News

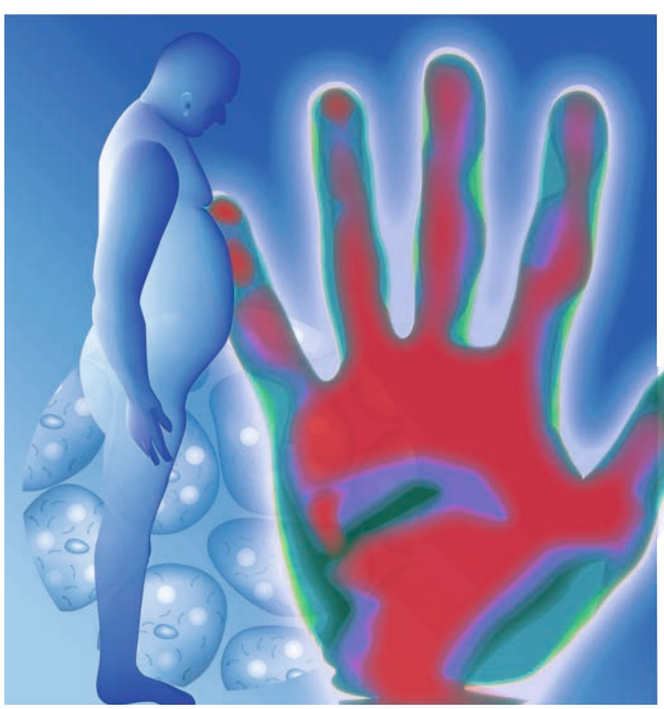
Research Highlights

# Thermal imaging of body fat shows potential in tackling obesity in the future

*Researchers at the University of Nottingham (UK) have developed a thermal imaging technique that they hope will give us greater insight into how energy is stored and used.*

Researchers at the University of Nottingham (Nottingham, UK) have embarked on ground-breaking research that has the potential to aid us in the fight against obesity. Obesity is one of the biggest health issues of the 21st century with 26% of adults and 29% of 2–15 year olds in England medically classified as such in 2010.

The study by Symonds *et al.* enrolled healthy volunteers who were divided into various age groups: 3–8 years old, 13–18 years old and 35–58 years old. A standard cool challenge was performed whereby subjects placed their hands or feet in water set at 20C. The effect on their superclavicular region, which contains brown adipose tissue (beneficial bodily fat) was measured using thermal imaging.



Thermal imaging can be used to identify reserves of brown adipose tissue because the tissue produces 300-times more heat than any other in the body. As a technique, it benefits greatly from its noninvasive nature and ability to perform repeat thermal imaging experiments on many different subjects.

Brown adipose tissue has a crucial role in the rate at which our bodies use calories as energy, therefore, reducing the amount that is stored in our bodies as white fat.

By locating reserves of brown adipose tissue it is hoped that we can gain a better understanding of the balance between the energy gained from food intake and the energy used by our bodies in conserving functions. Understanding this energy balance would then aid us in monitoring the amount of energy stored within the body as white fat.

"Potentially, the more brown fat you have or the more active your brown fat is, you produce more heat and as a result you might be less likely to lay down excess energy or food as white fat," explained Symonds, leader of the team at the University of Nottingham and Professor of Developmental Physiology in the School of Clinical Sciences.

Published in the *Journal of Pediatrics*, all of the age ranges demonstrated a highly localized increase in temperature where heat was produced as required. However, there was a significant age-related pattern where younger children were better able than subjects in the adolescent and adult age groups to do this.

Describing the significance of these results, Helen Budge, Clinical Associate Professor and Reader in Neonatology at the University of Nottingham explained "Babies have a larger amount of brown fat, which they use up to keep warm soon after birth making our study's finding that this healthy fat can also generate

heat in childhood and adolescence very exciting."

The study featured many researchers from the University of Nottingham's Early Life Nutrition Unit whose research currently focuses on controlling brown adipose tissue by methods such as nutrition, exercise and therapeutics. It is hoped that by finding ways to increase the amount of energy used as heat the amount of white fat stored will be reduced, and therefore limit weight gain that can lead to obesity.

In the future, this thermal imaging technique could be used alone or in combination with other techniques, to provide us a better understanding of how to effectively monitor and control energy that is gained from stored food intake. It could also shed light on the impact that different food types have on the activity and amount of brown adipose tissue and, therefore, calories burnt.

In conclusion, Symonds added, "This completely noninvasive technique could play a crucial role in our fight against obesity. Potentially we could add a thermogenic index to food labels to show whether that product would increase or decrease heat production within brown fat. In other words whether it would speed up or slow down the amount of calories we burn."

*– Written by Natasha Galukande*

*Sources: Symonds ME, Henderson K, Elvidge L* et al. *Thermal imaging to assess age-related changes of skin temperature within the supraclavicular region colocating with brown adipose tissue in healthy children.* J. Pediatr. *doi:10.1016/j.jpeds.2012.04.056 (2012) (Epub ahead of print); Non-invasive thermal imaging joins the fight against obesity: www.medicalnewstoday.com/releases/248023.php*

# Hybrid device for imaging brain electrical activity demonstrates promising precision

A study recently published by *Magnetic Resonance in Medicine* details the emergence of a novel device which combines whole head magnetoencephalography (MEG) with MRI technology to produce unparalleled precision in detailing brain electrical activity.

Combining MEG with MRI to obtain accurate images of the brain was previously impossible due to the respective magnetic fields interfering with each other. Now, with the advent of ultra-low field MRI, researchers have been able to achieve this. Unlike high-field MRI, ultra-low field MRI employs magnetic field sensors which have a magnetic field strength of only a few hundred-thousandths of its sister device, therefore, solving the previous problem.

The hybrid MEG-MRI device is modeled on a whole-head MEG device. It is anticipated that this hybrid will help simplify analysis of information obtained using MEG or MRI technology individually, as well as improving localization accuracy. It is also expected to reduce coregistration errors where information, which is obtained and collated from different methods, is then indirectly matched.

MEG and MRI technology both benefit from being noninvasive methods of measuring features of the brain. MEG measures neuronal activity by recording the magnetic fields that are found in the brain. Produced from electrical currents, they are then detected by magnetometers such as arrays of super coiling quantum interference devices.

> "Combining magnetoencephalography with MRI to obtain accurate images of the brain was previously impossible..."

A major disadvantage of MEG is that the maps of brain activity that it creates are not accurate enough to be independently relied upon for the sole diagnosis and basis upon which treatment decisions are made. MRI technology provides an image which distinguishes between different soft tissues of the body, therefore allowing specific structures of the brain to be identified. The scanners found within an MRI device rely on characterization of different tissue structures by their water abundance. Hydrogen originating from the water in different tissues responds to magnetic fields created by the scanner. Different amounts of hydrogen responding to these magnetic fields produces different signals which are then interpreted as originating from specific tissues.

The project, which was coordinated by Aalto University (Helsinki, Finland), brought together 13 different research groups. It is an important aspect of the European Commission Seventh Framework Program. Academy Professor Risto Illmoeniemi from Aalto University highlights the benefits it can provide in the future to patients suffering from different conditions as well as the financial benefits of the new technology:

"We expect that the new technology will improve the accuracy of brain mapping of patients with epilepsy. It may also improve the diagnosis of cancer patients because the improved image contrast may facilitate the characterization of cancer tissue. The innovative MEG-MRI device will allow brain imaging for new patients, such as those with metal implants. Also, the silent and open device will not scare children or make people feel claustrophobic. In the future, this development can also reduce costs as images can be obtained in one session rather than two."

*– Written by Natasha Galukande*

*Sources: Vesanen PT, Nieminen JO, Zevenhoven KC* et al. *Hybrid ultra-low-fiekd MRI and magnetoencephalography system based on a commercial whole-head neuromagnetometer.* Magn. Reson. Med. *doi:10.1002/mrm.24413 (2012) (Epub ahead of print); Unprecedented accuracy in locating brain electrical activity with new device: www.sciencedaily.com/releases/2012/07/120726102756.htm*

# Combining imaging modalities could lead to earlier diagnosis of gastrointestinal diseases

The quality of images gained from internal organs *in vivo* has been given a major boost by combining two already commonly used methods, photoacoustic imaging and ultrasound, to produce new images that are both high in contrast and resolution. The study, published by *Nature Medicine*, could lead to both an earlier and more accurate diagnosis of many cancers around the GI tract.

Using photoacoustic endoscopy, teams from the University of California (CA, USA) and Washington University (MO, USA) have gained high quality *in vivo* images from the GI tract where blood vessels and their surrounding tissue can be identified. This new simultaneous method of medical imaging presents doctors with a dramatically clearer picture than that achieved from ultrasound endoscopy.

The researchers added a photoacoustic imaging device to an ultrasound endoscope. The new method of imaging involves internally inserting the camera, which can then be used to shine a light on the organ tissue. After absorbing this light, the organ tissue increases in temperature before expanding. A sound pressure wave is created from this expansion, which is then registered and recorded on the ultrasound device that is attached to the endoscope.

Ultrasound endoscopy is critical for its use in many interventional procedures involving internal organs, where a camera is attached to the end of a flexible scope and placed in the body producing high-resolution images. However, when viewing soft tissue, which connects, supports and surrounds other structures, the quality of these high-resolution images is reduced by their low-contrast. In these cases, dim and hard-to-interpret pictures are gained. Novel research funded by the National Cancer Institute at NIH (MD, USA) has overcome this problem with the creation of photoacoustic endoscopy.

Photoacoustic endoscopy can provide doctors with greatly improved images of soft tissue due to it producing images with high optical contrast without decreasing the high resolution characteristic of ultrasound endoscopy.

"This is a first time that we have had small endoscopy with two imaging modalities," commented Qifa Zhou, a principal investigator and coauthor of this recent study, and a professor at the NIH Resource Center for Medical Ultrasonic Transducer Technology at the University of Southern California Biomedical Engineering (CA, USA).

"Photoacoustic endoscopy provides deeper penetration than optical endoscopy and more functional contrast than ultrasonic endoscopy," added Lihong Wang, another principle investigator and coauthor, in the Department of Biomedical Engineering in Engineering and Applied Science at Washington University.

This new technology, therefore, is hoped to lead to doctors safely gaining a clearer view of a patient's GI tract as well as earlier diagnosis of colon and prostate cancers.

*– Written by Natasha Galukande*

*Sources: Yang JM, Favazza C, Chen R* et al. *Simultaneous functional photoacoustic and ultrasonic endoscopy of internal organs* in vivo. Nat. Med. *doi:10.1038/nm.2823 (2012) (Epub ahead of print); Double vision: hybrid medical imaging technology may shed new light on cancer: www.sciencedaily.com/releases/2012/08/120813172640.htm*

# 3D view of the inflammatory response could lead to new biomarkers and therapeutic agents

Recent work which involved the collaboration of researchers from many different disciplines at Vanderbilt University (TN, USA) is hoping to discover previously unknown proteins to be implicated in the inflammatory response. Published in *Cell Host and Microbe,* researchers employed different imaging techniques to achieve a 3D outlook of the inflammatory response. It is anticipated that knowledge gained could lead to new biomarkers and therapeutic agents for infectious disease.

The researchers were interested in imaging infections in 3D. This was first achieved by infecting mice, achieving a whole-organism inflammatory response. Next MRI and mass spectrometry imaging were combined. The teams were then able to identify proteins produced at different sites of the infection.

The mice were infected with *Staphylococcus aureus,* by Ahmed Attia, a former member of Vanderbilt University, who recently transferred to Cario University (Egypt). *S. aureus* was selected in this experiment due its prevalence in humans. After infection Daniel Colvin, Vanderbilt University Institute of Imaging Science, imaged the mice using MRI before Kaitlin Scroeder and Erin Seeley, both from the Mass Spectrometry Research Center (TN, USA), employed mass spectrometry imaging techniques. The responsibility of collating information from the two areas was given to Kevin Wilson, Vanderbilt University Institute of Imaging Science, who crated algorithms to achieve consolidated 3D pictures.

Whilst imaging mass spectrometry provided the researchers with 3D information on the distribution of proteins involved with the immune response, MRI allowed this to be compared with information on the structure and soft-tissue contrast found within the mice. Eric Skaar, one of the senior coauthors of the paper commented "The technologies allow the investigators to see a single image of an infected animal, look at how proteins of the immune system are responding and identify where the infected tissue is located."

The success of this study is attributed to the access of different research groups to each other's resources, highlighting the importance of collaboration between the different expertise to advancement in the field "The fact that my research group, which studies infectious diseases, has access to these powerful imaging and mass spectrometry technologies is a real strength at Vanderbilt and has allowed us to develop these new tools that will enable high impact discovery," Skaar added. This is a matter which John Gore, the director of Vanderbilt University Institute of Imaging Science states is "Another example of the multimodality approach we have been pursuing in general within the Imaging Institute."

"The technologies allow the investigators to see a single image of an infected animal, look at how proteins of the immune system are responding and identify where the infected tissue is located."

The inflammatory response has key roles in fighting infectious and autoimmune diseases as well as cancer. Previous studies have involved focusing on a single organ system rather then the whole organisms, therefore, lacking spatial information. Furthermore, the number of proteins that can be analyzed in these previous experiments has been limited by their need for specific antibodies to also be available. "Imaging mass spectrometry is extremely valuable for the discovery process because it does not require a target-specific reagent such as an antibody – that is, you do not have to know in advance what you're looking for in order to correlate molecular changes with disease outcome," explained Richard Caproli, Director of the Magnetic Spectrometry Research Center. Although this recent study is limited by its noninvasive nature, in the future it is hoped that it could be applied to analyzing tissues of the human body that have been removed, such as tumors.

The researchers plan to continue their studies with the hope of discovering new biomarkers and targets for therapeutic intervention to aid in diagnosing and fighting infection by looking at "proteins that are important at the interface between the host and the pathogen – the battleground between the immune system and the bacteria," added Skaar, "Part of the strength of this work is not where the research is now, but where it allows us to go from here."

*– Written by Natasha Galukande*

*Sources: Attia AS, Schroeder KA, Seeley EH* et al. *Monitoring the inflammatory response to infection through the integration of MALDI IMS and MRI.* Cell Host Microbe *11(6), 664–673 (2012); Imaging the inflammatory response: www.medicalnewstoday.com/releases/248922.php*

# Knowing cholesterol levels like the back of your hand: is the cholesterol snapshot through hand imaging a diagnostic of the future?

In a recent issue of the *International Journal of Medical Engineering and Informatics*, researchers from India have developed a total cholesterol test utilizing a digital camera to take a snapshot of the back of a patient's hand rather than obtaining a blood sample. The resulting image is then cropped and compared with images in a database for known cholesterol levels.

NR Shanker and colleagues (Sree Sastha Institute of Engineering and Technology, Chennai, India) describe how they have developed the noninvasive technique to measure cholesterol levels in patients at increased risk of heart disease. The authors have created a large database of cholesterol levels recorded using standard blood tests and liked this to a corresponding image of the hand for each patient as cholesterol is concentrated in the creases of a patients fingers. The authors have also developed an image processing computer program that compares the image from a new patient with the database entries and matches this to a specific cholesterol reading.

Measuring circulating cholesterol levels and counts is important for determining risks in cardiovascular disease. Total cholesterol is a useful early indicator of disease, although more detailed testing that distinguishes between the HDL and LDL and triglycerides are needed for a more accurate health assessment of patients found to have high total cholesterol. It is the LDL, so-called 'bad' cholesterol that contributes to the formation of arterial plaques, atherosclerosis. The presence of different total levels of cholesterol can be revealed through image analysis of the skin.

A noninvasive and inexpensive method for cholesterol screening would allow this risk factor to be determined in much larger patient populations without the need for costly and inconvenient blood tests. The team also intent to publish details of the extension of this work in classifying cholesterol type using their approach.

*– Written by Michael Dowdall*

*Source: Shanker NR, Ezhil A, Archana S. Noninvasive method of detection of cholesterol using image processing.* Int. J. Med. Eng. Inform. *4(3), 223 (2012).*

# Study suggests coronary artery calcium most effective at identifying cardiovascular prognosis in intermediate-risk patients

A new study from the MESA study population has found that coronary artery calcium assessment was the best predictor of coronary heart disease in asymptomatic patients categorized as intermediate risk by the Framingham Risk Score (FRS). The results, published in a recent issue of *JAMA*, were heralded by the authors as a step forward in the attempt to fine tune the risk-guided management of the millions of patients in the cardiovascular 'no-mans land'.

Current cardiovascular risk guidelines use the FRS to classify individuals as high risk, intermediate or low risk of incident coronary heart disease, using the results to guide primary treatment with aggressive drug therapy or lifestyle measures.

Although this has helped to ensure treatment is appropriate for patients at high and low risk, for the 23 million Americans categorized as intermediate risk, the right management can be hard to determine.

Speaking to sister journal, *Expert Review of Cardiovascular Therapy*, Joseph Yeboah, Assistant Professor of Cardiology at Wake Forest Baptist (NC, USA) and lead author of the study explained the problem, "The intermediate-risk group is in no-man's land and it is unclear to clinicians what to do with them. But we know that a significant number of the 785,000 new heart attacks that occur every year in asymptomatic individuals in the USA (according to the CDC) occur in the intermediate-risk group. Hence the need to refine this risk category with novel risk markers."

Using data from the MESA study population, the researchers directly compared the top six assessment tests for risk prediction in 1330 intermediate-risk patients (FRS >5% to <20%): coronary artery calcium (CAC) score, ankle–brachial index, brachial flow-mediated dilation, carotid intima–media thickness, high sensitivity C-reactive protein and a family history of heart disease.

In the analysis, CAC score, ankle–brachial index, high-sensitivity CRP and family history were found to be independent predictors of incident coronary heart disease (myocardial infarction, angina followed by revascularization, resuscitated cardiac arrest or coronary heart disease death) and cerebrovascular disease in the ensuing 7.5 years of observation.

Of the six tests, the CAC score was found to be the best at predicting which patients in the category went on to have the highest amount of predictive power and improved risk reclassification when combined with other FRS and race/ethnicity.

Although the results suggest that CAC should be used for extensive screening in the asymptomatic population, Yeboah discussed the need for breakthroughs in reducing radiation exposure and cost. "Current research should focus on streamlining the CAC acquisition process (minimal radiation as possible), the cost and cancer risk of the small but nontrivial amount of radiation exposure."

The authors were hopeful that CAC can be used to improve management of millions of patients. As Yeboah summarized, "Our results clearly show the superiority of CAC for fine-tuning cardiovascular risk assessment in the intermediate-risk group. Therefore, if the limitations of CAC screening are addressed, CAC can be appropriately applied to the millions in this risk category to identify the high-risk individuals in this group and treated aggressively to reduce heart attacks in our communities."

*– Written by Louise Rishton*

*Sources: Yeboah J, McClelland RL, Polonsky TS* et al. *Comparison of novel risk markers for improvement in cardiovascular risk assessment in intermediate-risk individuals.* JAMA *308(8), 788–795 (2012); Newswise press release: www.newswise.com/articles/study-shows-heart-calcium-scan-most-effective-in-predicting-risk-of-heart-disease*

# Adherence to radiation reduction methods found to reduce exposure by 40% in cardiac procedures

Adherence to new radiation reduction measures by a team of researchers from the Mayo Clinic's cath laboratory (MN, USA) has been found to reduce radiation exposure by 40% over a 3-year period, reinforcing the achievability of targets to reduce risks to patients and staff during cardiac interventions.

The results, reported in *Journal of the American College of Cardiology: Cardiovascular Interventions*, were following technical modifications to the use of standard x-ray equipment coupled with intensive radiation safety training.

"Through our efforts, we were able to quickly cut the overall radiation exposure to patients by nearly half using simple but effective methods," reported Charanjit Rihal, chair of Mayo's Division of Cardiovascular Diseases. "We think this program could serve as a useful model for other cath laboratories in the USA."

X-rays are increasingly used in the cath laboratory to aid with diagnosis and guide procedures; however, exposure to excessive amounts of radiation can raise the risk of certain cancers and skin damage.

In the effort to reduce radiation during cardiac intervention, the Mayo Clinic instituted a program of technical changes such

as establishing standard x-ray imaging protocols, increasing the use of x-ray beam spectral filters, reducing the detector target dose for certain imaging techniques and reducing the fluoroscopy frame rate. Recognizing that practice changes can also be used to reduce exposure, they also put in place intraprocedure radiation dose announcements; the reporting of procedures of high air-kerma, including procedure air-kerma in the clinical report; and starting compulsory radiation safety training for investigators.

Comparing the cumulative skin dose after a total of 18,115 procedures performed by 27 staff cardiologists and 65 fellows-in-training over 3 years, the researchers found a 40% reduction from the end of the period compared with the beginning.

*– Written by Louise Rishton*

*Sources: Fetterly KA, Mathew V, Lennon R. Radiation dose reduction in the invasive cardiovascular laboratory: implementing a culture and philosophy of radiation safety.* JACC Cardiovasc. Interv. *5(8) 866–873 (2012); Newswise press release: www.newswise.com/articles/mayo-clinic-cardiologists-dramatically-cut-patient-radiation-exposure-from-x-rays*

# MRI-guided right heart catheterization shown to be feasible and safe

*A small-scale study has provided encouraging early evidence that MRI-directed heart catheterization could be a feasible alternative to the traditional x-ray-guidance.*

A preliminary study of 16 patients lead by Robert Lederman (NIH, MD, USA) has demonstrated that MRI-directed transfemoral right heart catheterization is feasible, exhibiting similar success rates and procedural durations to the traditionally used x-ray guidance. The technique could one day become an alternative to the current x-ray-directed methods, allowing reduced radiation exposure.

The study is the first to examine this type of catherization using entirely MRI guidance and is the only paired comparison of x-ray and MRI catheterization in the same patients. Researchers also compared MRI-guided catheterization using an air-filled balloon with the procedure using a balloon containing a 2% solution of diluted gadolinium.

Sixteen unselected patients scheduled for comprehensive transfemoral right heart catheterization underwent the procedure three-times: first, using standard x-ray guidance; second, using real-time MRI guidance with an air-filled balloon; and third, using real-time MRI guidance with a gadolinium-filled balloon. The MRI-directed catheterizations took place in an adjoining room to the x-ray-directed interventions, and procedures were carried out without using a guidewire due to the current lack of MRI-safe versions.

Authors compared success rate, time to perform key steps and catheter visibility between the different types of guidance.

All three image-guidance techniques produced a similar success rate for all chamber-entry tasks. A high success rate was observed – the team successfully performed 15 out of 16 catheterizations without a guidewire. The one procedural failure occurred in a patient with a large secundum atrial septal defect with large pulmonary arteries and moderate pulmonary hypertension. Both x-ray- and MRI-guided catheterization failed in this patient without a guidewire.

Overall, it did not take significantly longer to perform the MRI-guided procedures compared with the x-ray-guided version and navigation tended to be fastest using MRI-guidance with gadolinium-filled catheters when entering the left pulomary artery from the main pulmonary artery. A further encouraging finding was that operator confidence was reportedly equivalent over the three different image-guidance techniques, although there appeared to be a learning curve with the less familiar MRI-guidance: these procedures tended to be quicker in the second eight patients compared with the first eight.

X-ray guidance demonstrated the highest catheter visibility, with both tip and shaft continually visible. Only the catheter tip was visualized in MRI-guided procedures, but using a gadolinium-filled balloon proved more consistently conspicuous compared with their air-filled equivalents. This was thanks to the specific enhancement of the gadolinium using a 'saturation preparation' MRI mode.

While MRI-directed catheterization is a long way from broad clinical adoption, researchers hope that future use of this alternative image-guidance technique could reduce radiation exposure and allow interventionalists to benefit from improved tissue visualization. The study authors cite improved devices and workflows as essentials for making this one day become reality.

*– Written by Sarah Miller*

*Source: Ratnayaka K, Faranesh AZ, Hansen MS* et al. *Real-time MRI-guided right heart catheterization in adults using passive catheters.* Eur. Heart J. *doi:10.1093/eurheartj/ehs189 (2012) (Epub ahead of print).*

## About the News

The News highlights some of the most important events and research in the field of imaging in medicine. If you have newsworthy information, please contact: Sarah Miller, Commissioning Editor, *Imaging in Medicine,* s.miller@futuremedicine.com