

MI Lab

NTNU, Faculty of Medicine

MI Lab 2009



MI Lab partners



MI Lab leader Professor Olav Haraldseth

In 2009 MI Lab we succeeded in recruiting many high quality students, and we are now running at full budget capacity

with 26 PhD students/ post docs and 6 international guest professors. In this second full year of operation the academic record is starting to be satisfactory with a publication list for 2009 of 33 full scientific papers in international journals with referee.

As MI Lab leader I am happy about three things:

- It is nice to see the competence and enthusiasm of the group of PhD and post doc students. They obtain experience in medical technology R&D in the crossroad 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.
- Centres for Research-based Innovation is a new construction where 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 good commitment from the partners.
- MI Lab wants to be an integrated part of the total Ultrasound and MR research environment in Trondheim, and the experience so far is that the interaction is excellent between the MI Lab hired PhD and post doc students and the rest of the medical imaging community in Trondheim. I like to call this the "MI Lab family".

The main success story for MI Lab in 2009 was the new pocket-sized ultrasound scanner from GE Vingmed Ultrasound, Vscan. The research group of professor Hans Torp, both inside and outside of MI Lab, has contributed to the product, and further R&D on clinical application and further technology refinements will be a new focus area for MI Lab. The first study using Vscan in general practice is now performed in three GP offices in the Trondheim area.

Olav Haraldseth

MI Lab activities

The annual **MI Lab Day** was in **June** 2009 and the aim of this event is to bring together all the partners and all the researchers to a day of science and mingling. The main speakers were the two MI Lab guest professors Anders M. Dale from University of San Diego, USA and Arend Heerschap from the University of Nijmegen, the Netherlands.

In **March** 2009 MI Lab arranged an **all-day work-shop** on future ultrasound probe technology. The programme covered transducers, power requirements, beamforming and acoustic/electronic stack design, interconnect, and assembly. Main speakers were Jean-Francois Gelly and Kjell Kristoffersen from GE; Hans Torp, Trond Ytterdal and Bjørn Angelsen from NTNU; and Maaikje Visser Taklo from Sintef MiNaLab.

In **November** 2009 MI Lab arranged an **all-day seminar** on cardiac imaging and left ventricular mechanics. For this meeting a large group of researchers and PhD students from Katholieke Universiteit in Leuven, Belgium was invited and two of the main speakers were the Leuven professors Frank Rademakers and Jan D'hooge. The latter is also MI Lab guest professor.

The Norwegian Research School in Medical Imaging was an initiative from MI Lab leader Olav Haraldseth that ended up with the successful appointment from The Norwegian Research Council in September 2008 as one of five such national research programmes, and the only one in the area of medicine and health. It is a nationwide multidisciplinary network promoting high quality PhD and post graduate student training and is a tool for recruitment of the best master students and more women to a PhD and further research career. The programme includes not only MR and ultrasound, but also positron emission tomography (PET), image-guided surgery, biomedical optics and bio-nanotechnology. For more information see: www.ntnu.no/medicalimaging

Nansen Neuroscience Network (NNN) is a new national innovation cluster in neuroscience and neuromedicine initiated in 2009 by MI Lab together with the Centre of Molecular Biology and Neuroscience (CMBN) in Oslo and Innovation Norway. The aim is to copy the success of Oslo Cancer Cluster, and the official founding of NNN will take place on May 11 in 2010.

MI Lab and Centre of Molecular Biology and Neuroscience (CMBN) together with the Kavli Institute for Systems Neuroscience in Trondheim have in 2009 initiated the establishment of a national research infrastructure in neuroscience called **NORBRAIN**. The aim is to obtain a vertical integration from cellular biology (main focus of CMBN) through systems neuroscience research in animal models (main focus of the Kavli Institute) to research on patients and human volunteers with advanced MR technology (MI Lab). As part of NORBRAIN MI Lab has applied The Research Council of Norway for financing of a clinical 7 Tesla MR system for human research. With this new technology the spatial resolution of 0,1 mm for anatomy and 0,5 mm for functional studies will be possible.



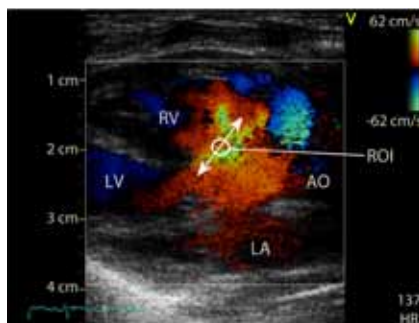
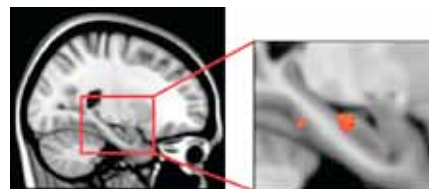
From HUNT Biobank at Levanger.

Ultrasound and MR imaging as research tools in population studies and preventive medicine

MI Lab is collaborating with HUNT (the North-Trøndelag Health Survey). As part of the third HUNT survey in 2007-2009 a total of 1300 advanced cardiac ultrasound and 1000 advanced MR imaging of brain were collected among a HUNT subpopulation self-reported to be healthy. These data are unique and can be used in many different ways. It is an unselected population based group of "normals" that can be used to analyze the normal variation in a population. Pathological changes in the images may be used as end-points for risk factors found in the previous HUNT 1 and HUNT 2 surveys. The pathological changes may furthermore be correlated to genomics and other high throughput analyses of the collected blood samples from the same persons. And lastly, different types of image based biological information may have a potential as predictors for later disease occurrence. Over time disease occurrence in the group of 2300 investigated persons may be collected from regional quality health registers and local hospital data. This opens a unique possibility for validation of imaging biomarkers in an unselected population.

Functional MR Imaging of episodic memories

PhD student Hanne Lehn together with the professors Asta Håberg and Menno Witter published in 2009 in Journal of Neuroscience the paper "A specific role of the human hippocampus in recall of temporal sequences." (J Neurosci. 2009;29:3475-84). The hippocampus and other parts of the medial temporal lobe are central to memory formation and recall. However, to obtain strong and reliable brain activation with functional MR studies has been a challenge. The study was based on the hypothesis that recall of the naturalistic sequence of past events would be particularly sensitive to hippocampal function, attributable to greater involvement of associative processes. To test this prediction, we let subjects watch a novel movie and later, during functional magnetic resonance imaging, asked them to rearrange and "replay" scenes from the movie in correct order. Hanne Lehn's scientific work is a collaboration between the fMRI group at the MR centre, MI Lab and the Centre for the Biology of Memory (Centre of Excellence at NTNU), and is part of a joint effort on development and scientific validation of new MR methods to be used in research on reduced memory function in dementia patients. The figures show the part of the hippocampus that was activated with this test of episodic memory. There was a positive correlation between the strength of the activation and number of correct answers.



Improved ultrasound of heart defects in newborns using high frame rate flow visualisation

There is a trade off between frame rate and image quality in Colour Doppler Imaging, for instance in newborns due to their high heart rates. In a MI Lab project this has been solved by using plane wave imaging (PWI). Plane unfocused beams can be emitted to avoid image artefacts while increasing the frame rate when receiving multiple image lines in parallel for every transmitted pulse. Using this technique, flow was visualized using both conventional Colour Doppler

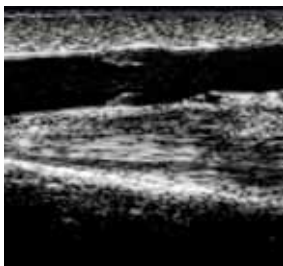
Imaging (CDI) and Blood Flow Imaging (BFI). BFI is a new visualisation technique extending CDI with an angle independent display of blood movement. Five newborns with complex congenital heart disease were examined. A fivefold increase in frame rate was achieved compared to conventional imaging in the same patients. This implied flow images with frame rates up to 100 frames per second. The improved data acquisition rate can be utilized to image rapid flow events, but also to improve the overall image quality.

Publication list 2009 – (only full scientific papers in international journals with referee)

1. Bjåstad T, Torp H. Single-pulse tissue doppler using synthetic transmit beams. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2009 Oct;56(10):2134-44
2. Skaug TR et al. Quantification of Mitral Regurgitation Using High Pulse Repetition Frequency Three-Dimensional Color Doppler. *J Am Soc Echocardiogr*. 2009 Nov 13. [Epub ahead of print]
3. Bjåstad T et al. Synthetic transmit beam technique in an aberrating environment. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2009 Jul;56(7):1340-51.
4. Hergum T et al. Fast ultrasound imaging simulation in K-space. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2009 Jun;56(6):1159-67.
5. Hergum T et al. Quantification of valvular regurgitation area and geometry using HPRF 3-D Doppler. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2009 May;56(5):975-82.
6. Swillens A et al. Assessment of numerical simulation strategies for ultrasonic color blood flow imaging, based on a computer and experimental model of the carotid artery. *Ann Biomed Eng*. 2009 Nov;37(11):2188-99.
7. Swillens A et al. Ultrasound simulation of complex flow velocity fields based on computational fluid dynamics. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2009 Mar;56(3):546-56.
8. Frijlink ME et al. Investigation of transmit and receive performance at the fundamental and third harmonic resonance frequency of a medical ultrasound transducer. *Ultrasonics*. 2009 Dec;49(8):601-4
9. Crosby J et al. The effect of including myocardial anisotropy in simulated ultrasound images of the heart. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2009 Feb;56(2):326-33.
10. Crosby J et al. 3-D speckle tracking for assessment of regional left ventricular function. *Ultrasound Med Biol*. 2009 Mar;35(3):458-71
11. Amundsen BH et al. Regional myocardial long-axis strain and strain rate measured by different tissue Doppler and speckle tracking echocardiography methods: a comparison with tagged magnetic resonance imaging. *Eur J Echocardiogr*. 2009 Mar;10(2):229-37
12. Thorstensen A et al. Reproducibility in echocardiographic assessment of the left ventricular global and regional function, the HUNT study. *Eur J Echocardiogr*. 2009 Dec 3. [Epub ahead of print]
13. Moholdt TT et al. Aerobic interval training versus continuous moderate exercise after coronary artery bypass surgery: a randomized study of cardiovascular effects and quality of life. *Am Heart J*. 2009 Dec;158(6):1031-7.
14. Aamot IL et al. Onset of exercise training 14 days after uncomplicated myocardial infarction: a randomized controlled trial. *Eur J Cardiovasc Prev Rehabil*. 2009 Nov 24. [Epub ahead of print]
15. Sandvei MS et al. Left ventricular myocardial function during the acute phase of a subarachnoid haemorrhage. *Scand Cardiovasc J*. 2009 Apr;43(2):110-6.
16. Rustad LA et al. Upright bicycle exercise echocardiography in patients with myocardial infarction shows lack of diastolic, but not systolic, reserve: a tissue Doppler study. *Eur J Echocardiogr*. 2009 Jun;10(4):503-8
17. Dalen H et al. Segmental and global longitudinal strain and strain rate based on echocardiography of 1266 healthy individuals: the HUNT study in Norway. *Eur J Echocardiogr*. 2009 Nov 28. [Epub ahead of print]
18. Stanton T et al. Interaction of left ventricular geometry and myocardial ischemia in the response of myocardial deformation to stress. *Am J Cardiol*. 2009 Oct 1;104(7):897-903.
19. Stanton T et al. Association of myocardial deformation with mortality independent of myocardial ischemia and left ventricular hypertrophy. *JACC Cardiovasc Imaging*. 2009 Jul;2(7):793-801.
20. Gulati S et al. Surgical resection of high-grade gliomas in eloquent regions guided by blood oxygenation level dependent functional magnetic resonance imaging, diffusion tensor tractography, and intraoperative navigated 3D ultrasound. *Minim Invasive Neurosurg*. 2009 Feb;52(1):17-24
21. Berntsen EM et al. Integrated pre- and intraoperative imaging in a patient with an arteriovenous malformation located in eloquent cortex. *Minim Invasive Neurosurg*. 2009 Apr;52(2):83-5
22. Solheim O et al. Intraseptal ultrasound in transsphenoidal surgery: a novel technique. *Neurosurgery*. 2010 Jan;66(1):173-85; discussion 185-6.
23. Lindseth F et al. Blood flow imaging: an angle-independent ultrasound modality for intraoperative assessment of flow dynamics in neurovascular surgery. *Neurosurgery*. 2009 Dec;65(6 Suppl):149-57
24. Nordgaard HB et al. Pulsatility index variations using two different transit-time flowmeters in coronary artery bypass surgery. *Eur J Cardiothorac Surg*. 2009 Dec 21. [Epub ahead of print]
25. Nordgaard H et al. Transit-time blood flow measurements in sequential saphenous coronary artery bypass grafts. *Ann Thorac Surg*. 2009 May;87(5):1409-15.
26. Nordgaard H et al. Different graft flow patterns due to competitive flow or stenosis in the coronary anastomosis assessed by transit-time flowmetry in a porcine model. *Eur J Cardiothorac Surg*. 2009 Jul;36(1):137-42
27. Lehn H et al. A specific role of the human hippocampus in recall of temporal sequences. *J Neurosci*. 2009 Mar 18;29(11):3475-84.
28. Askim T et al. Motor network changes associated with successful motor skill relearning after acute ischemic stroke: a longitudinal functional magnetic resonance imaging study. *Neurorehabil Neural Repair*. 2009 Mar-Apr;23(3):295-304
29. Martinussen M et al. Segmental brain volumes and cognitive and perceptual correlates in 15-year-old adolescents with low birth weight. *J Pediatr*. 2009 Dec;155(6):848-853
30. Skranes J et al. White matter abnormalities and executive function in children with very low birth weight. *Neuroreport*. 2009 Feb 18;20(3):263-6.
31. Wijnen JP et al. Short echo time 1H MRSI of the human brain at 3T with adiabatic slice-selective refocusing pulses; reproducibility and variance in a dual center setting. *J Magn Reson Imaging*. 2010 Jan;31(1):61-70.
32. Thuen M et al. Combination of Mn(2+)-enhanced and diffusion tensor MR imaging gives complementary information about injury and regeneration in the adult rat optic nerve. *J Magn Reson Imaging*. 2009 Jan;29(1):39-51.
33. Widerøe M et al. Manganese-enhanced magnetic resonance imaging of hypoxic-ischemic brain injury in the neonatal rat. *Neuroimage*. 2009 Apr 15;45(3):880-90.

MI Lab partner Medi-Stim released new product for improved quality control of heart and vascular surgery

In desember 2009, Medi-Stim released the new ultrasound based platform for intraoperative quality control, the VeriQC. The project has been going on since 2006 and the R&D has been performed in close cooperation with the MI Lab partner Sonowand AS and with Aurotech Ultrasound AS located in Tydal, and also with important contributions from the MI Lab research. Almost 20 systems are already out in the field enabling the surgeons to get highly detailed ultrasound images of the internal structure of the blood vessels. This, together with traditional transit-time blood flow measurements, provides documentation of the surgical outcome. MI Lab will perform research to further develop this technology to get even better images and probes for the intraoperative applications in heart and vascular surgery.



PROFESSOR HANS OLAV MYHRE RECEIVES PRIZE FOR HIS VASCULAR SURGERY RESEARCH



Photo: Frode Nikolaisen, St. Olavs Hospital

Professor Hans Olav Myhre has been a key person for the establishment of MI Lab. He received in February 2009 the Heart prize from the Norwegian Council on Cardiovascular Diseases [Nasjonalforeningens Hjerterpris]. It is the first time a vascular surgeon receives this prize.

Cited from the jury decision: "Myhre has contributed significantly to the understanding of failing blood supply to the legs and how this can be treated with surgical operation, image-guided interventions, and structured training programmes. Myhre has also translated his knowledge into practical clinical solutions. At St. Olavs Hospital in Trondheim he was a main person behind the "Operating Room of the Future", which opened in 2005 in collaboration with NTNU and Sintef."

Annual Accounts 2009

For MI Lab 2009 was the second full year of operation. The total costs in 2009 of 30,3 million NOK (app. 3,6 million Euro) were split equally between in-kind contributions from the partners (including the host NTNU) and cash contributions (15,3 and 15,0 MNOK respectively).



- Industrial Partners
- University (NTNU)
- Public partners (health care and SINTEF)
- Research Council of Norway

Table: Financial contributions to MI Lab, NTNU, Faculty of Medicine 2009

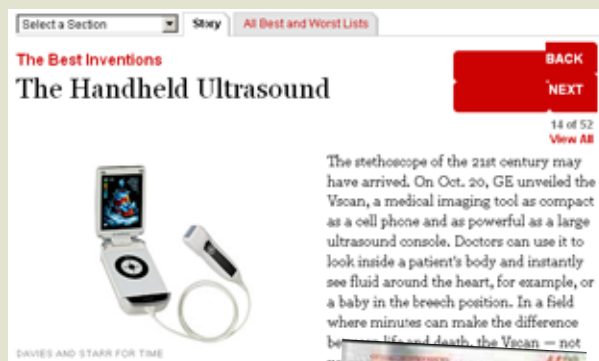
Vscan – made in Trondheim and Horten – the 2009 highlight for MI Lab

The main success story for MI Lab in 2009 is the new pocket-sized ultrasound scanner from GE Vingmed Ultrasound, Vscan. The research group of Hans Torp, both inside and outside of MI Lab, has contributed to the product, and further R&D on clinical application and technology improvements will be a new focus area for MI Lab. The first study using Vscan in general practice is now performed in three GP offices in the Trondheim area.

Vscan received much international and national attention. The CEO of the entire GE company, Jeff Immelt, chose to do the international release himself at the Web 2.0 Summit San Francisco in October. Vscan was ranked by Time Magazine as the 14th most important invention world-wide in 2009, and by Teknisk Ukeblad in Norway as the number one engineering achievement in Norway in 2009.

Vscan is a good exponent for one of the main research goals of MI Lab as it combines advanced imaging functions and high user-friendliness. The image quality is superb compared to other hand held ultrasound scanner. MI Lab plans to start a wide variety of projects with Vscan, ranging from detection of deep vein thrombosis in Norwegian nursing homes, diagnosis of rheumatic fever heart disease in rural Nepal, and to rapid assessment of cardiac function in emergency situations in ambulances and hospitals. MI Lab is also discussing with GE Vingmed Ultrasound and Faculty of Medicine at NTNU to furnish all medical students in one class with Vscan from day one in medical school as a test project for universal ultrasound training. The vision is that the future doctor will have the high-tech Vscan in one pocket and the good old stethoscope in the other pocket.

Facsimile time.com

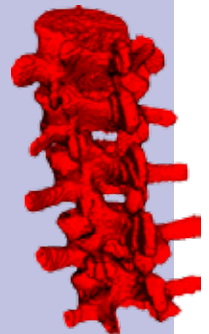


GE Chairman and CEO Jeff Immelt unveils GE Healthcare's new Vscan, at the Web 2.0 Summit in San Francisco on Tuesday, Oct. 20, 2009.

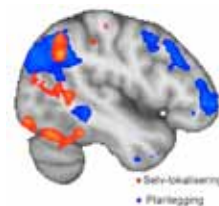


A new method for image guidance in spinal surgery

Spinal surgery is currently performed with no or little image guidance during the procedure, and positioning and level detection is performed using palpation and x-ray imaging. MI Lab post doc Ingerid Reinertsen has developed a new method based on image registration of pre-operative MR/CT images and intra-operative ultrasound to make it possible for the surgeon to use ultrasound imaging for level detection before surgery, and use pre-operative MR/CT data for navigation during the operation. This can be a valuable tool in order to identify lesions such as tumors and herniated discs and reduce the use of x-ray imaging during surgery.



NEW KNOWLEDGE ABOUT BRAIN FUNCTION USING VIRTUAL REALITY INSIDE THE MR SCANNER

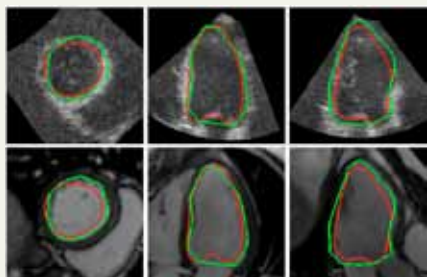


Professor Asta Håberg and the PhD students Hallvard Røe Evensmoen and Jian Xu have established a virtual reality program for functional fMRI studies of

navigation (finding your way) in a learned environment while the patient / test person is inside the MR scanner. Hallvard Røe Evensmoen had in October an oral presentation at the Society of Neuroscience annual meeting in Chicago. The study had focused on what parts of the brain that are activated during the different phases of navigation; especially the difference between first localizing where you are in the virtual reality environment ("self-localization"), and then planning what route to take to reach the goal. The former has strong activation in primary sensory areas while the latter also has activation in memory areas and pre-frontal areas related to planning. However, the most interesting finding was that the self-localisation and planning phases also activated different parts of the hippocampus.

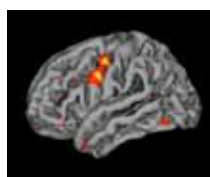


WHY IS THE MEASURED CARDIAC FUNCTION DIFFERENT WHEN BASED ON 3D ULTRASOUND COMPARED TO MR IMAGING?



Previous studies have reported significantly lower cardiac chamber volumes with ultrasound compared to MR imaging. With new 3D soft-ware developed by MI Lab, it is possible to directly compare the wall delineations in ultrasound and MR, and MI Lab post docs Gabriel Kiss (technologist) and Brage H. Amundsen (medical doctor) performed a scientific study to understand the sources of the difference. The study showed that differences between ultrasound and MR was mainly in the delineation of the inner wall (endocardium) in the lateral and anterior walls, which have a coarser inner surface (trabeculae) than other parts of the heart. These results are of great importance for development of better 3D ultrasound technology for quantification of cardiac function.

Reduced fine motor function is related to thinner motor cortex in adolescents born preterm

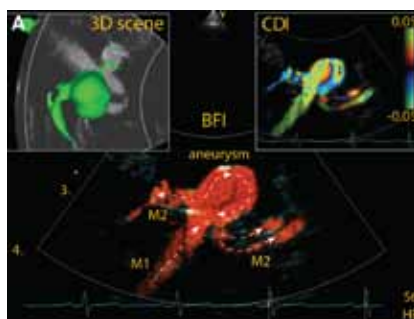


PhD student Kari Anne I. Evensen and the paediatrics professors Ann-Mari

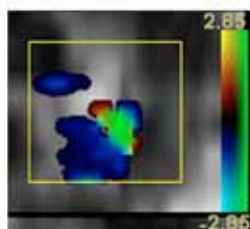
Brubakk and Jon Skranes have in collaboration with MI Lab performed a study of the correlation between brain function and brain changes in teenagers with previous preterm birth (birth weight <1500 g). A main finding was thinner motor cortex in the hand area of the precentral gyrus in preterm born teenagers who had poor fine motor function. The thickness correlated inversely with the severity of the problems. This proves that MR based measurements of cortical thickness is an important research tool both for understanding the cause of functional problems, and to monitor the effect of training and rehabilitation.

The potential of Blood Flow Imaging (BFI) in a Neurosurgical setting

BFI is an angle-independent 2-D ultrasound modality which is more intuitive compared to existing methods based on the Doppler-principle. When integrated with 3-D navigation technology, BFI provides a real-time and high-resolution visualization of both vessel geometry and flow direction in the brain vessels during the surgical operation. A recently published study (Neurosurgery 2009;65:149-57) showed that vascular flow direction was properly visualized in 3 cerebral aneurysms and 3 arteriovenous malformations. The use of navigation technology further allowed for identification of the vessels of interest. The surgeon found BFI to be more intuitive compared with conventional colour Doppler methods (CDI), which made it easier to quality control flow in distal arteries during aneurysm surgery, and to discern between feeding arteries and draining veins for arteriovenous malformations.



NEW ULTRASOUND METHOD FOR IMPROVED HEART VALVE DIAGNOSIS



MULDO is a new ultrasound method invented in Trondheim for improved diagnosis of valve disease in the heart. MULDO is based on high pulse repetition frequency 3D colour Doppler, and a main feature is the ability to quantify the volume of the leakage in cases of mitral regurgitation, and this is important for better diagnosis and treatment. PhD student and cardiologist Thomas Skaug has in a collaboration with post docs Torbjørn Hergum (technology) and Bjørn Olav Haugen (cardiology) used the method in a recently published study of twenty-seven patients to validate the accuracy of the measurements compared to MR Imaging (J Am Soc Echocardiogr 2010;23:1-8). For

moderate and severe regurgitation the agreement with MRI was good while mild regurgitation was overestimated with MULDO. These results will be used for R&D on further refinements of the method.

MI Lab 2009

ABOUT MI LAB

MI Lab is one of the 14 Centres for Research-based Innovation (in Norwegian: Senter for Forskningsdrevet Innovasjon – SFI) appointed by the Research Council of Norway 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, FAST, Medi-Stim, Sonowand, Nordic Neurolab, CorTechs Labs and Arctic Silicon Devices.

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 in the health care system 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 though 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 & flow quantification
- Ultrasound probe hardware

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

- Cardiac Ultrasound
- Pocket-sized Ultrasound

Research Task 3: Image guided minimally invasive surgery

- Neurosurgery
- Heart and Vascular surgery

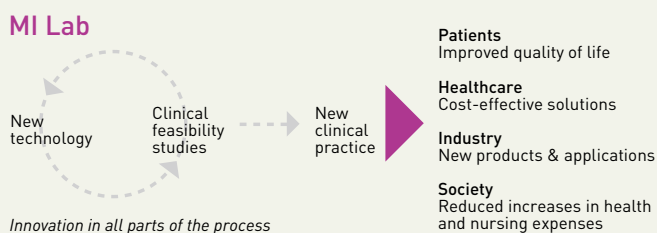
Research Task 4: Imaging based information to support medical decision making

- Advanced MR methods in clinical diagnosis
- Foetal Ultrasound
- MR in regenerative medicine & MR 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, Faculty of Medicine, NTNU

Medical Technology Research Centre, NO-7489 Trondheim.

E-mail: olav.haraldseth@ntnu.no