using low-power ultrasound bursts following an injection of an ultrasound contrast agent that consists of preformed microbubbles. By systematically focusing at multiple overlapping locations, one could prescribe the region in which the BBB is disrupted to conform to a desired target volume, permitting the delivery of therapeutic agents and reducing drug penetration to the rest of the brain. Ultrasound parameters suited for this procedure are compatible with a device that can focus through the intact skull. This presentation will describe recent research on this technique, discussing methodology, safety, possible mechanisms, and potential means to guide and monitor the procedure.

Microbubbles as a Tool for Targeted Ultrasound Imaging and Drug Delivery

A.L. Klibanov, C.T. Chin, W.T. Shi, M. Bohmer, C.S. Hall, J.J. Rychak, Y.K. Cho, A. van Wamel, N. de Jong, M. Celebi, T. Shevchenko, J. Backer, M. Backer, J. Hossack, K. Ley.

University of Virginia, Charlottesville VA , La Jolla Institute of Allergy and Immunology, La Jolla, CA, Erasmus MC Department of Biomedical Engineering, Rotterdam, Netherlands, Sibtech Inc., Brookfield, CT, Philips Research, Eindhoven, Netherlands and Briarcliff Manor, NY.

Gas-filled microbubbles stabilized with a thin lipid/polymer shell are nontoxic, fully biocompatible/biodegradable and freely circulate in the bloodstream. Despite their small size, microbubbles act as efficient contrast agents for ultrasound imaging and convert ultrasound energy for therapeutic applications.

Attachment of targeting ligands to the microbubble surface can be performed either by covalent coupling or via streptavidin bonding to biotinylated microbubble shell. A variety of ligands, such as antibodies against selectins or immunoglobulin superfamily molecules (ICAM-1, VCAM-1), Lewis^x-derived oligosaccharides or glycosulfopeptides (for targeting P- and E-selectin), VEGF for targeting VEGF receptors and other ligands can be attached to the bubble surface to achieve selective accumulation of microbubbles to the receptors that are expressed on vascular endothelium.

Microbubbles targeted in vivo can be detected by ultrasound imaging with dedicated preclinical small-animal scanners and clinical imaging systems. Successful targeted imaging was achieved in a variety of conditions, from TNFα-induced inflammation to ischemia-reperfusion injury to atherosclerosis and tumor vasculature imaging. We have achieved the ability to monitor molecular signature of tumor endothelium markers by repeated injections of ligand-carrying microbubbles during the course of tumor development in mice.

Liposomes and other nanoparticles capable of carrying anticancer drugs can be attached to microbubble surface by the same techniques as targeting ligands. Ultrasound treatment of such complexes results in microbubble destruction and release of microbubble-associated materials and their deposition in the tissue-mimicking gel phantom. Combination of focused high-intensity ultrasound and low-intensity nondestructive ultrasound imaging can achieve selective insonation and treatment monitoring in the desired tissue.

Cell Tracking and Cell Delivery: From Imaging to Intervention

Jeff W.M. Bulte, Dara L. Kraitchman, Aravind Arepally

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The clinical use of novel experimental cell therapies calls for suitable methods that can monitor the cellular biodistribution non-invasively following administration. Among the different clinically used imaging techniques, magnetic resonance (MR) imaging has superior spatial resolution with excellent soft tissue contrast. In order for exogenous therapeutic cells to be detected, they need to have a different contrast from endogenous cells. The most sensitive MR label to date are the superparamagnetic iron oxide nanoparticles or SPIOs. SPIOs are clinically approved and create strong local magnetic field disturbances that spoil the MR signal leading to hypo- or hyperintense contrast.

After approximately a decade of animal studies using MRI cell tracking these nanoprobes entered the clinic for cell tracking in 2004. The first phase I trial demonstrated the feasibility and safety of MRI (dendritic) cell tracking in cancer patients. A surprising finding, only observable by MRI, was that misinjection of cells occurred in half the patients. While the injection procedure was performed under ultrasound guidance, neither radionuclide or US imaging was able to reveal the failure of targeted cell delivery. Therefore, MR-guided targeted cell delivery may have significant advantages for clinical implementation of novel treatment paradigms using cellular therapeutics. This also applies to bone marrow stem cell transplantation in myocardial infarction. If this is done in real-time under MR guidance, then verification of accurate cell delivery in, adjacent, or remote from the infarct is mandatory.

Recently, we have developed several new technologies that can be used to monitor cell injection, tissue engraftment, cell survival, and cellular differentiation. The first group consists of magnetocapsules, perfluorobromide capsules, and radiopaque capsules that provide simultaneous immunoprotection and multimodal trackability. They are currently being used to improve islet cell and stem cell transplantation. The second group consists of firefly-derived bioluminescent as well as artificial MR reporter genes based on an abundance of exchangable amide protons. These are being applied to track cells, cell survival, and stem cell differentiation into downstream cell lineages. In order to enhance delivery and engraftment, we have developed stent designs that are fine-tuned towards islet cell and stem cell therapies. Our team is dedicated to help guide translating promising pre-clinical studies into the clinic using approved contrast agents, instruments, and devices.

Poster Abstracts

IGT Workshop Posters: Listed by category and the first author

Prostate:

Kruecker - Fusion of Pre-Acquired MRI with Transrectal Ultrasound for Real-time Interventional Guidance in the Prostate

Song - A Pilot Study of Intraoperative Dynamic Dosimetry using Registered Ultrasound and Fluoroscopy (RUF) for Permanent Prostate Brachytherapy

Fichtinger - Robotic Assistance for Ultrasound Guided Prostate Brachytherapy

Mozer - Fully-Automated Robot for MRI Guided Prostate Interventions

Krieger- MRI Guided Prostate Biopsy and Marker Placements

Mozer - Framework for 3D TransRectal Ultrasound (TRUS) Image-Based Tracking

Feleppa Planning and guidance of prostate-cancer therapy using tissue-type images generated from registered magnetic-resonance and ultrasound spectra

Josan - MRI-guided Cryoablation – Acute Cryolesion Assessment with T1 and T2 Imaging

Body:

Cheng - EM Tracking Guided Lung Biopsy – P. Cheng

Yaniv- Navigated Radiofrequency (NAV-RFA) Ablation of Liver Tumors

Armiger - An Intraoperative Biomedical Guidance System for Periacetabular Osteotomy

Iftima - Image-Guided Intervention System for Pancreatic Cancer screening and Therapy

Neurosurgery:

Zibly- MR-Guided High Intensity Focused Ultrasound (MRgHIFU) – Cranial Nerve Thermal Injury Preliminary Results

Xia- A Cooperatively-Controlled Image Guided Robot System for Skull Base Surgery

Levene- Aberration Correction of GRIN lenses for Multipohoton-Microscopy – Guided Neurosurgery

Clinthorne- xCAT: Mobile Intraoperative CT Scanners for Head and neck Surgery

Zhou - Protein-Based MR Imaging of Human Brain Tumors at 3T

Cardiovascular:

Chuech- Vascular Replicas for the Simulation of Image-Guided Stroke Therapy

Shmatukha- Vasculature-based Co-registration of X-ray and MR Images for the Guidance of Cardiovascular Interventions

Linte- Minimally Invasive Intracardiac Therapy Using Augmented Reality Enhanced Ultrasound

Wolf- In vitro ARFI Imaging of Cardiac Ablation Lesions

Nikoozadeh- Intracardiac Ultrasound Imaging Catheters Intergrated with Electrophysiology Electrodes and Ablation Devices

Wilson- Fabrication, Deflecftion, and Heating of Magnetically-Steered Catheters

Hetts- Magnetic Catheter Deflection and Navigation at 1.5 Tesla

Zhang- Image-guided Acoustic Droplet Vaporization (ADV) for Tissue Occlusion

Tempel-Brami- Image-Guided Vascular Targeted Photodynamic Therapy Using Photosensitized (Ps) Bold MRI

Imaging, Computation, & Visualization:

Miga- Model-based Approaches to Enhancing Guidance for Surgical Therapy

Papademetris- From Medical Image Computing to Computer Aided Intervention: Development of a Research Interface for Image Guided Navigation

Galeotti- Holographic Display for In-Situ Merger of Real-Time Tomographic Data with Direct Vision

Tgavalekos - Preliminary Results for Instrument Tip Tracking During Interventional Oncology Procedures

Todd- Using thermal model predictions to improve MR temperature imaging time resolution

Payne- Minimization of HIFU Treatment Time using Model Predictive Feedback Control

Mao- A Novel Algorithm for Automatic Detection of Multiple Internal Fiducial Markers on Onboard MV and kV Images

Wiersma- Combined kV and MV Imaging for Real-Time Tracking of Implanted Fiducial Markers

Fusion of Pre-Acquired MRI with Transrectal Ultrasound for Realtime Interventional Guidance in the Prostate

J. Kruecker[a], S. Xu[a], P. Pinto[b], I.B. Turkbey[b], P. Choyke[b], H.B. Hooper[b], A. K. Singh[c], Julia Locklin[b], and B. J. Wood[b]

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Purpose: To enable lesion-targeted prostate biopsy and localized therapy, by bringing target information from pre-acquired MRI into the transrectal ultrasound (TRUS)-based workflow, without requiring interventional MRI.

Methods: A TRUS probe is spatially tracked using an electromagnetic tracking system mounted near the patient. At the beginning of the procedure, a 3D ultrasound volume of the prostate is reconstructed from images obtained in a 2D manual sweep across the prostate. The 3D ultrasound is registered manually with a pre-acquired T2-weighted MRI. Subsequent realtime TRUS imaging shows the current ultrasound frame fused with the corresponding MRI multi-planar reconstruction (MPR). Target points selected in the MRI are automatically visualized in the corresponding location in the ultrasound. Semi-automatic image-based registration of the current ultrasound frame with the 3D TRUS image is used to compensate for intra-procedural prostate motion. This technique was evaluated and used in phantom studies and 17 patients

Results: In phantoms, the motion compensation achieved accuracy of 2.3 ± 0.9mm. In patients, the prostate overlap between MRI and TRUS was 77% ± 18% , which increased to 93% ± 5% with motion compensation . The 3D TRUS – MRI registration accuracy was 3.1 ± 0.9mm, based on manual segmentations in both image modalities. Positive lesion targeted biopsies were obtained in patients with prior false negative conventional systematic sextant biopsies.

Conclusions: Fusion of pre-acquired prostate MRI with realtime TRUS is feasible and may enable lesion-targeted interventional guidance without requiring an interventional MRI.

A Pilot Study of Intraoperative Dynamic Dosimetry using Registered Ultrasound and Fluoroscopy (RUF) for Permanent Prostate Brachytherapy

Danny Y Song*, Anton Deguet*, Ameet Jain*, Iulian Iordachita*, Elwood Armour*, E Clif Burdette†, Gabor Fichtinger§

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Purpose: Currently available brachytherapy techniques do not allow robust identification of seed positions intraoperatively resulting in lack of dosimetric quality control.

Materials/Methods: In contrast to prior approaches, we perform dynamic intra-operative dosimetry without major modification to conventional setup. A non-invasive, radio-opaque fiducial was utilized and 4 non-coplanar X-rays taken for reconstruction. 3D coordinates of segmented seeds are calculated upon resolving correspondence of seeds in C-arm images by formalizing seed-matching as network-flow problem. Calculated seed positions were imported into the treatment planning software for visualization of dosimetry intraoperatively. The treatment plan and/or total number of seeds were subsequently modified prior to completion of the procedure.

Results: Five patients were treated with permanent source brachytherapy using RUF. RUF calculation of seed positions was performed 3 times during each case, and subsequent seed placement modified as determined by physician judgment. 54-84 seeds were placed; based on RUF data, 3-10 seeds were added to the original treatment plan to alter areas of visualized underdosing. CT dose-volume histogram data are as follows: prostate D90 of 100-135%, V100 of 88.3-99.6% (in the patient with V100 of 88.3%, RUF indicated area of underdosage but all available seeds had been utilized), urethral D50 of 95-120%, and rectal R100 of 0.0-0.3cc.

Conclusions: RUF is achievable and feasible for use in a standard intraoperative setting, without major alteration of normal clinical setup. These pilot results indicate satisfactory performance with positive dosimetric outcomes.

Robotic Assistance for Ultrasound Guided Prostate Brachytherapy

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Goal: We develop an ultrasound image guided robotic assistance system for prostate brachytherapy.

Rationale: The system is expected to lead to more precise and consistent implants.

Design: The system consists of a transrectal ultrasound (TRUS) and a spatially co-registered robot integrated with an FDA-approved commercial treatment planning system. The salient feature of the system is a small parallel robot affixed to the mounting posts of the template. The robot replaces the template interchangeably and uses the same coordinate system. Established clinical hardware, workflow and calibration are left intact. In these experiments, we recorded the first insertion attempt without adjustment.

Results: The system was tested in training phantom All clinically relevant locations were reached. Non-parallel needle trajectories were achieved. The pre-insertion transverse and rotational errors (measured with Polaris optical tracker relative to the template's coordinate frame) were 0.25mm (STD=0.17mm) and 0.75^{o} (STD=0.37^{o}). The needle tip placement errors measured in TRUS were 1.04mm (STD=0.50mm). The system has been tested successfully in Phase-I clinical feasibility and safety trials. Results will be reported the conference.

Fully-Automated Robot for
MRI Guided Prostate Interventions

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Purpose: Transrectal ultrasound is commonly used to image the prostate but magnetic resonance imaging (MRI) provides better visualization for treatment planning and monitoring. The exact placement of needles in the gland is crucial to achieve diagnosis or deliver treatment. We present an MRI compatible robot for needle placement in the MRI scanner.

Methods: The system is specifically designed for transperineal percutaneous prostate interventions and is currently customized to perform fully automated MRI-guided brachytherapy. The system may be adapted for other image-guided interventions such as biopsy or cryotherapy. In order to achieve MRI compatibility, the entire robot is built of nonmetallic materials such as ceramics, plastics and rubbers. Additionally, a pneumatic stepper-motor was specifically developed for this application.

Results: Various preclinical experiments were performed to test the robot for precision and imager compatibility. The robot is fully operational within any MRI scanner. Compatibility tests in scanners of up to 7 Tesla showed no interference of the robot with the functionality of the imager. Precision tests in tissue mockups yielded a mean seed placement error of 0.72 mm (SD 0.36 mm). Cadaver and animal studies are in progress.

Conclusion: We present the first fully-automated MRI compatible robot. Prior to any clinical use, robot refinements and more extensive testing are being performed.

Acknowledgements: This work was supported by the National Cancer Institute, the Prostate Cancer Foundation, and the Patrick C. Walsh Foundation.

MRI Guided Prostate Biopsy and Marker Placements

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Purpose: To develop and evaluate the performance of a Magnetic Resonance Imaging (MRI) guided system for transrectal prostate interventions - such as needle biopsy, gold marker placement, and therapy delivery. MRI affords images with higher anatomical resolution and contrast than can be obtained using ultra sound, which is the present day standard for guidance of prostate interventions. This system is expected to ultimately lead to higher sensitivity in detecting prostate cancer and allow for more precise implants of gold markers to help guide external beam therapy.

Methods: The system consists of three major components: First, a needle manipulator with integrated endorectal MRI imaging coil to assist the physician in inserting a needle to a predetermined target. Second, a hybrid tracking method, comprised of fast, accurate, passive fiducial tracking for initial registration and incremental motion measurement along the degrees of freedom using fiber-optic encoders and mechanical scales. Third, a custom targeting software program, which automatically segments the fiducials for initial registration, displays MR images, calculates parameters to reach selected targets in the prostate, and provides an user interface for the physician.

Results: The performance of the system was evaluated in extensive phantom experiments and two clinical procedures. One procedure encompassed combined biopsy and marker placements, the second employed biopsy only. Mean targeting accuracy was 1.8mm for the clinical biopsies and 1.1mm for the marker. Prostate cancer was found in one case.

Conclusion: The phantom experiments and clinical procedures demonstrate accurate and fast MRI guided needle targeting of the prostate.

Framework for 3D TransRectal Ultrasound (TRUS) Image-Based Tracking
- Example of Use –
Evaluation of 2D TRUS Prostate Biopsies Mapping

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Purpose: Prostate biopsies are mainly performed under TransRectal UltraSound (TRUS) control by sampling the prostate according to a predefined pattern. From a clinical point of view, it could be useful to control the 3D spatial distribution of theses biopsies. We propose a 3D TRUS based tracking system for prostate biopsies localization and we use it to evaluate the ability of a clinician to perform biopsies under 2D TRUS control commonly used in clinical practice.

Methods: A single operator performed 12-core TRUS biopsies on 32 patients according to a classical pattern using a 2D-3D TRUS probe (RIC5-9 on a Voluson-i, GE).

• Before the first biopsy, a 3D reference volume is acquired.
• For biopsy targeting, the probe is switched to 2D mode.
• After each biopsy gun shot a 3D TRUS volume is acquired.
• After the biopsy session, the needle is segmented in each volume and is fused automatically into the reference with our rigid image-based registration algorithm.

Results: The registration method was validated on 237 images with an average error < 1.44 mm and a max error 3.84mm. Registration between each volume was computed in 6 seconds. The success rate of all the registration was 96.7%. The operator reached the target in 67% of all cases and a learning curve can be highlighted.

Conclusions: This study shows that our algorithm is robust and accurate. Moreover, it is difficult to reach targets using a 2D TRUS probe. Navigation systems and robots are needed to improve prostate biopsies.

Planning and Guidance of Prostate-Cancer Therapy using Tissue-Type Images Generated from Registered Magnetic-Resonance and Ultrasound Spectra

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Purpose: Prostate cancer cannot be imaged reliably using available imaging modalities including transrectal-ultrasound and magnetic-resonance (MR). Consequently, prostate biopsies typically are performed with minimal knowledge of where cancer is located. Ultrasound spectral (USS) parameters along with clinical parameters have been shown to identify cancerous regions in the prostate successfully. Prostate cancer also can be identified using magnetic-resonance spectroscopy (MRS) parameters. We aim to combine USS and MRS parameters by spatially co-registering 3-D volumes generated from ultrasound (US) and MR data to enhance our tissue-characterization methods.

Methods: 3-D volumes were generated from US and MR transverse scans acquired from clinical prostatectomy patients prior to surgery. These 3-D volumes were co-registered in two ways. In the first method of co-registration, the MR volume rendering was warped to match the volume rendering generated from US images using the gland boundary and urethra as landmarks. In the second method, a 3-D algorithm based on a soft-tissue deformation model was utilized to volumetrically match MR and US images.

Results: After warping, the 3-D volume generated from clinical MR images closely matched the volume generated from US images. Application of the 3-D algorithm to clinical data also resulted in good agreement between MR and US images. Both methods successfully compensated for different deformations introduced during the imaging procedures.

Conclusions: Distortions introduced during imaging were effectively minimized, enabling accurate co-registration of 3-D volumes generated by the two imaging modalities. Successful co-registration indicates that integration of USS and MRS parameters is feasible and may have great potential for identifying prostate cancer reliably.

MRI-guided Cryoablation – Acute Cryolesion Assessment with T1 and T2 Imaging

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Purpose: The appearance of acute prostate cryolesions on T1 and T2 weighted MR images varies among subjects. This work investigates the dependence of lesion contrast on freeze protocol, area, and time and compares lesion size with that on contrast-enhanced (CE) MR images.

Methods: Cryoablation was performed on 17 dogs in the 0.5T GE interventional MRI scanner using Oncura cryotherapy system. Two freezing protocols were used: A) single slow freeze; B) two fast freeze/thaw cycles. A regression of pre-to-post freeze T2 signal change with freeze protocol, freeze area, and time after maximum freeze was performed.

Results: The boundaries of T1 and T2 lesion corresponded well with the CE lesion.
Upon adjusting for effects of freeze area and time, T2 signal change was greater for protocol-B than protocol-A. For both protocols, T2 enhancement was higher for a smaller area, and a longer time. The effects of area and time on T2 enhancement were smaller for protocol-B.

On T1-weighted images, the cryolesion appeared iso or slightly hypo-intense, surrounded by a dark rim, however, it was observed only in 6 dogs for protocol-B, and 4 dogs for protocol-A. The conspicuity of protocol-B lesions was higher than protocol-A.

Discussion: We hypothesize that T2 signal enhancement is caused by fluid accumulation into the cryolesion from surrounding injured microvessels. In larger lesions fluid is distributed over a larger volume, producing less T2 enhancement. The central hemorrhagic region of the cryolesion appears iso- or hypo-intense on T1w images, while the dark rim could be a combination of hemorrhage and edema.

EM Tracking Guided Lung Biopsy

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Purpose: We have developed a navigation system based on the open source software library the Image-Guided Surgery Toolkit (IGSTK). We have obtained Institutional Review Board (IRB) approval and FDA Investigational Device Exemption (IDE) to use this system in a clinical trial for CT-guided lung biopsy. The clinical trial will evaluate the use of electromagnetic tracking as an adjunct guidance modality for these cases.

Methods: In contrast to traditional CT-guided or fluoroscopy-based interventions, this navigation system uses a pre-operative CT image volume and an electromagnetic tracking system to provide real-time feedback of the biopsy needle position overlaid on the CT images. The first step is to scan the patient with skin fiducials and an 18-gauge respiratory motion monitoring needle placed near site of interest. We then transfer the CT images to the navigation workstation, perform paired-point registration, and plan the biopsy trajectory. The interventional radiologist then places a tracked needle using the image overlay. When the radiologist believes the biopsy needle has reached the desired target, he will check the actual position with CT fluoroscopy. If the needle position is deemed acceptable, a core biopsy will be done. If the position is deemed unacceptable, we consider that the navigation system will not be helpful and finish the procedure with the standard CT fluoroscopy guided technique.

Results: The navigation system has been successfully tested on a respiring phantom in the clinical environment. We believe that the navigation system will be able to target lesions at greater (or at least equivalent) accuracy and reduce radiation exposure compare to fluoroscopy guidance. We also hope that this system will reduce the complexity (advance and check with fluoroscopy versus real-time feedback) in this commonly performed procedure and lower the experience level needed to successfully target small lesions.

Conclusions: We have developed a working system for electromagnetically guided lung biopsy based on an open source software package. The system has been tested on a phantom in the clinical environment. We are now recruiting patients for a clinical trial as described in this abstract.

Navigated Radiofrequency (NAV-RFA) Ablation of Liver Tumors

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Purpose: We are developing a Navigated Radio Frequency Ablation (NAV-RFA) system for treatment of liver tumors based on Slicer 3.0 and the Image-Guided Surgery Toolkit (IGSTK). Our goal is to provide the physician with an optimal ablation plan and intraoperative guidance using electromagnetic tracking.

Methods: To achieve clinical acceptance for our NAV-RFA system we have designed it such that image acquisition, ablation planning, and navigation are all performed in-situ in the Interventional Radiology suite. Preoperatively a cone beam CT of the liver is acquired. The data is segmented into four structures: ribs, liver, tumor, and vasculature. The physician indicates regions that should not be crossed by the RFA probe, and regions that should not be treated. Based on this data, a pre-emptive goal programming method is used to compute a set of planned trajectories and ablation locations. The image data is registered to the patient and navigation information is provided by overlaying the probe location onto the images.

Results: A proof of concept system using manual segmentation and an IGSTK based interface was successfully completed in a single swine animal trial targeting an artificially introduced lung nodule. The computed plan consisted of one skin entry point, two needle trajectories, and four ablation locations. Computation time was approximately eight minutes.

The physician navigated the RFA probe using electromagnetic tracking and performed the ablations. Pathologic analysis of the burn showed that histologic cell death was achieved only for approximately 50% of the estimated necrotic area.

Conclusions: We have developed a proof of concept NAV-RFA system. The next phase of development has started with the integration of IGSTK tracking into Slicer 3.0, and development of a semi-automatic segmentation framework.

An Intraoperative Biomechanical Guidance System for Periacetabular Osteotomy

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Purpose: Our ongoing effort has been to develop a software suite that allows a clinician to surgically plan and execute a periactetabular osteotomy with feedback based on both the internal joint stress state during activities of daily living and computer-simulated radiological information.

Methods: The navigation system with Biomechanical Guidance (BGS) allows the clinician to graphically load CT scan data and characterize a patient's malformed dysplastic hip using conventional radiological angle measurements as well as biomechanical methods. Using the navigation system intraoperatively, the biomechanical model is updated in real-time to reflect improved stress distribution within the hip joint during re-alignment.

Results: The first round of clinical-setting trials included 10 patients with operations beginning in November 2005 and ending in September 2006 (four males, six females, age: 22-47. Each patient underwent a unilateral osteotomy following a modified Ganz protocol. In all cases, the surgeon reduced the contact pressure by a median of 45% (Range 14 to 445%). The BGS preoperative plan for the PAO cases, based on the principle of reducing the peak contact pressure agreed with the surgeon's preoperative plan for realignment based on radiological data (Median: 3.4 degrees; Range: 0.1 to 15.4 degrees).

Conclusion: The surgeon is faced with trade-offs during surgery that may deviate the final surgical outcome from the preoperative plan. For the surgeon this new navigation offers the chance to look at, not only the peak pressure, but to foresee the radiographical angles in real-time while he struggles with the fragment fixation.

Image-Guided Intervention System for Pancreatic Cancer Screening and Therapy

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An image-guided intervention clinical instrument that has the potential to significantly increase the yield of CT and EUS guided procedures for pancreatic cancer screening and to offer a real-time monitored therapy option is presented. A common path fiber optic-based catheter is used for both imaging and therapy. The yield increase will be accomplished by providing high-resolution (micron scale) cross-sectional optical coherence tomography (OCT) images of the ductal or cystic lining epithelium that will allow for better differentiation between non-neoplastic and neoplastic lesions. The therapeutic capability will be added by sending a laser beam through the same catheter, which will thermally coagulate (cause necrosis of) the diseased epithelial tissue layer. With the laser therapy and OCT imaging combined, the dual capability system will have the potential for performing both diagnosis and real-time monitoring of therapy. None out of these features are currently available to the physician.

This system is currently being tested at the Massachusetts General Hospital on excised pancreatic tissue specimens. The very preliminary results show that OCT provides the necessary resolution to distinguish between the normal and malignant epithelium. Also, thermal ablation of the ductal epithelium, as well as induced necrosys on cystic tissue is demonstrated.

The proposed system can be engineered to work in conjunction with existing clinical EUS and CT systems. With two new added capabilities, high resolution imaging and laser therapy, these systems would allow for increased diagnostic yield and will offer a therapeutic option for early stage pancreatic tumors.

MR-Guided High Intensity Focus Ultrasound (MRgHIFU):
Cranial Nerve Thermal Injury - Preliminary Results

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Purpose: MRgHIFU is an emerging modality for non-invasive ultrasound-based treatment of deep-seated tissues. This study was designed to evaluate the efficacy and safety of thermal injury to cranial nerves by MRgHIFU using the optic nerve as model.

Methods: Five pigs underwent a bifrontal craniectomy one week before MRgHIFU (Exablate 2000, 1.15 MHz) treatment. Targeting was performed using pre-treatment T2 MRIs. Sonication duration and energy were 6-10 sec and 50-200 Joule. Brains were extracted immediately post treatment and subjected to histological analysis.

Results: In an animal treated up to 50ºc, as depicted by real-time thermal mapping, there were no signs of tissue damage neither in MRI nor in histological examination. In an animal treated up to 60ºc, there where clear signs of tissue damage in the MRI as well as a region of necrosis with sharp boundaries in the histological examination, surrounded by a narrow region of edema. In an animal treated up to 70ºc, there where signs of tissue damage in the MRI and the histological examination depicted necrosis in the treatment region surrounded by a wider transitional zone within the target nerve.

Conclusions: We showed that for the discussed setup, the thermal threshold for tissue damage was 50^{o}c. Higher temperatures induced increased tissue damage, well confined within the targeted nerve. These preliminary results demonstrate the feasibility of using MRgHIFU for accurate and safe tissue disruption in cranial nerves in vivo.

A Cooperatively-Controlled Imaged Guided Robot System for Skull Base Surgery

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Purpose: We created an image-guided robot system to create a cavity in the skull base to allow access for neurosurgical interventions. The motivation for introducing an image-guided robot is to improve safety by preventing the surgeon from accidentally damaging the critical neurovascular structures during the drilling procedure.

Methods: We used the NeuroMate robotic arm with a 6 degree-of-freedom force sensor. The force sensor, the Stealthlink optical tracking interface, and additional software allow the robotic arm to be used in a navigated, cooperatively-controlled fashion by the surgeon. We employed "virtual fixtures" to constrain the motion of the robot-held cutting tool so that it remains in the safe zone that was defined on a preoperative CT scan.

Results: We performed experiments on both foam skull and cadaver heads. The results for foam blocks cut using different registrations yielded an average placement error (due to calibration and registration error) of 0.6mm and an average dimensional error (due to system compliance) of 0.6mm. In the cadaver, we drilled the posterior porus acusticus and the entire clivus. We obtained postoperative CT to assess accuracy. Some bone was undercut, likely due to using a large 5 mm cutter. Maximum overcut is about 2.5 mm, with an average overcut of 1mm.

Conclusions: The system appears to be feasible for skull base drilling. We have since implemented measures to improve the accuracy by reducing the cutting tool compliance.

Aberration Correction of GRIN lenses for Multiphoton Microscopy-Guided Neurosurgery

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Purpose: Gradient index (GRIN) lenses are needle-like lenses that can be used to extend the reach of multiphoton microscopy (MPM) to deep brain structures. We are developing a GRIN-lens-based MPM microscope for use in image-guided biopsy and implantation of deep-brain stimulating electrodes. GRIN lenses, however, suffer from significant spherical aberrations. The purpose of this work was to use a combination of glass coverslips and a standard microscope objective correction collar to correct for spherical aberration in GRIN lenses.

Methods: We performed ray-trace analyses of the GRIN lens system using ZEMAX to find the optimum glass thickness for aberration correction. We corrected for spherical aberrations in GRIN lenses by first over-compensating with a glass coverslip. This enabled cancellation of the remaining aberration using the correction collar on a long-working distance microscope objective. Aberration correction was evaluated by measuring the longitudinal point-spread function by taking z-stacks of the surface of a fluorescent slide.

Results: Ray-trace calculations demonstrated that the optimum glass thickness to compensate for spherical aberrations in GRIN lenses is ~80 microns. We demonstrate a 3-fold reduction in the longitudinal point-spread function using #0 coverslips. The improved results were also demonstrated by in vivo imaging of dendritic spines in mouse brain.

Conclusions: Choosing the appropriate thickness of glass to place in front of a GRIN lens is a simple and effective way of reducing spherical aberration and significantly improving imaging resolution for MPM-guided neurosurgery.

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xCAT: Mobile Intraoperative CT Scanners for Head and Neck Surgery

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Purpose Use of 3D image guidance in surgical procedures has been steadily increasing; however, surgical navigation systems typically rely on pre-operative datasets, which cannot account for manipulations during the procedure. To eliminate the issue, the Xoran xCAT volume CT scanners were developed.

Methods The first product in the xCAT series was designed to provide intraoperative 3D image support for sinus, temporal bone, and skull base surgery; a neurosurgery product is under active development. The scanner comprises a large-area flat-panel xray detector, low-power x-ray source, and weighs 450 pounds. It is easily moved into place for CT images during procedures. Data acquisition for a full volume dataset takes 40 seconds and a reconstructed volume having isotropic spatial resolution is available for viewing two minutes later. An important benefit is that the updated images can be used to replace the pre-operative scan in the navigation system. Because the radiation dose is significantly lower than conventional CT head scans, updates can be performed several times during a surgical procedure if necessary.

To gauge the benefits of having readily available 3D images, xCAT images were obtained near the conventonal endpoint of surgical procedures to evaluate the need for additional intervention during navigation-assisted endoscopic sinonasal, and skull base surgery, as well as during trauma procedures.

Results Preliminary results based on more than 50 cases show that the CT images indicated that additional intervention was necessary in a significant fraction.

Conclusions Indications support the value of CT image support during surgery.

Protein-Based MR Imaging of Human Brain Tumors at 3T

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Purpose: To develop a totally new protein-based MRI approach for imaging of human brain tumors.

Methods: Nine patients with brain tumors of varying grade were scanned at 3T. The new technique used is called amide proton transfer (APT) imaging, in which the imaging intensity was quantified as a change in bulk water intensity due to chemical exchange with amide protons of cytosolic proteins. We assigned areas with conventional MRI abnormality as tumor, in which Gd-enhancing regions were assigned as tumor cores, and the rest as tumor periphery.

Results: Gd-enhancement was observed for six patients with high-grade tumors and not for three patients with low-grade tumors. In high-grade tumors, APT intensities were significantly higher in the Gd-enhancing tumor core than in tumor periphery ($P = 0.01$) and in normal appearing white matter (NAWM, $P = 0.008$). Regions of increased APT (presumably due to higher cellular protein content in gliomas) extended outside of the core into peripheral zones (due to the infiltrative nature of gliomas), but smaller than the abnormal areas designated as tumor on conventional MRI. Conversely, APT intensities in tumor were indistinguishable from NAWM ($P = 0.8$) in patients with low-grade tumors. Even though the sample size was limited, a clear correlation with grade could be established ($r = 0.92$).

Conclusions: The higher concentration of cytosolic proteins in tumor cells allows us to visualize brain tumors and distinguish grade at the protein level. These unique features may prove valuable for maximizing diagnostic accuracy and guiding surgical resection of human brain tumors.

Acknowledgments: The authors thank Jaishri Blakeley, Craig Jones, Michael Schlosser, John Laterra, Martin Pomper, Jun Hua, and Mina Kim for collaboration on this project and Terri Brawner, Kathleen Kahl, and Ivana Kusevic for experimental assistance. This work was supported in part by grants from NIH (RR015241, EB002634, and EB002666), Whitaker Foundation, and Dana Foundation.

Vascular Replicas for the Simulation of Image-Guided Stroke Therapy

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Purpose: Our goal is to develop an innovative and practical method for batch manufacturing of patient-specific silicone vascular replicas for simulation of image guided stroke therapy. The silicone models are designed to be elastic, true-to-scale, and optically transparent with uniform thickness.

Methods: The 3D morphology of the target vessels were acquired and reconstructed by using medical imaging modalities such as computed tomography, magnetic resonance imaging and 3D rotational angiography. The reconstructed image was first edited and optimized in image post-processing and then used as a template to create a core-shell model. The rapid prototyping machine transformed the virtual core-shell design into the physical mold for silicone injection. Two different silicone rubbers, Sylgard 184 and LIM 6030, were used in this study. After injection, the silicone was cured at 50^{o}C for 12 hours. The whole mold was immersed in xylene to remove the model material.

Results: LIM 6030 has a more cloudy appearance than Sylgard 184 does; however, they are both optically transparent. The stress-stretch curve of both silicone rubbers were obtained by means of the Instron. Like human blood vessel, silicone rubber exhibits the nonlinear stress-stretch relationship, and LIM 6030 has similar elastic modulus to the middle cerebral artery under pressure up to 0.05 MPa.

Conclusions: This method successfully fabricated silicone cerebral aneurysm replicas with characteristics that fulfill the aforesaid requirements and the replicas have been applied for the assessment of the safety and efficacy of devices for the mechanical obliteration of clot in acute stroke applications.

Vasculature-based Co-registration of X-ray and MR Images for the Guidance of Cardiovascular Interventions

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Purpose: Simultaneous use of MRI and X-ray during interventions allows combining cross-sectional soft-tissue and functional display with real-time visualization of interventional devices. Co-registration of MR and X-ray images is usually achieved with the help of markers attached to the patient's body and to moving scanner components. The anatomy of interest position must be derived indirectly from the marker positions, using time-consuming image post-processing and equipment calibrations. Our X-ray/MRI fusion technique automatically co-registers anatomical features of interest, without any markers or hardware calibrations. It derives the relationship between the coordinate systems of two different scanners by calculating the transformation required to overlay representations of a selected blood vessel on both scanners, with the derived relationship applicable to any other anatomy of interest.

Methods: Phantom images were acquired on a combined X-ray/MRI interventional suite. The phantom mimicked MRI and X-ray appearances of a blood vessel within soft tissue and an anatomy of interest to be displayed on the fused image. Series of MR and X-ray images of the phantom were acquired, and "vessel" representations on them were automatically co-registered. The calculated transformation was automatically applied to the MRI representation of the "anatomy" of interest, and fused XMR images were automatically generated.

Results: Fused XMR images demonstrated good agreement between X-ray and MRI representations of phantom. Image fusion inaccuracies were of the order of a few millimeters, well within the clinically acceptable limit.

Conclusions: The described technique allows using MRI soft tissue and functional information as a roadmap during real-time X-ray guidance of interventions.

Minimally Invasive Intracardiac Therapy Using Augmented Reality Enhanced Ultrasound

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Purpose: The progress towards minimally invasive approaches to reduce morbidity during cardiac interventions has been hampered by the lack of adequate visualization and insufficient surgical guidance required to manipulate instruments inside the beating heart. Consequently, most intracardiac procedures are still performed on the arrested heart and rely on cardiopulmonary bypass.

Methods: We have developed a surgical guidance platform that provides the surgeon with a virtual surgical environment that accurately represents the real surgical field, eliminating the limitations arising due to the absence of direct vision. The virtual environment integrates intra-procedure trans-esophageal echocardiography images for real-time image guidance displayed within their anatomical context, provided by means of pre-operative, subject-specific, dynamic cardiac models. Ultimately, the environment is complemented with virtual representations of the surgical instruments utilized in the procedure and tracked in real-time with respect to the other virtual components using the NDI Aurora™ magnetic tracking system.

Results: Following extensive laboratory testing, we have translated the work into the operating room and report our experience during *in vivo* porcine studies. After building the pre-operative models of the porcine heart and fusing them with the intra-procedurally acquired US images, we employed our surgical navigation system to successfully guide typical intracardiac interventions *in vivo*, such as a mitral valve implantation and atrial septal defect repair.

Conclusions: Given its extensive capabilities in providing the necessary guidance for surgical instrument navigation and on-target manipulation for therapy delivery in absence of direct vision, our surgical guidance system constitutes an ideal candidate for performing interventions inside the beating heart.

In vitro ARFI Imaging of Cardiac Ablation Lesions

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Purpose: Acoustic radiation force impulse (ARFI) imaging has shown promise as a modality for characterizing cardiac ablation lesions. ARFI images are created by displaying tissue displacement caused by an acoustic pulse. The ARFI imaging contrast between normal and ablated myocardium is unknown. The goal of this study is to compare lesion histology to ARFI parameters *in vitro* where the imaging can be controlled.

Methods: An apparatus was constructed to image lesions with precise and known alignment of the imaging plane. The device controlled the angular rotation and the 3D location of an AcuNav™ ICE catheter. The apparatus housed a tissue chamber, which could be aligned with the imaging plane. A Siemens Antares scanner was used to image RF ablation lesions with both B-mode and ARFI. The lesions were positioned on the tissue to be transected by the image plane. The tissue was then cut along the plane using the chamber as a guide. Photographs of the cut/imaging plane were compared to B-mode and ARFI images.

Results: Statistical results were not available at the time of writing; however, the images below show typical results. There is a marked stiffening of the ablated tissue as shown by reduced displacement. The lateral boundary of the lesion is well defined but the lesion depth is less discernable.

Conclusion: ARFI imaging can be used to image ablation lesions otherwise invisible to ultrasound. The effectiveness of the technique is attenuated with depth and additional pushing force will be required to image the full extent of the lesion.

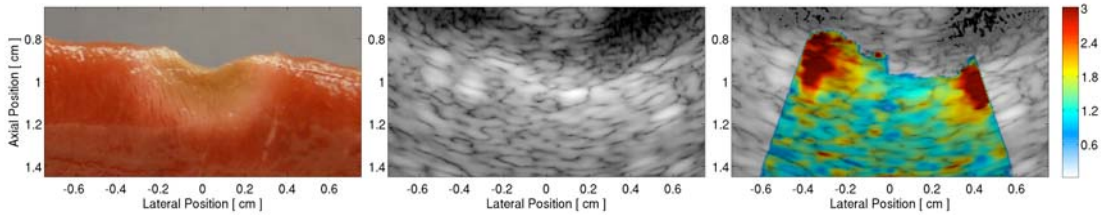

Fig 1. Photograph, B-Mode image, and ARFI image(peak displacement) of an ablation lesion

Intracardiac Ultrasound Imaging Catheters
Integrated with Electrophysiology Electrodes and Ablation Devices

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Purpose: Catheter ablation has revolutionized the management of cardiac arrhythmias. Currently, in these procedures fluoroscopy is the standard method for navigating catheters in the heart. Multiple catheters are used for electrophysiology assessment and ablation. We are developing intracardiac ultrasound imaging catheters integrated with EP electrodes and ablation devices to simplify interventions in the heart.

Methods: We are developing two types of forward-viewing ultrasound imaging arrays based on the capacitive micromachined ultrasonic transducer (CMUT) technology: A 14-MHz, 24-element microlinear (ML) array with a 1.7x1.3-mm footprint, and a 2-mm diameter, 10-MHz, 64-element annular ring array. Both arrays are integrated with custom designed front-end electronic transmit-receive circuits to overcome the performance degradation associated with long cables in the catheter. The ML-CMUT array provides a 2-D image in front of the catheter tip. The CMUT ring array provides a 3-D image. The central lumen available in the ring array geometry enables the convenient delivery of different therapeutic devices such as HIFU transducers.

Results: With the ML-CMUT array, we demonstrated ex-vivo images of the left atrial appendage in a Langendorff isolated perfused rabbit heart model and in-vivo images of heart through the open chest in a porcine animal model.
We used the CMUT ring array to demonstrate 3-D images of coronary stents and an anatomic cast of a left atrial model.

Conclusions: These results show that the CMUT technology is ideal for implementing high-frequency, minia-ture transducer arrays with integrated electronics to guide catheter-based intracardiac and in-travascular interventions.

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Fabrication, Deflection, and Heating of Magnetically-Steered Catheters

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Purpose: To test the ability to fabricate, manipulate, and cool coil-tipped catheters in the magnetic field of the MRI scanner.

Methods: Orthogonal copper coils were mounted on 3-French microcatheters using laser lithography. The catheters were suspended in a simple water phantom in the bore of the 1.5 T MR imager (Philips Medical Systems). Currents were applied to the coils at varying magnitudes (100-400 mA), polarities, and combinations to induce catheter tip deflection. Movement of the catheter was imaged using a real-time bFFE sequence (1-3 frames/sec). Heat generation in the catheters was quantified with a thermocouple at the tip. Cooling effects of dripping normal saline through the catheter was measured.

Results: Reproducible fabrication of orthogonal coils on the microcatheter tips was possible using laser lithography. The orthogonal coils predictably deflected the catheter tip in multiple directions. Application of a saline drip through the catheter cooled the tip when current was applied to the coils.

Conclusions: Dual, orthogonal coil-tipped microcatheters were reproducibly constructed, predictably deflected, and effectively cooled with a saline infusion.

Magnetic Catheter Deflection and Navigation at 1.5 Tesla

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Introduction: Interventional MRI is growing into an accepted therapeutic modality given all the advantages MRI has to offer in terms of imaging and physiologic assessment. A further advantage of MRI would involve exploiting the magnetic environment of the MR scanner to control the movement of a catheter that was inherently sensitive to the ambient magnetic field of the Magnet. Magnetic catheter navigation would broaden the range of therapeutic options and improve the safety profile of such procedures.

Purpose: To test the feasibility of controlling and imaging the movement of magnetically sensitive catheters in a 1.5 T MRI scanner by regulating the voltage applied to the copper coils on the catheter tip.

Methods: A 5 French angiographic catheter was modified by winding 38 gauge insulated copper magnet wire around the distal I cm of it's the catheter tip. The wire ends were run down the length of the catheter to allow for them to be connected to a remote voltage source. The catheter was suspended in a simple cylindrical water phantom, and this system was positioned in the center of the bore of the MR imager (1.5 T Intera, Philips Medical Systems). Varying voltages (1.5, 3, 6, and 9 V) were applied to the copper wire ends in alternating polarities. As the voltages were applied, the resultant movement of the catheter was imaged using a real-time bFFE rapid imaging sequence (1-3 frames/sec). The angle of catheter deflection was measured at each voltage level. Subsequently, the same catheter was placed in a y-shaped tubular phantom and again a voltage was applied to the catheter as it approached the "bifurcation" of the phantom in order to deflect the catheter down one limb of the other.

Results: Catheter tip movement could be imaged in real-time with the bFFE sequence. Catheter deflection was achieved at all applied voltages. The angle of deflection increased with increasing applied potential in a linear fashion. Application of voltage to the catheter also permitted catheter tip deflection down either limb of the bifurcated phantom.

Conclusions: The coil-tipped angiographic catheter design effectively demonstrated the feasibility of magnetic catheter deflection and concomitant visual tracking of such movement in the B_0 field of the 1.5 T MR imager when the coil is energized by an external voltage source

Image-guided Acoustic Droplet Vaporization (ADV) for Tissue Occlusion

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Purpose: Acoustic vaporization of liquid droplets with boiling points below body temperature shows promise as a spatially and temporally selective method for vascular occlusion and tissue ablation. The initial time of droplet circulation necessitates accurate and sensitive targeting.

Methods: Before the focused vaporization, therapy transducer is carefully aligned with the imaging array. The vaporizing focal point is marked on the ultrasound imager screen. *In vivo* color flow and pulse wave (PW) Doppler imaging are employed to identify the target arteries or tissues and avoid major adjacent veins. Test firings at low droplet concentration allow verification of the vaporization at the therapy transducer focus in the presence of aberrating tissues. Short tone bursts with 0.25% duty cycle are used to vaporize droplets with concentrations comparable to clinical ultrasound contrast agent use.

Results: Bubble production by ADV in arteries or tissues is easily visible in gray scale images. Our three canine studies with ADV in the renal artery generated substantial vascular occlusion as seen by high gray scale echogenicity and acoustic shadowing with multiple scattering. Concurrent with this was the detection of the blood flow reversal by PW Doppler, along with a narrowing of the waveform. A canine prostate was also occluded using the same commercial linear array for ADV and targeting.

Conclusions: Image guidance of ADV is particularly critical for targeting supply arteries when small vessels are the location of droplet vaporization for occlusion. Image guidance for vaporization in target tissues is also important for precise treatment.

Image-Guided Vascular Targeted Photodynamic Therapy Using Photosensitized (Ps) Bold MRI

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This study describes a photochemical mode of MR imaging in which pulsed light projected onto live rats (intravenously injected with a bacteriochloropyll derived photosensitizer, WST11) can be dynamically viewed by psMRI.

Upon circulating through an illuminated blood vessel network during vascular-targeted photodynamic therapy, the drug is instantly photosensitized, generating an intravascular burst of cytotoxic reactive oxygen species (ROS), coupled with local consumption of molecular blood oxygen. The resulting local rise in paramagnetic deoxyhemoglobin, increases the image contrast, as detected by Blood Oxygen Level Dependent (BOLD)-MRI. This oxygen-radical mediated photo-consumption of oxygen and the ensuing hemodynamic response differs from the metabolically based oxygen consumption underlying classical BOLD contrast generation.

Here we show that psMRI allows online detection of spatio-temporal information of incident light images displayed on tumors or normal striated muscle of the rat. Light image registration is computed by correlating BOLD-MRI-contrast responses to the light-sequence-triggering paradigm. The regions with enhanced BOLD contrast relative to the surroundings (range 7-61 fold) are deduced as illuminated and found to match the shape and exposure time of illumination. However, the resolution at which BOLD changes can be detected is limited by vascular density.

The described phenomenon may enable exciting experimental possibilities at lower photo-damage levels, such as the use of 3D vascular networks as screens for probing optical transparency of tissues, or correlating hemodynamic response maps to light induced hypoxic sinks. psMRI has the potential of serving as a tool for Image-Guided Therapy for photodynamic interventions. *This research was supported by Steba-Biotech, France.*

Model-Based Approaches to Enhancing Guidance for Surgical Therapy

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Purpose: The delivery of therapy has three general classifications – invasive (e.g. open-cranium neurosurgical guidance), minimally-invasive (e.g. laparoscopic procedures), and non-invasive (e.g. radiation therapy). Each of these can benefit from the real-time correlation with highly-resolved computational models that assist in their respective guidance. Within our laboratory, the focus has been concerned with developing techniques to augment therapy within the first two classifications and with the added constraint that the approaches are economically scalable to medical centers worldwide.

Methods: The general approach consists of two stages. The first stage augments existing guidance systems with low-cost digitization technology and computer models to compensate for organ presentation changes resulting from the intervention itself. The second stage uses localized imaging technology to fine-tune the delivery of therapy. With respect to this particular presentation, the approaches to the first stage are explored in two soft-tissue organ systems, i.e. brain and liver.

Results: Thus far, preliminary results within image-guided neurosurgery and image-guided liver surgery have been forthcoming. As an example, a neurosurgical guidance system has been augmented with laser range scanning technology which is used to track the cortical surface during surgery (semi-automatically at this time). Once measurements are made, they are used to constrain computer model predictions of soft tissue deformations, and updates to the guidance system are performed. The modeling platform is capable of simulating gravity-induced organ deformation, volumetric contraction due to hyperosmotic drugs, edema-induced swelling, retraction, and resection. In testing within animals and humans, the results suggest that 70-80% of deformation compensation is possible.

The results in image-guided liver surgery are still in development. Currently, a new salient feature registration method has been employed for initial registration and clinical data has been processed. In addition, information regarding the extent of intraoperative liver deformation due to surgical manipulation has been performed. An initial realization of model-based compensation has been implemented and tested within phantoms and limited clinical data. In this context, the results are encouraging that a similar strategy will be possible within the liver.

Conclusions: The need for cost-conscious approaches to improving surgical therapy is of critical importance. To achieve this, computer modeling approaches will be essential and multiple teams around the country are exploiting this valuable tool for changing the face of technology-guided therapy.

From Medical Image Computing to Computer Aided Intervention: Development of a Research Interface for Image Guided Navigation

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Purpose: This paper describes the development and application of techniques to integrate research image analysis methods and software with a commercial image guided surgery navigation system (BrainLAB VectorVision).

Methods: We describe a research interface implementing a custom client/server architecture termed VectorVision Link (VVLink) which extends functionality from the Visualization Toolkit . VVLink enables bi-directional transfer of data such as images, visualizations and tool positions in real time. The server is integrated into the VVCranial System and we designed a client integrated into the Yale BioImage Suite program.

Results: As part of the quantitative evaluation of the performance of the interface we demonstrate that tool positions were transferred through the interface to the client workstation at speeds comparable to those obtainable by direct connection of the tools to a workstation, demonstrating the efficiency of the protocol. In addition we demonstrate the use of VVLink in both phantom experiments and in actual neurosurgeries.

Conclusions: This type of interface enables the testing of newly developed image analysis methods within the surgical environment without the need for the research groups to actually design, build and test a custom image-guided navigation system. It also allows the implementation of research protocols for algorithm testing within the operating room environment without the need to have the surgeons use anything other than the same image-guided navigation system that they rely on for surgeries routinely. In this way, the research protocol can be performed in a “minimally invasive” manner with respect to its effect on the actual surgery.

Holographic Display for In-Situ Merger of Real-Time Tomographic Data with Direct Vision

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Purpose: The present work presents the first Real-Time Tomographic Holography (RTTH) optical system. The goal of RTTH is to holographically place a viewpoint-independent real-time (live) virtual image precisely into its actual anatomic location, enabling natural hand-eye coordination to guide invasive procedures, without requiring tracking or a head- mounted device. Derived from a similar mirror-based approach (previously used in our ultrasound guidance device, the Sonic Flashlight), RTTH has the added capability of generating large in- situ virtual images from a small display chip. As opposed to existing "head-up" holographic displays (e.g., for fighter pilots), ours places the image in the near field rather than at infinite distance.

Methods: We used a commercial program to simulate and optimize our design, which ultimately utilized a square (5x5in) optically fabricated holographic optical element (HOE) to project a 92x88mm planar virtual image at a distance of 1m from the HOE. Other components included an off-axis, 532nm-laser-illuminated 19x16mm LCD image source, and additional optics located near the LCD.

Results: Our system's virtual image appeared stable and well focused. Its highest measured viewpoint-induced error in location is < 3mm. An unexpected first-order astigmatism distortion produces a 3cm (3% of 1m) ambiguity in depth, typically unnoticed by human observers. The worst-case blur-induced minimum displayable feature size is <1mm.

Conclusions: We have successfully designed, built, and tested the first RTTH optical system. It displays a stable virtual image at 1m. A planned second-generation will produce images closer than 1m, suitable for deep ultrasound guided procedures such as liver biopsy and amniocentesis.

Preliminary Results for Instrument Tip Tracking During Interventional Oncology Procedures

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Purpose: Compared to optical tracking system, electromagnetic (EM) technology enables navigation of devices like needles where only the instrument tip is tracked. Radiofrequency ablation of liver tumors where tip position is crucial could benefit from this EM microsensor technology. The goal of this study is to provide an accurate system to target the tumor and reduce the iterative workflow that exists in regular oncology intervention.

Methods: In our studies, we used an EM tracker (GE Healthcare, Lawrence, MA) with an embedded microsensor, whose nominal outer diameter value is 0.75mm, into the tip of a needle. We simulated dynamic tracking by moving the tip of the instrument, against a glass plate in a circular motion. Different heights were used making sure the entire surgical volume was cover. To assess the instrument accuracy we applied the mathematical best-fit plane method.

Results: In a clean environment with non-magnetic materials, our results demonstrate that the dynamic accuracy of the microsensor over a range of 30x30x25cm was 1.4mm(p95) with 0.6mm mean.

Discussion: Our preliminary results confirm that in this specific configuration the range of the EM microsensor covers the clinical region of interest. The next step is to optimize the registration accuracy between the instrument tip and the CT-images taking into account the correction of the respiratory motion. More accuracy results in clinical environment will be shared during the conference.

Using Thermal Model Predictions to Improve MR Temperature Imaging Time Resolution

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Purpose: To improve the temporal resolution of MR temperature imaging scans by combining predictions from a pre-identified thermal model with undersampled MR data.

Methods: HIFU heating experiments were performed using a 256-element phased array transducer and an agar phantom. A site-specific thermal model of the tissue thermal response is identified prior to treatment by applying mild heating. HIFU heating of the phantom is then performed using higher power values, and fully sampled PRF temperature images are acquired. Undersampled k-space data is created by retrospectively zeroing out phase encode lines.

Temperature maps are created in a multi-step recursive process. The model forward predicts the temperature distribution from time (n) to time (n+1); a complex image is formed at time (n+1) by using the phase information from the temperature distribution at time (n+1) and the magnitude of the image at time (n); this complex image is projected into k-space and all phase encode lines acquired at time (n+1) are inserted; the data is projected back into image space, and then converted to an updated temperature map for time (n+1).

Results: Temperature maps were produced using one half, one fourth, and one sixth of the fully acquired k-space. The standard deviation of the error remained below ± 1.5°C for all reduction factors.

Conclusions: The reconstruction method presented here allows accurate temperature maps to be created using only a fraction of the normally acquired k-space data. Fewer acquired k-space lines can be parlayed into faster scan times, greater volume coverage or higher spatial resolution.

Minimization of HIFU Treatment Time using Model Predictive Feedback Control

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Purpose: Test that HIFU treatment times can be minimized, while protecting normal tissue, through the optimization of individual pulse heating and cooling times using model predictive control (MPC).

Methods: Simulations and experimental results were obtained using a 256 element phased array transducer.

Simulations: An extension of the traditional angular spectrum method was used to simulate the ultrasound beam propagation and power deposition in a homogeneous tissue region. Temperature responses were predicted using the 3D Pennes' BHTE. Treatment time was minimized by optimizing individual heating and cooling times for each pulse while keeping normal tissue temperatures below a constraint value.

Experiments: Agar phantom and *ex vivo* tissue samples were treated using a fully 3D model predictive controller. Temperatures were measured non-invasively with a 3T MRI scanner using the proton resonance frequency method. A nine position (3x3 grid) region (~1.5 cm^3) was treated. Individual pulse times were adjusted using MPC. Heating times were predicted using a full order Pennes' BHTE identified model, while cooling times were adjusted using an approximate exponential model.

Results: Up to a 65% decrease in treatment time was achieved when compared to times acquired by using fixed heating and cooling times for each pulse. Such time reductions are seen both in experiments and simulations.

Conclusions: The use of optimized, 3D model predictive feedback control provides significant reductions in treatment time and more uniform distributions of thermal dose while ensuring normal tissue safety. Optimized MPC promises to make HIFU treatments more clinically practical, particularly around critical normal tissues.

A Novel Algorithm for Automatic Detection of Multiple Internal Fiducial Markers on Onboard MV And kV Images

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Purpose: Develop a fully automatic algorithm to track spherical or cylindrical fiducial markers on onboard MV and kV images.

Methods: A new pattern matching method was developed to calculate the similarity between pre-calculated patterns and target features. Both correlation efficiency and signal intensity were obtained and used to detect markers. The whole projection of any spherical marker was matched since it depended on its diameter only. For cylindrical markers, a new filter was applied to determine the orientations of the marker projections, then the cross sections of cylindrical markers were matched because they were unique and independent on the projection lengths. Five gold cylindrical fiducials (Φ1.2 x 5 mm) were embedded in a head phantom, which was studied on a Trilogy. Images from pancreas and prostate patients were analyzed too.

Results: More than 2000 kV and MV phantom and patient images were acquired to test this algorithm and all fiducials were successfully detected. 3D positions of the markers were accurately obtained from kV and MV image pairs.

Conclusions: This algorithm has high efficiency of fully automatically detecting cylindrical fiducials on both MV and kV images, which enables tracking markers during treatment by utilizing the actual MV treatment beam and one onboard kV imaging system. This will reduce diagnostic doses comparing with using multiple kV imaging systems.

Combined kV and MV Imaging for Real-Time Tracking of Implanted Fiducial Markers

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Purpose: In the presence of intra-fraction organ motion, target localization uncertainty can greatly hamper the advantage of highly conformal dose techniques such as intensity modulated radiation therapy (IMRT). To minimize the adverse dosimetric effect caused by tumor motion, a real-time knowledge of the tumor position is required throughout the beam delivery process. The aim of this study is to demonstrate a near real-time 3D internal fiducial tracking system based on the combined use of kV and MV imaging.

Methods: A radiotherapy system equipped with both kV and MV imaging systems was used in this work. A hardware frame grabber was used to capture both kV and MV video streams simultaneously at 30 fps. The geometric tracking capabilities of the system were evaluated using a pelvic phantom with embedded fiducials placed on a moveable stage.

Results: The fiducial locations were extracted from the kV and MV images using a software tool. The maximum 3D tracking speed of the kV/MV system is approximately 9 Hz. The geometric accuracy of the system is found to be on the order of less than 1 mm in all three spatial dimensions.

Conclusions: A real-time 3D fiducial tracking system using combined kV and MV imaging has been successfully demonstrated for the first time. This technique is especially suitable for RT systems already equipped with on board kV and EPID imaging devices. Given its simplicity and achievable accuracy the approach should find widespread clinical application in real-time monitoring of the tumor position for 4D radiation therapy.