More than the eye can see: existing MRI images can now be reevaluated with ARDX. The mathematical method diagnoses incipient Alzheimer's by detecting information that cannot be seen with the naked eye.

Photo: Christina Körte and Torsten Kollmer

MEDICAL IMAGE ANALYSIS

SEEING MORE THAN THE DOCTOR

Photo: Christina Körte and Torsten Kollmer

The volume of the hippocampus is the key marker. If it has degenerated to a greater extent than is normal, it may indicate the start of Alzheimer's. ARDX supports the diagnosis of the status quo. However, it is not yet possible to predict dementia. "ARDX is a low-threshold test offered to people with memory impairment who fear they are suffering from early Alzheimer's dementia," explains Dr. Lothar Spies, managing director of jung diagnostics. The Hamburg company has specialized in medical image analysis services. It is the first company worldwide to have developed an image-based Alzheimer's risk diagnostic method and has marketed this as an approved medical product.

Every specialist, neurologist, psychiatrist and general practitioner can offer ARDX. Patients are first subjected to a memory test and examined radiologically with a conventional MRI system. At jung diagnostics, the MRI image data is then checked to ensure that the quality is good enough and analyzed with the aid of the computer. This means that a patient's data set is deformed in such a way that it fits optimally onto a standard head, a so-called atlas. However, the individual characteristics of the brain are also retained.

The computer program then analyzes the images of the brain regions pixel by pixel and recognizes them as gray or white substance or cerebral fluid. With the aid of mathematical and statistical methods, the distribution of the gray substance is then compared to a collective of healthy test persons. Finally, the result is documented in a report that is automatically generated by the program. However, no report leaves the lab without being checked first. "We subject every report to a comprehensive final check and review the results for consistency," emphasizes Dr. Spies. "In doing so, we use an extensive list of plausibility criteria."

EXCEPTIONAL ANALYTICAL PERFORMANCE THANKS TO MATHEMATICAL ALGORITHMS

The algorithm, which forms the basis for the exceptional analytical performance of ARDX and which jung diagnostics has refined for use in routine clinical work, originates from the Fraunhofer Institute for Medical Image Computing MEVIS in Lübeck. This is where Prof. Dr. Herbert Thiele and his team work in the image registration project

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Good prospects for patients, as ARDX can analyze the previously generated MRI scans of the brain regions pixel by pixel. With the aid of mathematical and statistical methods, it delivers evidence of early dementia.

The Fraunhofer researchers cover a huge range. The current projects range from algorithms aimed at improving tumor diagnosis in digital pathology to the optimized positioning of brain stimulation electrodes for Parkinson's patients. To bring together the right partners in these complex subjects, the professor says that the good network of clinics, business and research that Life Science Nord Management GmbH has helped to create is especially valuable. "The support the agency gives us is very effective," says the professor. "And this is a key factor in scientific and commercial success."

EARLY ALZHEIMER DIAGNOSIS WITH THE HIPPOCAMPUS VOLUMETRY METHOD

ARDX shows what can be created when the right partners come together. Even though the method of hippocampus volumetry is still too complex and costly to be available as a standard procedure in general healthcare, the market is growing. "At present, we are pioneers in this field," tells Dr. Spies. "However, the technology is also increasingly being used in specialized clinics and experts to diagnose dementia. This is arousing the interest of other firms that now also see opportunities." A further positive signal is that the assessment of the hippocampus as a biomarker of Alzheimer's disease has been incorporated into the European guidelines on the diagnosis of Alzheimer's. While patients still have to pay for ARDX themselves, the managing director of jung diagnostics is convinced that the method's economic benefits will be accepted in the future. "If Alzheimer's can be diagnosed earlier with our methods, this will help not only patients, but will also lower the costs for the health insurance carriers in the long term."

Until then, the research team headed by Prof. Thiele and jung diagnostics are already working on the next joint project: "We are developing a method to measure the spinal cord in the region of the cervical spine," says Dr. Spies. In the case of multiple sclerosis patients, pathological changes that could lead to paralysis occur there. Once again, the computer can extract more from the image data than a human, and accordingly these changes can be detected at an early stage and therapy can be adapted accordingly. Does that represent a further step in computer-assisted image analysis – namely that that the doctor will be completely replaced eventually? "I can't see that happening," says Prof. Thiele, and Dr. Spies also shakes his head. "Our technology aims to assist health professionals in time-consuming routine tasks and give them more time for demanding diagnoses. The human factor will still play a role even in medical image analysis."   hk
Further information: www.jung-diagnostics.de
www.mevis.fraunhofer.de

group on new possibilities of computer-assisted analysis of medical image data. "Our research is practice-oriented," says the project coordinator, emphasizing the significance of the close collaboration between science and industry. The Lübeck project group is well known for its expertise in image registration. Together with the Bremen parent institute, it is, for example, researching into and developing interactive assistance systems for daily use in clinics – including algorithms that can help doctors evaluate computer medical image data and identify risk factors.

The cooperation with jung diagnostics started with a personal meeting at an event. "At that time, we very quickly decided to pool our know-how in a joint project," recalls Prof. Thiele, who sees huge potential in collaborating with small and mid-sized firms. "If firms have small or no development departments, we can jointly extend their innovative lead. The types of collaboration are very individual and range from providing advice to product component development."

WILL CAD REVOLUTIONIZE DIAGNOSIS?

What role can mathematical and statistical methods play in the future in providing diagnostic support?
We pose three questions to three experts: Prof. Dr. Jörg F. Debatin, former CEO of amedes Holding AG and now Vice President and Chief Technology Officer at GE Healthcare; Prof. Dr. Jürgen Stettin, CEO Prosystem AG; and Klaus Rupp, Head of Care Management at Techniker Krankenkasse.

How do you assess the medical and economic potential of mathematical and statistical methods to aid diagnosis?
Debatin: In my view, the potential for computer-assisted diagnosis (CAD) is vast. In modern medicine, it is necessary to filter out the relevant aspects from a flood of data. Computers provide ideal support here. They can also make a decisive contribution when it comes to correctly interpreting data. It is also conceivable that patient-specific data in the cloud can be compared to well-known patterns and thus the diagnosis can be finalized.
Stettin: In the future, these methods will frequently be used for diagnostic support purposes in medical technology. A second opinion aided by this method is also conceivable – in radiology for example. Adaptive systems, which help to avoid or minimize errors of use, are a further area.
Rupp: Mathematical and statistical methods calculate probabilities and do not deliver definitive prognoses or diagnoses. Their potential depends on the degree to which such methods can be used in a targeted manner, how well they are validated and how well doctors and patients are able to interpret and evaluate the test result. Often, the additional benefit of new methods is unclear and questions remain unanswered.

To what extent does this issue play a role in your daily work?
Debatin: We are at the very start of CAD implementation. The first applications can be seen in laboratory analysis and CAD is being used in some cases in radiology: in most cases, the computer flags abnormalities – for example on CT images of the lung or in a mammography.
Stettin: The incorporation of such methods into medical products is progressing very slowly for approval reasons. However, in the field of medical apps, we are currently seeing a boom in such applications – for example to evaluate blood sugar levels, for drug dosage or even to offer a full diagnostic assessment. But frequently there are software producers involved that have never heard of the strict requirements that medical products have to meet. This means that a great deal of support is still needed.
Rupp: Methods designed to provide mathematical and statistical support to diagnostic work have appeared increasingly in the market in
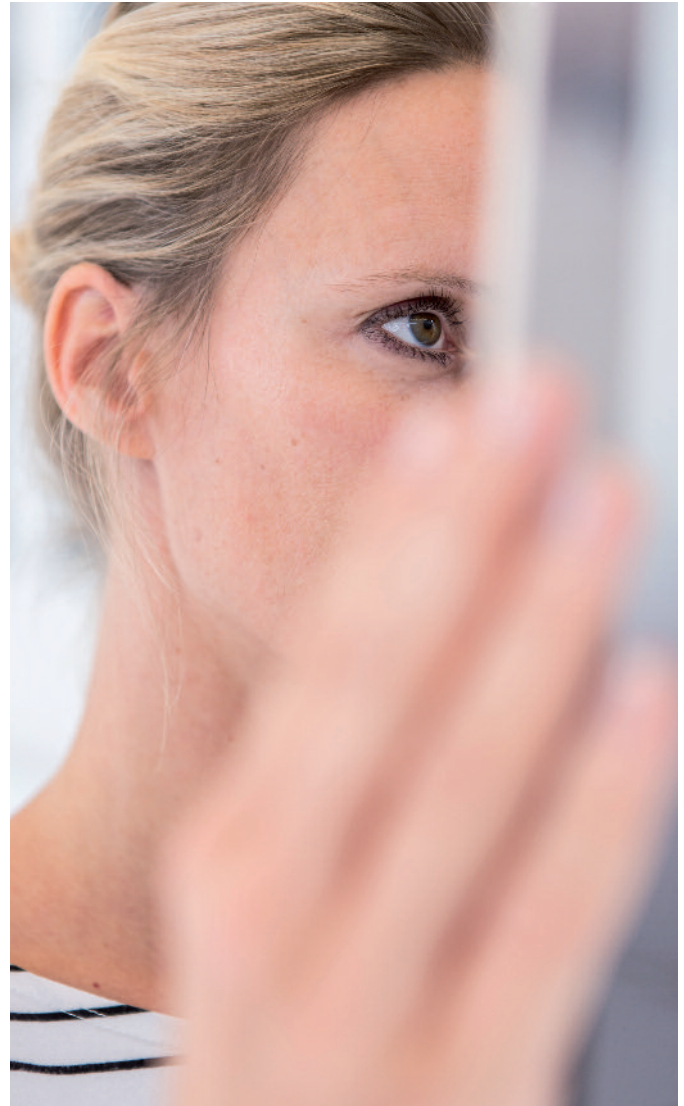
Photo: Christina Körte and Torsten Kollmer

recent years. As these methods are insufficiently covered by the fees for physicians contracted to the state healthcare system or not at all, we are often asked whether we will cover the costs. However, we ourselves attempt to filter out methods that demonstrably help to improve the care of our insured members.

Will this type of diagnostic support become established in Germany in the foreseeable future?
Debatin: Over the coming decade, CAD will revolutionize diagnostics in many ways. The doctors themselves are the biggest obstacle, since many are afraid that their work will be replaced by computers. Personally, I believe that CAD will remain just an aid. However, it will make a major contribution towards making diagnosis more efficient and above all more accurate medically.
Stettin: These methods will certainly become established. Verification, validation and approval are problematic.
Rupp: It is hardly possible to make a generally valid forecast at present. How well a method can become accepted depends on a range of factors – not least the additional clinical benefit, the alternatives that are available and the price. Each individual method has to be reviewed and assessed on its own.