

# MI Lab 2010



**MI•Lab**

**sfi** = Centre for  
Research-based  
Innovation  
Established by the Research Council of Norway

 **NTNU**

Norwegian University of  
Science and Technology

MI Lab partners



**MI Lab leader**  
**Professor Olav Haraldseth**  
 Olav.Haraldseth@ntnu.no

In 2010 MI Lab underwent two international expert evaluations (see the column to the right). I

am especially proud about the conclusion in the midway evaluation expert panel report from the Research Council of Norway:

*"MI Lab started up rapidly and efficiently and now produces results of world class quality that are bound to result in important innovations in medical imaging."*

As MI Lab's leader, I am happy about two things:

- It is gratifying to see the competence and enthusiasm of the PhD and postdoc student group. They obtain experience in medical R&D at the crossroads between university, industry and hospital, and will be a future pool for recruitment of high-quality personnel for Norwegian industrial R&D, health care and academia.
- The Centres for Research-based Innovation represent a new scheme in which several industrial partners and the university work together in an open research environment. Our experience so far is that we in MI Lab are able to build an arena for open innovation and long-term industrial research with high scientific quality and commitment from the partners. In 2010 this resulted in publication of 31 refereed articles in international journals and many important inventions that are in different phases of the patenting and licensing process.

The main success story for MI Lab in 2009 was the new pocket-sized ultrasound scanner from GE Vingmed Ultrasound, Vscan. We continued to receive positive international attention for this pioneering technology in 2010. MI Lab has several ongoing research projects to evaluate how this handheld ultrasound scanner with greatly improved image quality and user-friendliness can enable new clinical applications of ultrasound in health care and how these applications result in more cost-efficient patient management.

*Olav Haraldseth*

**Two international expert panel evaluations of MI Lab in 2010**

In 2010 MI Lab underwent two evaluations from international expert panels: the MI Lab Scientific Advisory Board and the Research Council of Norway's midway evaluation of all the 14 Centres for Research-based Innovation.

**Citations from the Research Council of Norway (RCN) midway evaluation expert panel report:**

*"The current and proposed research activities of the MI Lab are excellent and cover very well the current medical needs of improvement in ultrasound imaging, MRI and image guided therapy"*

*"Novel opportunities are being picked up, such as nano-particle based imaging and drug delivery"*

*"The students constitute an interesting interdisciplinary mix of engineers, physicists, mathematicians and physicians that has the potential to lead to a very fruitful innovative environment."*

*"The Centre is hosted within a "showpiece" facility within St Olav's Hospital. NTNU is the host institution with excellent facilities concentrated to one floor at St Olav. The Centre is a key component of St Olav's strategy as a healthcare provider."*

*"The Centre aims to act as a melting pot that is both multidisciplinary and, importantly, bridges academia, the clinic and business. This approach is critical to product innovation in the medical technology area - co-location of the three in a single facility is distinctive .. this is to be applauded and should be recognised as a benchmark for others."*

**Citations from the MI Lab Scientific Advisory Board report:**

*"MI Lab is composed of world-class investigators working in a uniquely collaborative environment with clinicians and industry. It is to be congratulated on its culture for multidisciplinary research and training: it is a clear leader in its field."*

*"It is striking that the majority of the quite large budget of MI Lab is devoted to the funding of graduate education and training .. The students we met, and whose publications we have read, impressed us with their high academic and intellectual level, their commitment and their maturity. We see this as a very positive aspect of the project."*

*"NTNU's international reputation is founded on a strong record of success in the translation of ideas into both clinical care and commercial innovation. No amount of planning can create a culture of this quality: it has arisen out of the work of several generations of visionary researchers at NTNU, and represents the fundamental asset upon which MI Lab is designed to build. We regard this as representing excellence at an international level."*

## Vscan in 2010

### - World Expo in Shanghai and the first research results

The pocket-sized and handheld ultrasound scanner Vscan from GE Vingmed Ultrasound, which Time magazine ranked as No. 14 among the 50 most important inventions of 2009, was demonstrated at the *World Expo 2010* in Shanghai. Ole Christian Mjølstad, consultant in cardiology at St. Olavs University Hospital and PhD student at MI Lab, presented research projects, potential clinical applications and practical use to enthusiastic visitors.

The first results from scientific projects using the Vscan were presented by Dr Mjølstad at the 22nd International Conference of the Society for Medical Innovation in Trondheim. A novel automatic method that tracks the mitral annular motion and enables inexperienced users to evaluate left ventricular systolic function was tested on patients examined by general practitioners. The results indicate that non-expert users can assess heart contractility using pocket-sized ultrasound scanners.

The first head-to-head comparison between Vscan and high-end scanners performed by cardiologists was presented at the European Society of Cardiology Con

gress EUROECHO 2010 in Copenhagen. Håvard Dalen, consultant cardiologists at Levanger Hospital and postdoc fellow at MI Lab, found that semi-quantitative evaluation of cardiac anatomy and function with a pocket-sized ultrasound scanner showed substantial to almost perfect agreement with reference echocardiographic examination for most indices (Dalen, Haugen, Mjølstad, Graven. *European Journal of Echocardiography* 2010;11-Suppl. 2: ii182).



## Blood Flow Imaging improves the visualization of the lung veins in newborns

Blood Flow Imaging (BFI) is a new ultrasound modality developed to overcome technical limitations in the standard flow modality, Colour Doppler Imaging (CDI). BFI visualizes blood cell movement in any direction of the image, providing a detailed image of blood flow. The lung veins are often involved in diagnostic errors in paediatric echocardiography. In 2010, paediatric cardiologist and MI Lab PhD student Siri Ann Nyrnes published (Nyrnes, Lovstakken, Haugen et al. *Echocardiography* 2010;27:1113-19) a study where 26 neonates with suspected congenital heart disease were prospectively examined with full echocardiography and BFI of the pulmonary veins after parental consent. Four

observers consistently ranked Blood Flow Imaging as better than Colour Doppler Imaging for visualization of the pulmonary veins for all observers and questions (all p-values < 0.01). This study attracted much media attention in Norway.

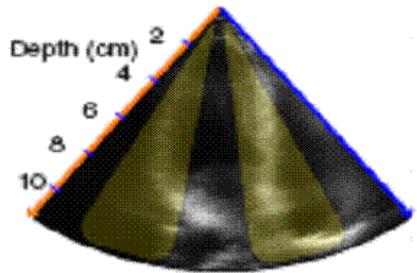
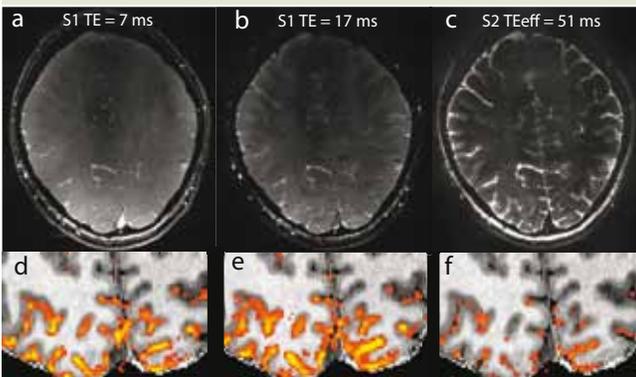


## High-resolution functional MRI of humans at 7 Tesla

As part of NORBRAIN, a national research infrastructure in neuroscience on the Research Council of Norway roadmap for large infrastructures, MI Lab wants to finance a clinical 7 Tesla MR system for human research in Trondheim. With this new technology, spatial resolution of 0.1 mm for anatomy and 0.5 mm for functional studies will be possible. In 2010, Pål Erik Goa, an MR physicist at St. Olavs Hospital, had a 6-month research stay at Erwin L. Hahn Institute in Essen, Germany to learn about clinical MR Imaging at 7 Tesla. Goa developed a multi-echo non-balanced steady-state free precession (nb-SSFP) sequence that was used for the first time in a high-resolution fMRI study at 7 Tesla. nb-SSFP has the unique property that both T2\*-weighted and T2-weighted signals can be acquired simultaneously, opening new possibilities for studying the individual contributions to the total functional contrast. NORBRAIN is a collaboration between MI Lab, the Centre of Molecular Biology and Neuroscience (CMBN) in Oslo and the Kavli Institute for Systems Neuroscience in Trondheim.

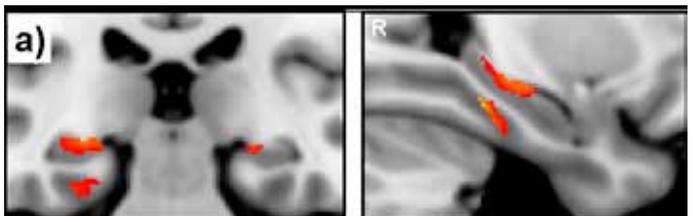
## MI Lab invention speeds up cardiac ultrasound to 1000 image updates per second

In 2010 the MI Lab postdoc fellows Svein Arne Aase and Tore Bjåstad, together with professor Hans Torp, developed an invention that greatly improves frame rate (temporal resolution) in cardiac ultrasound. At present the frame rate is between 50 and 150 updates of image information per second. The new invention enables a frame rate of close to 1000 images per second (and heart beat). The invention combines real-time automatic segmentation of the heart with beamforming directed only to the cardiac walls. No other non-invasive medical imaging method is close to achieving such a real-time temporal resolution, and this technology will provide new knowledge about cardiac function and cardiac wall motion both in the normal state and in heart disease. MI Lab will explore the potential for improved diagnosis and disease monitoring for patients with heart failure, focusing on diastolic dysfunction, myocardial deformation and fibrosis.



## Functional organization in the brain detected with virtual reality and fMRI

The Trondheim fMRI group in collaboration with MI Lab published in 2010 a study of the functional organization in the human brain of the ability to navigate (find your way) in a familiar environment (Xu, Evensmoen, Lehn, Pintzka, Håberg. Neuroimage. 2010;52:1654-66). Navigation is closely related to memory, and reduced ability to find your way in familiar environments is often a first symptom of dementia and Alzheimer's disease. A functional segregation along the posterior-anterior axis of the medial temporal brain lobe (MTL) has been suggested, and different phases of navigation should thus recruit different structures within the MTL. The Trondheim fMRI group has created a virtual reality environment that can be used during fMRI, and this study was the first to show that the different phases of navigation (self-localization, target localization, planning and finding your way) are localized in different parts of the MTL of the brain.

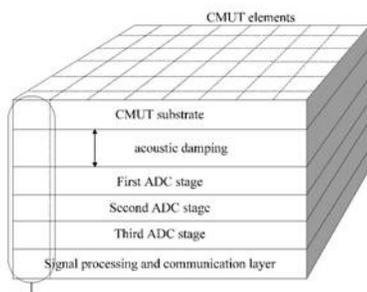


## AUROTECH Ultrasound AS new MI Lab partner

We are very happy to welcome AUROTECH Ultrasound AS, as new MI Lab partner. AUROTECH Ultrasound AS was founded in 1990, in the small municipality of Tydal, about 1,5 hour drive from Trondheim. The company still operates from Tydal, but has also established an office in Trondheim, and expects to grow rapidly during the next couple of years. AUROTECH develops digital signal processing ultrasound systems and offers high-end digital ultrasound platforms to OEMs (Original Equipment Manufacturers) or license partners. The platform offered; MANUS - Miniaturized Application Neutral Ultrasound System, has the same high-speed data collection and image processing capabilities as high-end scanners due to its special use of FPGA (Field-Programmable Gate Array) technology. The MANUS platform is unique, and combines flexibility, image quality and size with low manufacturing costs. We look upon the partnership as an important contribution to the total ultrasound technology competence in MI Lab.



## New invention - ultrasound transducer technology

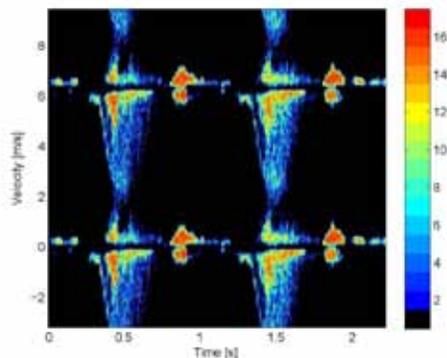
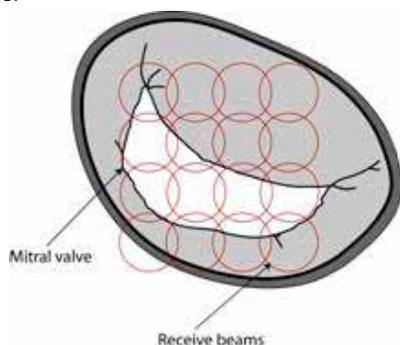


A research group in electronics at NTNU has in collaboration with MI Lab patented a manufacturing process for making transducers in CMUT (Capacitive Micromechanical Ultrasound transducer) technology. CMUT is nanoscale microelectronics technology, and with such miniaturization it is possible to improve image quality through greatly increased number of transducer elements. Furthermore, the patented manufacturing process opens the possibility of low cost production of complex transducer assemblies such as required in disposable probes for intravenous and surgical applications.

## New MI Lab invention

### - improved ultrasound based grading of heart valve leakage

Determining the severity of leaking valves in the heart is a tough job even for specialists. If you miss a severe leakage it might lead to heart failure and death. If you overestimate the leakage and decide to operate, you split open the chest and the heart of the patient – unnecessarily. Tonje D. Fredriksen and Torbjørn Hergum at MI Lab have together with professor Hans Torp invented an ultrasound-method that use parallel beamforming in combination with pulsed wave spectral Doppler to obtain both semi-quantitative and quantitative information about the severity of a leakage – in real time! This is done by recording a matrix of Doppler spectrums in parallel from the area around the leaking valve. If the leakage is large, many of the beams will intersect with it, while a small leakage might show up in just a few spectrums. This quantitative information is then used to colorize the Doppler spectrums.



## Publication list 2010 – (only full scientific papers in international journals with referee)

1. Nyrnes SA, Lovstakken L, Skogvoll E, Torp H, Haugen BO. Does a new ultrasound flow modality improve visualization of neonatal pulmonary veins? *Echocardiography*. 2010 Oct;27(9):1113-9. PMID: 21039814
2. Hergum T, Bjastad T, Lovstakken L, Kristoffersen K, Torp H. Reducing color flow artifacts caused by parallel beamforming. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2010;57(4):830-8. PMID: 20378446
3. Swillens A, Degroote J, Vierendeels J, Lovstakken L, Segers P. A simulation environment for validating ultrasonic blood flow and vessel wall imaging based on fluid-structure interaction simulations: ultrasonic assessment of arterial distension and wall shear rate. *Med Phys*. 2010 Aug;37(8):4318-30. PMID: 20879592
4. Swillens A, Segers P, Lovstakken L. Two-dimensional flow imaging in the carotid bifurcation using a combined speckle tracking and phase-shift estimator: a study based on ultrasound simulations and in vivo analysis. *Ultrasound Med Biol*. 2010 Oct;36(10):1722-35. PMID: 20800949
5. Swillens A, Segers P, Torp H, Lovstakken L. Two-dimensional blood velocity estimation with ultrasound: speckle tracking versus crossed-beam vector Doppler based on flow simulations in a carotid bifurcation model. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2010;57(2):327-39. PMID: 20178899
6. Skaug TR, Hergum T, Amundsen BH, Skjaerpe T, Torp H, Haugen BO. Quantification of mitral regurgitation using high pulse repetition frequency three-dimensional color Doppler. *J Am Soc Echocardiogr*. 2010;23(1):1-8. PMID: 19914037
7. Yu A, Lovstakken L. Eigen-based clutter filter design for ultrasound color flow imaging: a review. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2010;57(5):1096-111. PMID: 20442020
8. Dalen H, Thorstensen A, Vatten LJ, Aase SA, Støylen A. Reference Values and Distribution of Conventional Echocardiographic Doppler Measures and Longitudinal Tissue Doppler Velocities in a Population Free from Cardiovascular Disease. *Circ Cardiovasc Imaging*. 2010 Sep 1;3(5):614-22. PMID: 20581050
9. Aase SA, Bjørk-Ingul C, Thorstensen A, Torp H, Støylen A. Aortic Valve Closure: Relation to Tissue Velocities by Doppler and Speckle Tracking in Patients with Infarction and at High Heart Rates. *Echocardiography*. 2010;27(4):363-9. PMID: 20331696
10. Thorstensen A, Dalen H, Amundsen BH, Aase SA, Støylen A. Reproducibility in echocardiographic assessment of the left ventricular global and regional function, the HUNT study. *Eur J Echocardiogr*. 2010;11(2):149-56. PMID: 19959533
11. Dalen H, Thorstensen A, Aase SA, Ingul CB, Torp H, Vatten LJ, Støylen A. Segmental and global longitudinal strain and strain rate based on echocardiography of 1266 healthy individuals: the HUNT study in Norway. *Eur J Echocardiogr*. 2010;11(2):176-83. PMID: 19946115
12. Ingul CB, Malm S, Refsdal E, Hegbom K, Amundsen BH, Støylen A. Recovery of function after acute myocardial infarction evaluated by tissue Doppler strain and strain rate. *J Am Soc Echocardiogr*. 2010;23(4):432-8. PMID: 20202790
13. Hovland A, Staub UH, Bjørnstad H, Prytz J, Sexton J, Støylen A, Vik-Mo H. Gated SPECT offers improved interobserver agreement compared with echocardiography. *Clin Nucl Med*. 2010 Dec;35(12):927-30. PMID: 21206222
14. Nestaas E, Støylen A, Brunvand L, Fugelseth D. Longitudinal strain and strain rate by tissue Doppler are more sensitive indices than fractional shortening for assessing the reduced myocardial function in asphyxiated neonates. *Cardiol Young*. 2011 Feb;21(1):1-7. Epub 2010 Oct 6. PMID: 20923594
15. Ericsson M, Andersson KB, Amundsen BH, Torp SH, Sjaastad I, Christensen G, Sejersted OM, Ellingsen O. High-intensity exercise training in mice with cardiomyocyte-specific disruption of *Serca2*. *J Appl Physiol*. 2010;108(5):1311-20. PMID: 20167673
16. Aamot IL, Moholdt T, Amundsen BH, Solberg HS, Mørkved S, Støylen A. Onset of exercise training 14 days after uncomplicated myocardial infarction: a randomized controlled trial. *Eur J Cardiovasc Prev Rehabil*. 2010;17(4):387-92. PMID: 19940774
17. Solheim O, Selbekk T, Jakola AS, Unsgård G. Ultrasound-guided operations in unselected high-grade gliomas—overall results, impact of image quality and patient selection. *Acta Neurochir (Wien)*. 2010 Nov;152(11):1873-86. PMID: 20652608
18. Jakola AS, Sørlie A, Gulati S, Nygaard OP, Lydersen S, Solberg T. Clinical outcomes and safety assessment in elderly patients undergoing decompressive laminectomy for lumbar spinal stenosis: a prospective study. *BMC Surg*. 2010 Nov 22;10:34. PMID: 21092227
19. Berntsen EM, Gulati S, Solheim O, Kvistad KA, Torp SH, Selbekk T, Unsgård G, Håberg AK. Functional magnetic resonance imaging and diffusion tensor tractography incorporated into an intraoperative 3-dimensional ultrasound-based neuro-navigation system: impact on therapeutic strategies, extent of resection, and clinical outcome. *Neurosurgery*. 2010;67(2):251-64. PMID: 20644410
20. Solheim O, Selbekk T, Lovstakken L, Tangen GA, Solberg OV, Johansen TF, Cappelen J, Unsgård G. Intrasellar ultrasound in transsphenoidal surgery: a novel technique. *Neurosurgery*. 2010;66(1):173-85. PMID: 20023548
21. Selbekk T, Brekken R, Solheim O, Lydersen S, Hernes TA, Unsgård G. Tissue motion and strain in the human brain assessed by intraoperative ultrasound in glioma patients. *Ultrasound Med Biol*. 2010;36(1):2-10. PMID: 19854562
22. Nordgaard H, Swillens A, Nordhaug D, Kirkeby-Garstad I, Van Loo D, Vitale N, Segers P, Haaverstad R, Lovstakken L. Impact of competitive flow on wall shear stress in coronary surgery: computational fluid dynamics of a LIMA-LAD model. *Cardiovasc Res*. 2010 Dec 1;88(3):512-9. PMID: 20581004
23. Nordgaard HB, Vitale N, Astudillo R, Renzulli A, Romundstad P, Haaverstad R. Pulsatility index variations using two different transit-time flowmeters in coronary artery bypass surgery. *Eur J Cardiothorac Surg*. 2010;37(5):1063-7. PMID: 20031439
24. Xu J, Evensmoen HR, Lehn H, Pintzka CW, Håberg AK. Persistent posterior and transient anterior medial temporal lobe activity during navigation. *Neuroimage*. 2010;52(4):1654-66. PMID: 20677377
25. Palmer HS, Garzon B, Xu J, Berntsen EM, Skandsen T, Håberg AK. Reduced fractional anisotropy does not change the shape of the hemodynamic response in survivors of severe traumatic brain injury. *J Neurotrauma*. 2010;27(5):853-62. PMID: 20199173
26. Heldahl MG, Bathen TF, Rydland J, Kvistad KA, Lundgren S, Gribbestad IS, Goa PE. Prognostic value of pretreatment dynamic contrast-enhanced MR imaging in breast cancer patients receiving neoadjuvant chemotherapy: overall survival predicted from combined time course and volume analysis. *Acta Radiol*. 2010;51(6):604-12. PMID: 20429756
27. Jensen LR, Huuse EM, Bathen TF, Goa PE, Bofin AM, Pedersen TB, Lundgren S, Gribbestad IS. Assessment of early docetaxel response in an experimental model of human breast cancer using DCE-MRI, ex vivo HR MAS, and in vivo 1H MRS. *NMR Biomed*. 2010;23(1):56-65. PMID: 19650073
28. Askim T, Indredavik B, Håberg A. Internally and externally paced finger movements differ in reorganization after acute ischemic stroke. *Arch Phys Med Rehabil*. 2010 Oct;91(10):1529-36. PMID: 20875510
29. Hak S, Reitan NK, Haraldseth O, de Lange Davies C. Intravital microscopy in window chambers: a unique tool to study tumor angiogenesis and delivery of nanoparticles. *Angiogenesis*. 2010;13(2):113-30. PMID: 20623252
30. Reitan NK, Thuen M, Goa PE, de Lange Davies C. Characterization of tumor microvascular structure and permeability: comparison between magnetic resonance imaging and intravital confocal imaging. *J Biomed Opt*. 2010;15(3):036004. PMID: 20615006
31. Olsen Ø, Kristoffersen A, Thuen M, Sandvig A, Brekken C, Haraldseth O, Goa PE. Manganese transport in the rat optic nerve evaluated with spatial- and time-resolved magnetic resonance imaging. *J Magn Reson Imaging*. 2010 Sep;32(3):551-60. Epub 2010 Jun 10. PMID: 20815052

## PhD dissertations 2010

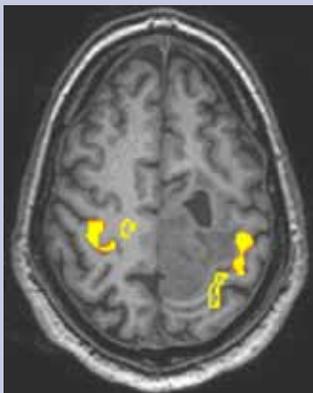
### Medical doctors

1. Håvard Bersås Nordgaard. Transt-time flowmetry and wall shear stress analysis of coronary artery bypass grafts – A clinical and experimental study.
2. Jian Xu. Blood oxygen level dependent functional magnetic resonance imaging and diffusion tensor imaging in traumatic brain injury research.
3. Håvard Dalen. Echocardiographic indices of cardiac function – Normal values and association with risk factors in a population free from cardiovascular disease, hypertension and diabetes.
4. Toril Skandsen. Moderate and severe traumatic brain injury. Magnetic resonance imaging findings, cognition and risk factors for disability.
5. Roar Johansen. MR techniques in evaluation of breast cancer patients with poor prognosis.
6. Khalid Shaker Ibrahim. Intraoperative ultrasound assessment in coronary artery bypass surgery – with special reference to coronary anastomoses and the ascending aorta.

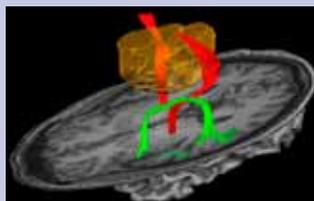
### Technologists

7. Fredrik Orderud. Real-time segmentation of 3D echocardiograms using a state estimation approach with deformable models.
8. Thomas Moe Halvorsrød. On Low Power, Analog Modules for Medical Ultrasound Imaging Systems.
9. Øystein Olsen. Analysis of manganese enhanced MRI of the normal and injured rat central nervous system.
10. Line Rørstad Jensen. Evaluation of treatment effects in cancer by MR imaging and spectroscopy.

## Benefit of advanced MR methods in minimally invasive neurosurgery



In 2010 Erik Magnus Berntsen (MD, PhD) together with collaborators from MI Lab, NTNU, St. Olavs Hospital and SINTEF published a study in the journal *Neurosurgery* on preoperative functional and diffusion tensor MRI combined with intraoperative 3D ultrasound used for minimally invasive neurosurgery (Berntsen et al., *Neurosurgery*, 2010;67:251-64). The results indicated that the tumor resections were performed as a successful compromise between maximal tumour removal and avoiding damage to crucial brain areas.



## Annual Accounts 2010

The total costs in 2010 of 32,2 million NOK (app. 4,1 million Euro) were split between cash contributions of 18,3 MNOK and own effort contributions from the partners (including the host NTNU) of 13,9 MNOK.

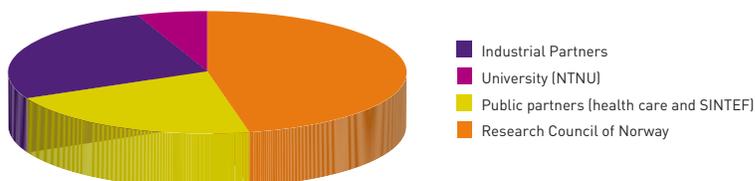


Table: Financial contributions to MI Lab 2010

# MI Lab 2010

MI Lab is one of the 14 Centres for Research-based Innovation (in Norwegian: Senter for Forskningsdrevet Innovasjon – SFI) appointed by the Norwegian Research Council in 2007.

MI Lab is hosted by NTNU, and the partners are the university hospital St. Olavs Hospital, the Central Norway Regional Health Authority, the research organisation SINTEF, and the industrial partners GE Vingmed Ultrasound, Medi-Stim, Sonowand, Nordic NeuroLab, CorTechs Labs, Arctic Silicon Devices, FAST and Aurotech Ultrasound.

MI Lab has a total budget of app. 30 MEuro for the 8 years period 2007–2014, and the contribution from the Research Council of Norway is 10 MEuro.



## MI LAB VISION AND RESEARCH PLAN

The vision is to facilitate cost efficient health care and improved patient outcome through innovation in medical imaging, and to exploit the innovations to create industrial enterprise in Norway.

Innovation in medical imaging can contribute to improved cost efficacy on several levels, and MI Lab has chosen to focus on three important areas:

- high quality medical imaging products and applications for non-expert users at the initial point of care
- less complications and more rapid rehabilitation with image-guided minimally invasive surgery
- more rapid and more precise choice of efficient treatment through decision-making based on advanced medical imaging

As Trondheim has a long history of basic ultrasound technology research, this is a fourth main area.

Inside this framework, MI Lab has the following project structure:

### Research Task 1: Ultrasound technology

- Ultrasound image improvement

### Research Task 1: Advanced imaging applications for non-expert user

- Cardiac Ultrasound
- Pocket-sized Ultrasound

### Research Task 3: Image guided minimally invasive surgery

- Neurosurgery
- Cardiac & Vascular surgery

### Research Task 4: Imaging based information to support medical decision making

- Advanced MR methods in clinical diagnosis
- Foetal Ultrasound
- MR in regenerative medicine & nanoparticles for imaging

## MI LAB STRATEGY

The strategy is to establish a creative melting pot for medical imaging research through:

- Bringing together on a daily basis researchers from university, hospital and industry
- Establish a large multi-disciplinary research environment including medicine, ICT, physics, mathematics, cybernetics, electronics, physiology, molecular biology, neuroscience, psychology etc.

### MI Lab



### Patients

Improved quality of life

### Healthcare

Cost-effective solutions

### Industry

New products & applications

### Society

Reduced increases in health and nursing expenses