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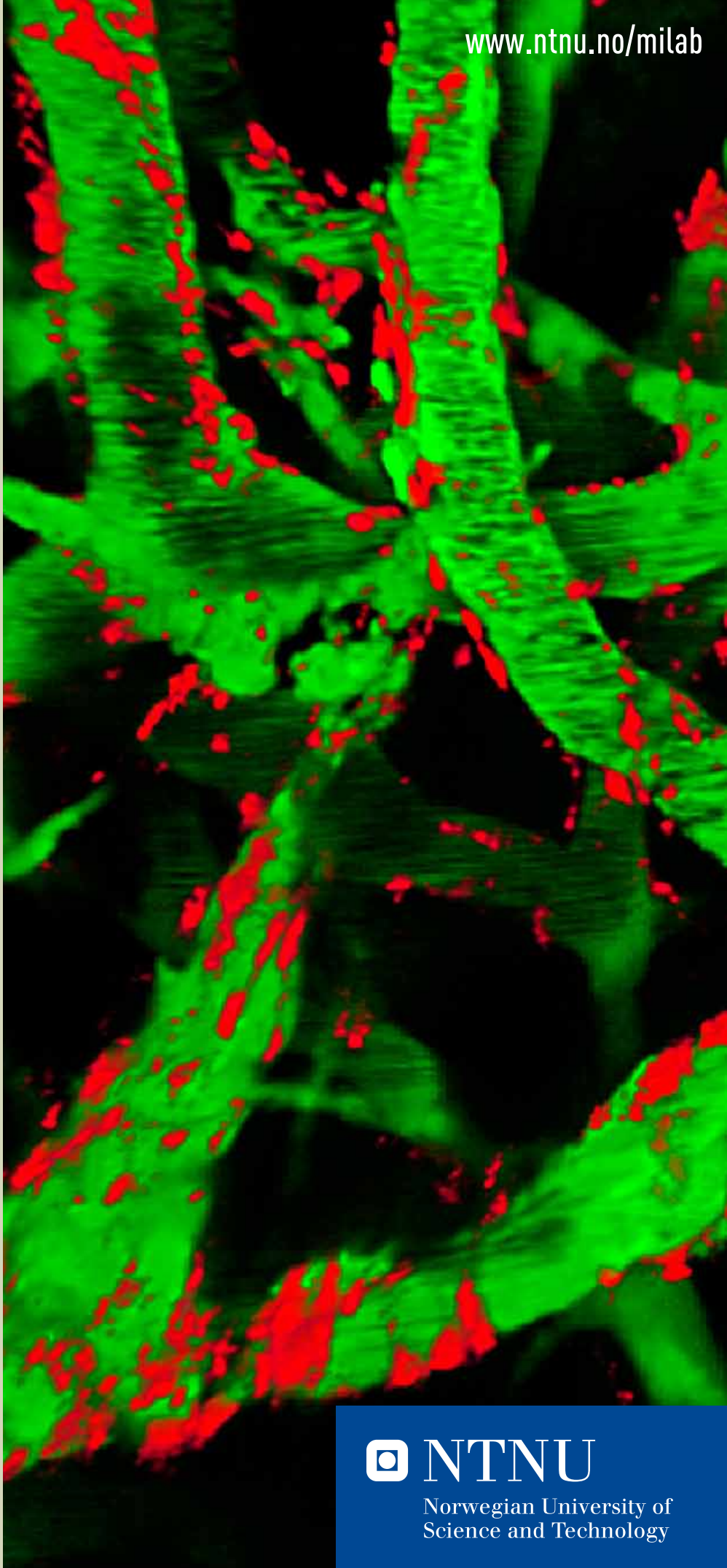
MI Lab 2011



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

For MI Lab 2011 was a good year.

We now have a broad research activity with a multi-disciplinary group of 31 on-going PhD students and post doctoral fellows, and we continuously get new ideas that have potential for the MI Lab vision of inventions that may facilitate cost efficient health care and improved patient outcome.

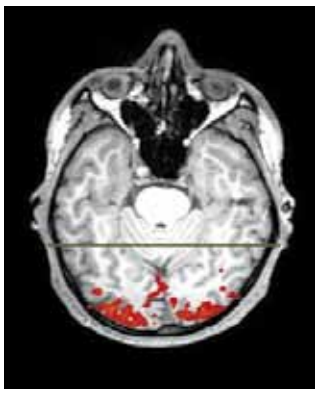
The MI Lab partner MediStim ASA obtained an official recommendation in the United Kingdom of the health benefits of the ultrasound system VeriQ: "The case for adopting the VeriQ system in the National Health System for assessing graft flow during coronary artery bypass graft surgery is supported by the evidence. The evidence suggests that intra operative transit time flow measurement .. may reduce perioperative morbidity and mortality. The VeriQ system is associated with an estimated cost saving of £115 per patient." A main success story for MI Lab has been the new pocket-sized ultrasound scanner from GE Vingmed Ultrasound, Vscan, and in 2011 the first full scientific papers with scientific evidence of the clinical benefits of Vscan were published. These two landmarks confirm the MI Lab vision that innovations in medical imaging can facilitate cost efficient health care and improved patient outcome at the same time.

As MI Lab leader I am happy about two things:

- It is nice to see the competence and enthusiasm of the group of PhD and post doc students. They obtain experience in medical 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.
- 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. In 2011 this resulted in a publication list of 34 scientific papers printed in international journals with referee, and MI Lab also have several important inventions in different phases of the patenting and product development process. In 2012 we expect the first of these inventions to be part of the industrial partners' products.

Technical improvements in MRI of brain function – accelerated using compressed sensing

PhD students Jørgen Avdal and Jarle Ladstein in collaboration with MR physicist Pål Erik Goa have successfully developed and implemented a method for speeding up the acquisition of functional MRI using compressed sensing. While traditional whole brain fMRI acquisitions have a frame rate of 2-3 seconds, utilizing this technique allows for subsecond imaging of the entire brain. In vivo evaluation of the method has indicated a significant increase in statistical power for the fMRI analysis of brain activity and localization. The increased frame rate is an important step towards better detection and removal of physiological noise in fMRI and also improves the ability to accurately determine the hemodynamic response function.



Scientific evidence for clinical benefit of the pocket-sized ultrasound Vscan

Three scientific papers published and/or in press in 2011 demonstrate the clinical benefit of using Vscan on new patients at admittance to the hospital. The studies were performed at the community-based Levanger Hospital 80 km from Trondheim. One study (Skjetne et al. European Journal of Echocardiography 2011;12:737-43) included 119 patients admitted to the cardiovascular unit, and it was found that in 55% of the patients Vscan was useful for the patient management, and in 16% of the patients Vscan enabled correction of the diagnosis. Another study (Mjølstad et al. European Journal of Internal Medicine, in press) included patients admitted to the internal medicine unit and used Vscan for both cardiac and abdominal ultrasound. Their main conclusion was: "By adding a pocket-sized ultrasound examination of < 10 min, we made important diagnostic changes in 1 of 5 patients, resulting in a completely different treatment strategy without time delay".

Pope Benedict XVI receives Vscan as a gift to a health care project in Congo (image to the left), and the hospital doctors Håvard Dalen and Torbjørn Graven at Levanger Hospital (image to the right)

MI Lab also performs research on further technical improvements of Vscan, and three scientific papers (Aase et al. European Journal of Echocardiography 2011;1:3-10, Snare SR et al. Ultrasound Med. Biol. 2011;4:617-31 and Snare SR et al. Comp. Meth. Progr. Biomed. 2011) describe the following improvements of user-friendliness for non-expert users: cardiac ultrasound without ECG, automatic measurement of mitral annulus excursion, and automatic measurement of heart septum thickness. The two latter are important for diagnosis and assessment of severity of heart failure and hypertension.

Technical improvements in MRI of brain function – reduction of phsyological noise

Functional MRI is a powerful tool for new knowledge about how the brain works, both to understand normal brain function and to study the pathological changes in a wide range of brain diseases. However, the method is still limited by relatively poor spatial resolution, image distortions and artefacts, and suboptimal sensitivity. The method requires very rapid image acquisition of typically 50-100 ms per brain slice, and this is mainly obtained by so-called echo planar imaging (EPI). A promising improvement is to move from 2D to 3D EPI acquisitions, and the St. Olav's Hospital MR physicists Anders Kristoffersen and Pål Erik Goa had recently a publication in Journal of Magnetic Resonance Imaging: "Cardiac-induced physiological noise in 3D gradient echo brain imaging: effect of k-space sampling scheme", where they show a new technological solution for strong reduction of image distortions caused by physiological noise, and in this case especially the small brain movements that follow the heart beat.

$$\Re[p_S(z,t_0)/e^{2\pi i K z}] = \frac{1}{2}[h(z+\zeta)+h(z-\zeta)]\cos[2\pi(t_0/T_{\text{phys}}-K\zeta)]$$
$$\approx h(z)\cos[2\pi(t_0/T_{\text{phys}}-K\zeta)],$$
$$\Im[p_S(z,t_0)/e^{2\pi i K z}] = -\frac{1}{2}[h(z+\zeta)-h(z-\zeta)]\sin[2\pi(t_0/T_{\text{phys}}-K\zeta)]$$
$$\approx -\zeta h'(z)\sin[2\pi(t_0/T_{\text{phys}}-K\zeta)],$$

Description of the MR signal and the noise

Publication list 2011

1. Hoilund-Kaupang H et al. Transmit beamforming for optimal second-harmonic generation. IEEE Trans Ultrason Ferroelectr Freq Control. 2011 Aug;58(8):1559-69. PMID:21859575
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4. Näsholm SP et al. Post-processing enhancement of reverberation-noise suppression in dual-frequency SURF imaging. IEEE Trans Ultrason Ferroelectr Freq Control. 2011 Feb;58(2):338-48.
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8. Thorstensen A et al. Peak systolic velocity indices are more sensitive than end-systolic indices in detecting contraction changes assessed by echocardiography in young healthy humans. Eur J Echocardiogr. 2011 Dec;12(12):924-30.
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PhD dissertations 2011

Medical doctors

1. **Ole Solheim.** Ultrasound guided surgery in patients with intracranial tumours.

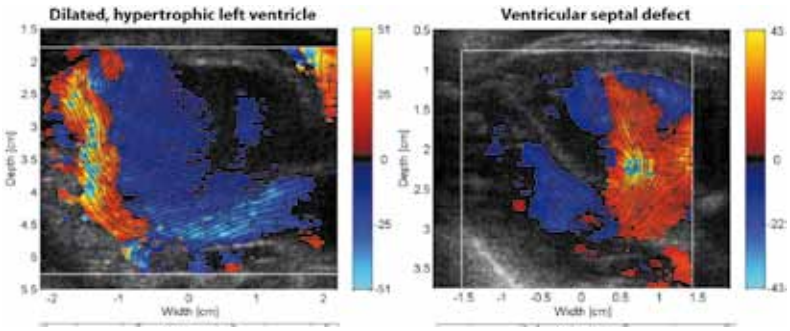
Technologists & others

2. **Halvard Høilund-Kaupang.** Models and methods for investigation of reverberations in nonlinear ultrasound imaging.
3. **Benjamin Garzon Jimenez de Cisneros.** Clinical applications of multimodal magnetic resonance imaging.
4. **Ioanna Sandvig.** The role of olfactory ensheathing cells, MRI and biomaterials in transplant-mediated CNS repair.
5. **Sten Roar Snare.** Quantitative cardiac analysis algorithms for pocket-sized ultrasound devices.
6. **Marianne Gjervik Heldahl.** Evaluation of neoadjuvant chemotherapy in locally advanced breast cancer based on MR methodology.
7. **Guro Fanneløb Giskeødegård.** Identification and charcterization of prognostic factors in breast cancer using MR metabolomics.

Better visualisation of cardiac flow in newborns with heart defects

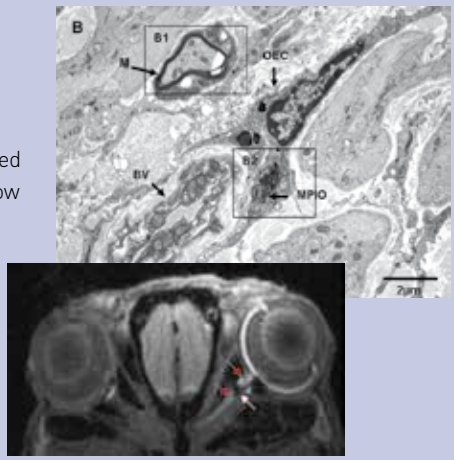
There is an emerging interest in studying the relation between intra-cardiac flow patterns and cardiac function and remodeling. At MI Lab an approach suitable for diagnosis and follow-up in newborns and children has been developed, able to quantify complex flow patterns due to pathology with a higher accuracy than traditional Doppler approaches.

The method is based on an ultrahigh frame rate imaging setup, for which the tracking of blood flow patterns over time becomes feasible. The method is currently evaluated in clinical feasibility studies. Preliminary results presented at the 2011 EuroEcho conference was selected and highlighted as a high-rank abstract.



First MI Lab PhD in MR guidance of regenerative medicine

October 2011 Ioanna Sandvig defended her PhD thesis "The role of olfactory ensheathing cells, MRI and biomaterials in transplant-mediated CNS repair". One of the main achievements in her work was to show how combinations of different MR methods could simultaneously monitor over time the in-vivo localisation of labelled cell grafts and the nerve fibre regeneration (and remyelination) in an animal model of nerve damage. Another paper was research on a new contrast agent for controlled release of manganese using alginate nanoparticle technology developed in collaboration with the Department of Biotechnology at NTNU. Manganese-enhanced MRI is an important complementary MR method for guidance of regenerative therapy in the brain as it can detect the function of active transport in the regenerating nerve fibers. However, because of a relatively small window between diagnostic and nerve toxic dose of manganese, new types of controlled release contrast agents must be developed. These results are promising for the potential of in-vivo guidance of regenerative therapy after spinal chord trauma and brain diseases with white matter pathology.



Bottom an MRI of rat head with transplanted cells in optic nerve (white arrow) and regenerating nerve fibers (red arrows). Top confirmation with electron microscopy: regenerating nerve fiber (B1) and transplanted cell (B2).

Annual Accounts 2011

The total costs in 2011 of 33,8 million NOK (app. 4,4 million Euro) were split between cash contributions of 19,4 MNOK and own effort contributions from the partners (including the host NTNU) of 14,4 MNOK.

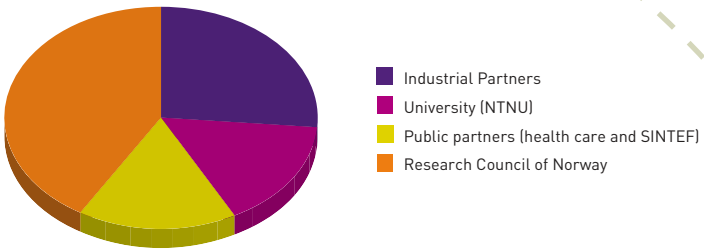
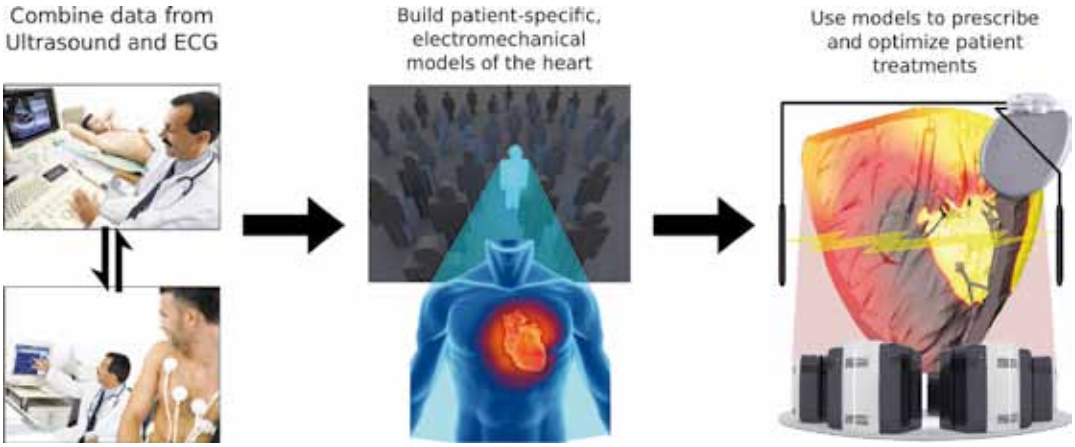


Table: Financial contributions to MI Lab 2011



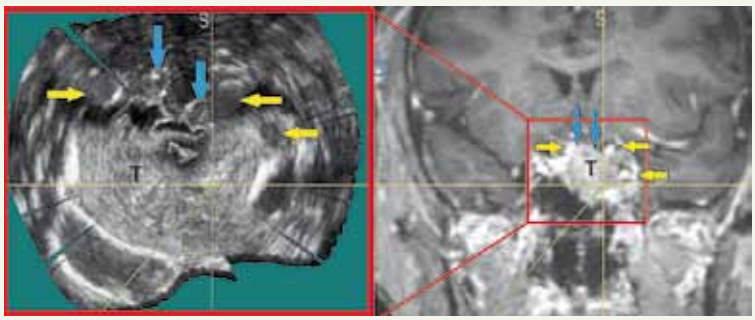
The goal of Centre for Cardiological Innovation is to combine electrical, mechanical, and anatomical information in a new integrated 3- dimensional cardiac scanner system that will provide diagnostic information for better treatment of patients at risk of sudden cardiac death or suffering from heart failure.

MI Lab partner GE Vingmed Ultrasound had success with new Centre for Research-based Innovation application

The Research Council of Norway appointed in 2011 seven new Centres for Research-based Innovation (CRIs). Only one of these where in the area of health and medicine, the Centre for Cardiological Innovation, hosted by Oslo University Hospital and with GE Vingmed Ultrasound as one of the main industrial partners. About the new CRI in medical ultrasound MI Lab leader Olav Haraldseth says: "First of all it is yet another proof of the high international quality of the R&D activities in GE Vingmed Ultrasound. It is also important for further growth and success for the ultrasound industrial cluster in Norway and the ultrasound research activities in Norwegian universities and university hospitals. This is an area where Norway is establishing a leading international role."

3D Ultrasound for pituitary surgery

The pituatiry gland is at the base of the brain and difficult to reach for the surgeon. The preferred surgical approach for pituitary tumours resection is the transsphenoidal route starting from the nose cavity. Residual tumours are unfortunately common (35-60% in unselected series) along with postoperative aquired hormone deficiencies (≈20%), and this surgical outcome may be improved with proper image guidance of the operations. Standard imaging technology useful for other intracranial tumors is not necessarily helpful for this purpose, and as a collaboration between several partners at NTNU, SINTEF and St. Olavs Hospital a prototype 10-13 MHz linear array, "side-looking" ultrasound probe dedicated for intraoperative ultrasound in transsphenoidal surgery was developed (Solheim et al, Neurosurgery 2010;1:173-85). It was shown that 2D ultrasound is feasible for this purpose, however, images from odd image planes can make interpretation challenging. We are therefore developing a method for recording 3D ultrasound images based on electromagnetic tracking of the probe. The 3D ultrasound image information can be co-registered to pre-operative MR images, and it allows the surgeon to look at any plane in the 3D volume. This will enable navigated resection (perhaps with navigated surgical curettes) and will ease image interpretation for the surgeon.



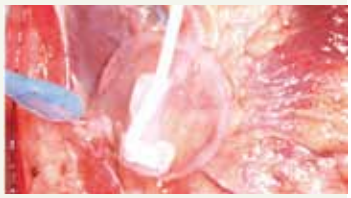
A reconstructed intraoperative ultrasound view of the tumor (T) to the left and the corresponding, navigated pre-operative brain MR image to the right.

The arrows point to structures that must not be damaged (blue arrow: optic nerves, yellow arrows: carotid arteries).

Official recommendation in the United Kingdom of health benefits of the ultrasound system VeriQ from MI Lab partner MediStim ASA

The British National Institute for Health and Clinical Excellence (NICE) was set up in 1999 to reduce variation in the availability and quality of National Health Service (NHS) treatments and care. In November 2011 they published an official recommendation of the VeriQ system: "The case for adopting the VeriQ system in the NHS for assessing graft flow during coronary artery bypass graft (CABG) surgery is supported by the evidence. The evidence suggests that intra operative transit time flow measurement is effective in detecting imperfections that may be corrected by graft revision. This may reduce the incidence of graft occlusion and may reduce perioperative morbidity and mortality. The VeriQ system is associated with an estimated cost saving of £115 per patient."

MediStim CEO Kari E. Krogstad comments: "It is our hope that the NICE recommendations will enable UK surgeons to adopt the objective and reliable measurements offered by the VeriQ system. We also believe this endorsement has the potential to impact practice in many other countries". This case confirms the MI Lab vision that innovations in medical imaging can facilitate cost efficient health care and improved patient outcome at the same time.



VeriQ in the operation theatre (top), and the VeriQ dedicated Doppler probe placed on the arterial anastomosis on the heart surface (bottom).

Chronic pain patients have to recruit more brain resources to perform everyday cognitive tasks

Humans have evolved to pay attention to pain to survive and avoid harm. Sometimes the source of pain is not dangerous, but the effects of pain on cognition can become harmful themselves. Many patients with chronic pain experience cognitive problems, but the neuronal correlates behind this are poorly understood. The results from a collaboration between MI Lab and the NTNU fMRI group indicate that it is the chronic sleep deprivation experienced by pain patients, and not the pain itself, that have the largest impact on how the brain works differently in those suffering from chronic pain compared to healthy controls. It seems that the sleep deprived brain of someone in chronic pain has fewer resources available, and so has to work harder to keep up with cognitive tasks. In the football analogy, the chronic pain team has to work harder because they play with fewer players than the opposition. Although more research is needed, our findings might help improve the quality of life for those suffering from the effects of chronic pain.

Prize for outstanding contribution to medical ultrasound

The Norwegian Academy of Technological Sciences (NTVA) Prize of Honour 2011 was awarded to Kjell Kristoffersen, Bjørn Angelsen and Kjell Arne Ingebrigtsen for their outstanding contribution to the development and commercialization of ultrasound for medical imaging. Bjørn Angelsen pioneered ultrasound Doppler imaging of the heart in the 1970s, and Kjell Arne Ingebrigtsen and Kjell Kristoffersen were key persons in the founding in 1985 of Vingmed Sound, the company that today is the MI Lab partner GE Vingmed Ultrasound AS. Kjell Kristoffersen is today one of the seniors in ultrasound technology in GE globally as Chief Engineer, and is responsible for international co-ordination of all GE R&D activities in ultrasound technology. He is also professor at the Department of Circulation and Medical Imaging at NTNU and scientific supervisor for several MI Lab PhD students. Kjell Arne Ingebrigtsen is now professor emeritus, but is still involved in ultrasound innovation and commercialisation, one on-going project is the NTNU patented manufacturing process for making nanosize ultrasound transducer elements, CMUT. Kjell Arne Ingebrigtsen was also leader of the MI Lab board until June 2011.

From left: Kjell Kristoffersen, Bjørn Angelsen, Kjell Arne Ingebrigtsen

MI Lab 2011

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, MediStim, Sonowand, Nordic Neurolab, CorTechs Labs, Arctic Silicon Devices 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 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

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

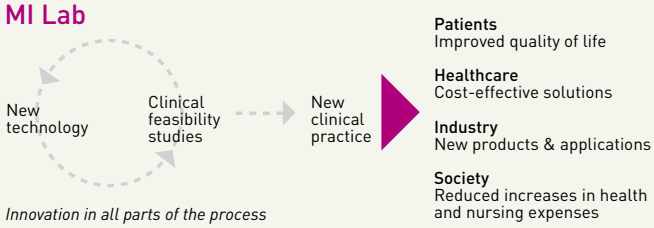
Research Task 4: Imaging based information to support medical decision making

- 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.



Innovation in all parts of the process

MI Lab, Faculty of Medicine, NTNU
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*On the cover: **Nanoparticles in the battle against cancer***
This image shows tumor bloodvessels in green and nanoparticles accumulated in the blood vessel walls in red. The goal is to make nanoparticles which specifically accumulate in tumors. If those nanoparticles contain diagnostic or therapeutic agents this approach is expected to improve diagnosis and therapy of cancer. Images like this are used to analyze how and where the nanoparticles accumulate in the tumor vasculature. The picture is a 3D composition of a stack of images taken with confocal microscopy.
Picture by: Sjoerd Hak, MI Lab

Photo: MI Lab and Geir Mogen.
Miljømerket trykkeri, lisensnr. 241 811
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