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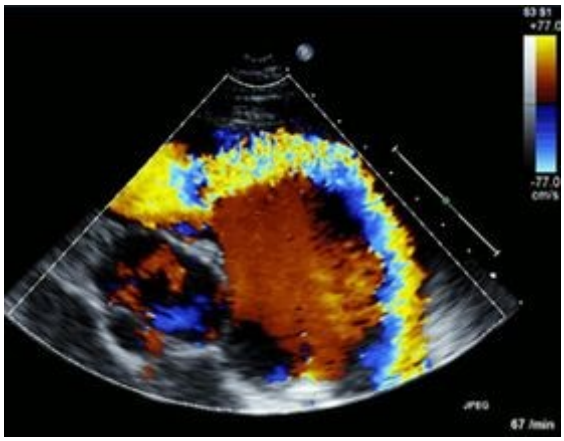
Combining bio- and medtech for the diagnosis of cardiac diseases

The Department of Cardiology at Heidelberg University Hospital and Siemens Corporate Technology have been working together since 2011 to develop new software that improves the diagnosis of heart diseases. The new software analyses and manages data related to the genetic causes of cardiomyopathy and presents the data to physicians in a clear manner. Specific microRNAs in the blood of patients have the potential of being used as new biomarkers, thus making diagnosis of a heart attack more rapid and reliable.



Colour Doppler echocardiography for the functional diagnosis of the heart (the photo shows the blood flow in a patient suffering from severe pulmonary valve stenosis).

People suspected to have suffered a heart attack, which is one of the main causes of death in industrial countries, need to be treated and diagnosed immediately. If their condition has been caused by the occlusion of coronary arteries, medical treatment (e.g. catheterisation to open the blocked artery) needs to be initiated within an hour of the first symptoms occurring in order to prevent the blood clot from blocking the artery and starving the heart muscle of oxygen, causing permanent damage and even cardiac death. ECG (electrocardiography) is currently the method of choice for identifying how much damage has occurred to the heart muscle; long-term ECG is the standard method for identifying continuous or undetected blood-flow disorders of the heart. However, ECG only detects typical heart attack signs in about 50% of patients and does not enable heart attacks to be differentiated from other cardiac disorders and diseases. A reliable diagnosis can only be made by also taking other criteria into account.

Morphofunctional characterisation of cardiac diseases

Control of cardiac function
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In addition to ECG, echocardiography is one of the most widely used non-invasive diagnostic tests in cardiology where it can provide information on the structure and function of the heart. Echocardiography creates ultrasound images of the heart. The Heart Centre at Heidelberg University Hospital carries out around 20,000 echocardiographies per year. The technology has made impressive progress, which can however only be briefly mentioned here. Several types of echocardiography are now used clinically: continuous wave, pulse wave, colour Doppler, tissue Doppler and two-dimensional and three-dimensional echocardiography. The procedure allows doctors to visualise structural and functional alterations of the heart in real time.

Dr. Benjamin Meder, a cardiologist in the Department of Cardiology, Angiology and Pneumology at the Heidelberg University Hospital (Medical Director: Professor Dr. Hugo A. Katus), uses echocardiography to obtain information on morphofunctional alterations and identify the causes of cardiac diseases. His major research focus concentrates on cardiomyopathies, which are diseases of the heart muscle rather than diseases resulting from cardiovascular or heart valve diseases such as myocardial infarction.

Cardiomyopathies are a rather heterogeneous group of diseases. They are often genetically triggered deterioriations of the function of the myocardium, but the symptoms can also be caused by toxic damage, a viral infection or a circulatory disorder. Researchers have identified more than 50 genes that can cause cardiomyopathies or increase their severity if they are defective. Currently available diagnostic techniques cannot definitely determine the genetic causes of this cardiovascular disease. “The problem is that knowing the precise cause is very important when choosing treatments and making medical prognoses,” said Meder.

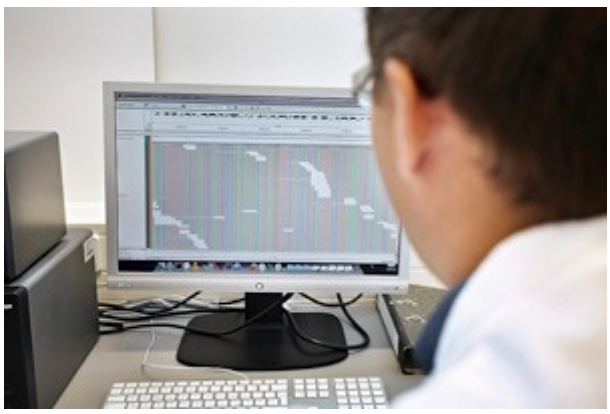
Using genome data for the diagnosis of heart diseases

Siemens software helps cardiologists to analyse genetic data.
© Siemens

With this in mind, cardiologists from Heidelberg University Hospital teamed up in 2011 with colleagues from Siemens Corporate Technology, the global leader in ultrasound diagnostics and medical imaging, to develop new software that not only analyses and manages the huge amount of data generated by genetic tests, but also presents it to physicians in a very clear manner. "Here we used tried and tested software as a basis and then recombined the software components in an intelligent way," said Dr. Andreas Keller, a researcher from the Chief Technology Office of Siemens' Healthcare sector.

In September 2012, Siemens installed an initial demonstration unit for improved genetic analysis of heart muscle weakness (dilated cardiomyopathy) at Heidelberg University Hospital. The cardiologists in Heidelberg already have datasets for around a thousand patients and Keller believes that another 150 datasets will be added to the collection each year. This will provide doctors with an increasingly solid foundation for future studies. Keller added that the challenge is also to make sure that a physician is not just given simple lab results, as was previously the case, but is instead issued gigabytes of information on each patient. "This will not be a problem given the fact that Siemens has many years of experience and expertise in evaluating large amounts of data and extracting clinical information that doctors can understand," said Keller. The demonstration unit will initially be used for the diagnosis of cardiomyopathy, but the systems can also be modified and used to detect other cardiovascular diseases, and even be applied to completely different areas, such as the early detection of cancer.

Blood biomarkers for the diagnosis of heart attacks



The genome offers a plethora of information

Laboratory investigations are of huge importance for quickly and reliably diagnosing a heart attack. The common practice for this was to analyse a patient's blood for proteins that are released by the heart muscle during a heart attack. Troponin T is currently the most important biomarker for the diagnosis of a heart attack. In contrast to previously used markers such as creatine kinase and lactate dehydrogenase, troponin T is highly specific for heart injury (other tests may also be positive in skeletal muscle injury) and is released into the blood during a heart attack. The test was developed by Professor Katus and is currently the gold standard in the diagnosis of myocardial infarction. It is used in laboratories around the world.

However, significantly elevated troponin T quantities are only detected between three to six hours after a heart attack. In addition, the presence of troponins can also have many different causes, which can make it very difficult to quickly differentiate between a heart attack and a heart muscle infection. Therefore, researchers around the world are looking for better and more rapid ways to diagnose a heart attack. The cooperation between cardiologists from Heidelberg led by Dr. Meder and the bioinformatician Dr. Keller from Siemens who previously worked at Saarland University and the Heidelberg-based Biomarker Discovery Center has led to a completely new approach.

The researchers decided that a better way to diagnose a heart attack would be to look for specific microRNAs in the patient's blood or serum. MicroRNAs (miRNAs) are small RNA molecules around 25 nucleotides long. They bind to messenger RNA (mRNA), thereby playing a key role in the expression of genes. 1500 different miRNAs have since been identified. miRNAs are rather stable molecules that can also be detected in the blood. Meder explains that miRNAs are either released when heart tissue dies, or there is a change in the miRNAs in cell types such as leukocytes and thrombocytes that occurs as a reaction to the traumatic event. miRNAs can be identified very quickly after a heart attack has occurred. These findings have been substantiated by recent work by the scientists who found an miRNA subgroup as well as new miRNA molecules that are deregulated soon after a first heart attack has occurred and also during the further acute phase of the heart attack.

The identification of tissue-specific miRNA signatures in the blood, which can be used as biomarkers for numerous diseases, including tumours, seems possible, at least in principle. This was shown by a large multicentre study (published in Nature Methods, 4th September 2011: "Towards the blood-borne miRNome of human disease"), which was designed and coordinated by Dr. Keller in cooperation with human geneticists Professor Eckart Meese and Dr. Petra Leidinger from Saarland University. Although it is basically possible to identify such markers for diagnostic purposes, the laboratory techniques required for this are time-consuming and expensive.

According to information from Siemens, Erlangen-based Siemens Corporate Technology researchers have taken up the challenge and are examining whether a type of "lab-on-a-chip" platform could be developed that would allow such tests to be conducted simply and quickly. The researchers are mainly focusing on better methods for the diagnosis of heart attacks on the basis of miRNAs.

Article

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Medical technology – serving healthcare

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