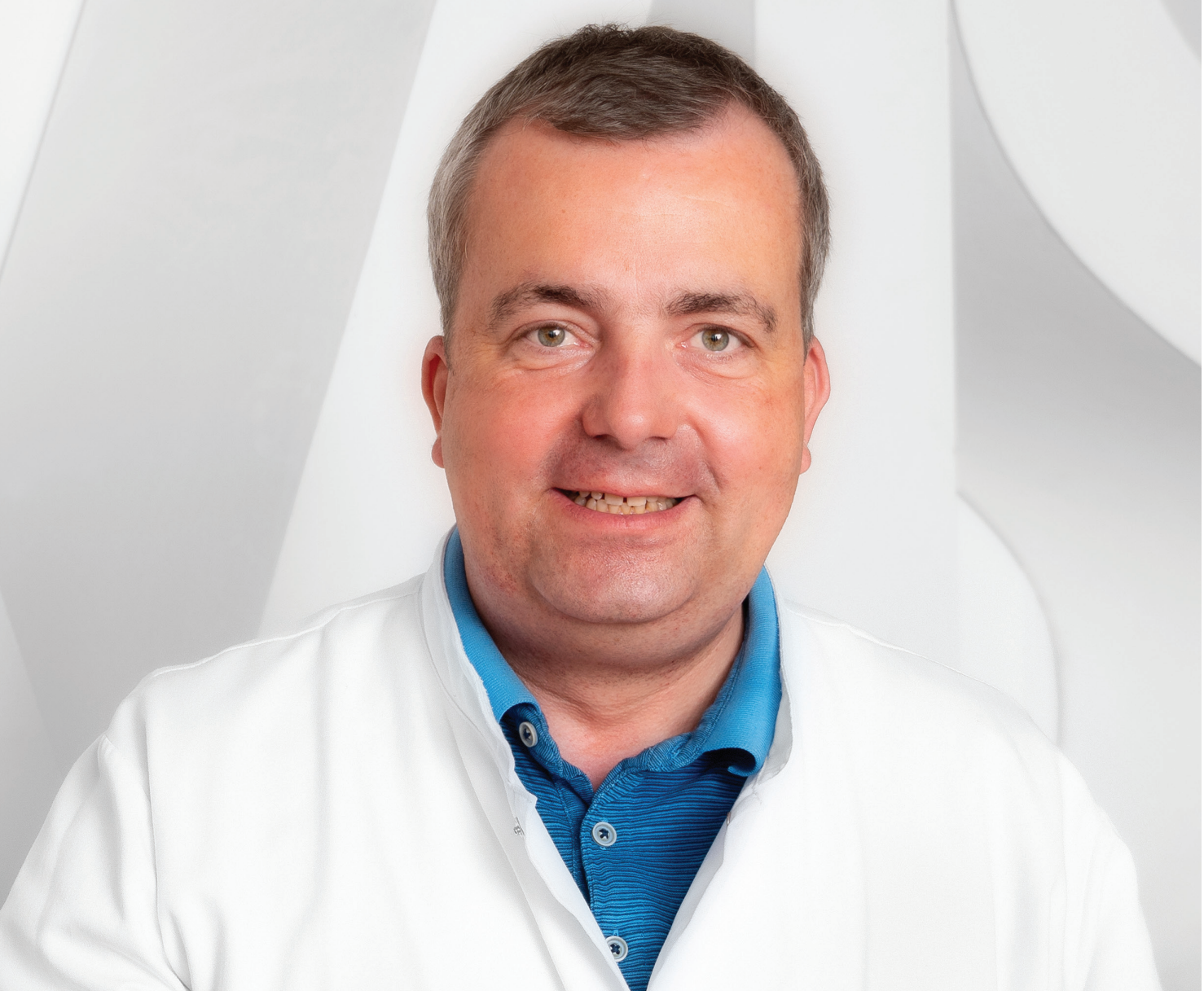


‚The ‚digital twin' can really improve MS care'

Interview with Prof. Dr Tjalf Ziemssen, Director of the Centre for Clinical Neurosciences and Deputy Clinical Director of the Clinic and Polyclinic for Neurology at the Centre for Clinical Neurosciences at the Neurological University Hospital Dresden.

Prof. Dr Tjalf Ziemssen sees himself as a digital pioneer with a lot of passion. Alongside and parallel to his day-to-day work at the Centre for Clinical Neurosciences at the Neurological University Hospital Dresden, treating patients with multiple sclerosis, he and his team are developing the concept of the ‚digital MS twin'. This can be thought of as a virtual copy, a digital dashboard or, in modern parlance, an avatar of a patient that is able to quantitatively describe the individual disease. The beauty of this is that a combination of artificial intelligence, machine learning and data analysis enables digital twins to uncover problems before they occur and optimise processes.

>> Prof. Ziemssen, you are a neurologist who has been treating multiple sclerosis patients since 2003. In 2006, you founded the MS Centre at the Carl-Gustav-Carus University Hospital in Dresden, where you and your colleagues treat over 1,000 patients from all over Germany; the total cohort consists of more than 2,000 MS patients. The special thing about it: all those who agree to this - and that will probably be most of them, otherwise they would probably not make the journey to the capital of the Free State of Saxony - are treated according to the concept of the ‚digital MS twin'. Firstly, what is the concept behind it?

A digital twin is based both on the data that is available on a single individual and on the procedures that are crucial for individual patient management.

The term ‚digital twin' is almost 30 years old in the industry. The idea of digital twin technology was described as early as 1991 in a publication by David Gelernter, which he called ‚Mirror Worlds' at the time. Dr Michael Grieves, who was still a lecturer at the University of Michigan at the time, then adopted the concept of digital twins and applied it to industrial production in 2002, thus creating the software concept of the digital twin.

What is the difference between a ‚digital twin' and the term simulation, which is more commonly used in this country?

These are two completely different but interrelated concepts. A simulation, as we know it from the coronavirus pandemic, for example, includes digital models that can show, replicate and predict various system processes based on certain assumptions.

A ‚digital twin', on the other hand, is first and foremost a vivid collection of relevant health and disease data, in our case of MS patients: A real virtual copy of the patient that quantitatively describes the disease. This can be imagined as a digital environment, perhaps also as an avatar, which can provide much more extensive information in addition to its patient-relevant presentations of patient data, because it can itself carry out an almost unlimited number of simulations and analyse several processes running simultaneously.

Cui bono: research or the patient community?

I would reverse the order, even if this may require some explanation. Let's stick with the technical wording for now: In fact, a digital twin is a virtual model of a product, process, system or plant - whether that's a T-shirt, hoover, electric car or state-of-the-art wind turbine. Their digital images, based onthe respective data of the real object, are used to better understand its performance and structure and to continuously improve it: Process optimisation is the buzzword here. This has long been standard practice in industry. The advantage of this is that a combination of artificial intelligence (AI), machine learning and data analysis enables digital twins to detect problems before they occur, helping not only to optimise processes but also to avoid serious errors before they can cause any damage.

When was the transfer to medicine?

Relatively late. The digital twin concept was first used in oncology around five years ago, then in cardiology, because these disease entities can be characterised very well and the relevant parameters are clear and limited. Since 2019, there have been a number of scientific papers dealing with the question of how digital twins can be used to personalise medicine, such as those by Prof. Dr Bergthor Björnsson from Linköping University in Sweden (1) or Dr Tina Hernandez-Boussard from Stanford University in the USA (2). We ourselves are currently preparing a scientific paper on the subject.

How does the patient benefit? A kind of data copy in a new form? A kind of avatar like an immunological twin. What interpretation do you use?

Just as they should be stored in the electronic patient file (ePA), for example, until it is sufficiently filled at some point. These are two completely different concepts: The ePA is nothing more than a rather wild and disorganised and also possibly incomplete collection of data, consisting largely of text documents, PDFs, images and other file formats. This reveals a typical German data collection mania that will be of little help to either patients or the doctors treating them, and therefore also to research. On the contrary: if a patient comes to me today with a DIN A4 folder, I can still somehow organise the individual documents on my desk. But try to get an overview of 100 or even 1,000 PDF documents on the PC screen - it's almost impossible. For me, the ePA is a form of patient documentation that I can't get used to - and for the patients too, by the way, because they can do little or nothing with it.

What does the ‚digital twin' do better?

If you ask me: everything.

You have to back that up.

As with the ePA, personalised patient data is of course the basis of the ‚digital twin'. The key difference in the concept isthat we are trying - and we have already made quite a bit of progress here - to move away from qualitative data or so-called secondary data, which is usually available in text form. Quantitative or primary data is crucial, which is then visualised in a completely new way so that patients and treating physicians can recognise the most important facts and trends at a glance and interpret them for themselves. Parallel to data collection, however, there is a second, integral part in which procedural data from real care - from the clinic, outpatient or telemedical track - is stored. This is where we integrate the digital clinical pathway, a signpost that guides patients and doctors through the jungle of a complex MS disease. The big picture is the important thing.

How does the patient benefit?

The patient benefit is the decisive factor for me, because patient-centredness is crucial for the data protection concept - the patient

has and uses their data. The digital MS twin is first and foremost a strategic concept to get patients on board on their patient journey and to constantly ensure that the information that is urgently needed firstly arrives and secondly can be understood. Every patient - and not every doctor, by the way - doesn't need as much data as possible, but the right data at the right time and in a way that can be understood and comprehended.

‚Every patient - and every doctor, by the way - doesn't need as much data as possible, but the right data at the right time.'

Is that what your patients want?

Of course they do, that's why they come to Dresden. Even if the concept is called a ‚digital twin', it means an absolute paradigm shift: the individual patient is at the centre of attention, because they agree to have their data and procedures available by mirroring their patient-specific data - initially without any AI. Secondly, a fairly sophisticated computer model can then take us to a whole new level of disease and patient management and the patient journey. This means that the ‚digital twin' is far more than just a collection of data, but can act as its own pilot using a kind of cockpit - with the treating doctor as co-pilot, so to speak - to organise the management of the illness itself in a meaningful way and even look into the future to a certain extent. And of course this is especially true when the patient is not in the doctor's surgery or in a specialised clinic like ours, which is the case 99% of the time each year.

Looking to the future?

This becomes clear if I use an example from multiple sclerosis. In MS, new inflammatory lesions develop again and again as the disease progresses. These changes in the brain can be depicted very well using imaging, which is then converted into radiological text volumes that most patients despair of. In the ‚digital twin', on the other hand, there are no longer any radiological images or text findings. A second point also becomes clear here: these comparisons using AI are only possible if the imaging is standardised and of high quality. Standardised data must therefore be available in high raw data quality.

What happens to it?

The imaging results in a visualised dashboard that allows the patient to see at a glance after each examination how the brain volume is developing, whether it remains stable, is changing or whether new lesions have appeared. Next, we are in the process of visualising the results of neurological examinations in order to move away from the miserable text findings here too.

Is this a vision or already a reality?

Certainly still a vision in the final stage of development. But we have already taken many important steps along the way and have been able to realise expansion stages that are enormously beneficial for patients and treating physicians. However, it is an immense effort that we have to make - in addition to our daily work in care and research, mind you.

And as is the case with every digital project ...

... we will never be completely finished. We simply have to say goodbye to this very German idea: Digitalisation has no final stage, but consists of a series of iterations that are constantly being improved. That's why you can only approach such complex projects in a modular way, developing one tool after another and gradually releasing them. As with the MS twin: first the imaging, then digital biomarkers such as the results of neurological examinations and then further laboratory data such as liver values etc..

What is the main challenge here?

The principle is always similar. However, you not only need different structures for each type of data, but also the know-how on how to collect certain quantitative data in a standardised way, how to evaluate and visualise it. Finally, this data must also be visualised in such a way that it reflects the actual state and probabilities in order to make predictions. Of course, this is always coupled with the very difficult task of doing this in such a way that the patient is as well informed as possible, but not frightened or even scared. It must therefore be adaptive and customisable to the respective situation.

Is the patient community involved in the development?

Of course, we work together with proven specialists and patients in the field of visualisation and representation as well as simulation and prediction. However, this alone would not get us any further, as real patient-centredness can only be achieved together with patients. This is where our patient board, which enthusiastically participates in the ‚digital twin', helps us.

Is the term ‚twin' perhaps not entirely appropriate?

I don't see it that way. Our task is to collect and communicate patient data and procedures of varying complexity. This broad spectrum, from simple visualisation of collected structured data to complex prediction, can be flexibly implemented with the tool and can therefore be individually adapted. What is misleading about the concept of the ‚digital twin' is that some people claim that it should be kept extremely far away from the patient, as statements about the course of the disease could possibly lead to irritation, anxiety or, in the worst case, even suicidal thoughts. Our interpretation is different: Every patient has the right to the information that concerns them. And it is our task to present it in an appropriate, i.e. understandable, form. However, we also have a duty to familiarise the patients who entrust us with their individual disease data and, above all, to present it in such a way that the disease data can support the patient journey, but can also be correctly classified both rationally and emotionally. This is certainly not an easy task, but it requires us doctors.

This is the fine art of communication, which you don't learn as a doctor.

Unfortunately, but it is getting better among current students. Yet communication is so important.

What about healthcare research?

With our approach, we prioritise patient-centredness, followed by the benefits for treating physicians in the clinic and also in the outpatient sector. Of course, we can conduct scientific research with the data available to us, to which our patients give us almost 100 per cent consent. A cohort of over 1,000 digital MS twins already has a lot of power and enables relevant research, in which we are also

very active.

For example?

I have already mentioned digital biomarkers, which have so far been underrepresented in research.

What exactly do you mean by that?

In multiple sclerosis, we need to record the functional systems that are affected differently and individually as quantitatively as possible in order to identify relevant changes, particularly during the course of the disease: for example, walking function, upper limb function or cognition. To test the lower extremities, for example, we ask our patients to jump up a few times on a high-tech force measurement platform, which we have modelled on that used by competitive ski jumpers. The information on coordination, strength and sensory function that we obtain from the simple jump - which takes perhaps five seconds - is of much higher quality than that from a complete, more time-consuming and therefore much more expensive neurological examination of the lower extremities.

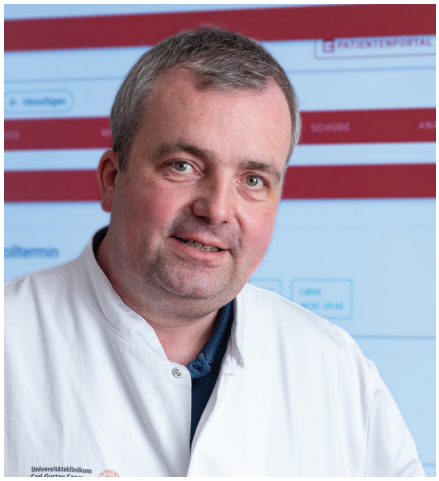
In the field of cognition, we also use AI for speech analyses. Cognition can be measured using a fairly simple question-and-answer system, but it can also be used to determine whether depression or fatigue is present. A speech test of this kind takes around ten minutes and the key neurological function results are available almost simultaneously, which we have not been able to quantify at all until now. The great thing about it is that every patient can take such language tests from home via telemedicine to test themselves in the event of any uncertainties during MS relapses.

The ‚digital twin' is therefore not only a completely new treatment concept, but also a new care concept.

Exactly. But also a monitoring concept for better quality of care. A look at a complete data collection, including the procedures carried out, also shows whether or not the treating physicians are working in accordance with the guidelines. For example, according to the guideline, every MS patient should have an MRI once a year.

What does the reality of care look like?

On average, patients only get an MRI every five years, with the exception of those patients who are treated in specialised centres like ours. However, according to the guideline, blood samples should also be taken at defined times for certain therapies. However, when we analyse the data available to us, we see that in reality this is also carried out much less frequently than is actually prescribed for safety monitoring. However, if the patient sees on their digital pathway that this blood sample is actually necessary but is not being taken, they can and must take action. My petition is therefore that we must use concepts such as the ‚digital twin' in order to optimise real care. This is the only way we will be able to achieve better, perhaps even high-quality care.



Univ.-Prof. Dr. med. Tjalf Ziemssen

is Professor of Clinical Neurosciences and Director of the Centre for Clinical Neurosciences as well as Deputy Clinical Director of the Clinic and Polyclinic for Neurology at the Centre for Clinical Neurosciences at the Neurological University Hospital Dresden. During his postdoctoral stay at the Max Planck Institute of Neurobiology, Department of Neuroimmunology in Munich-Mar tinsried, he worked on neuroimmunological issues. After returning to Dresden in 2004, he set up the Neuroimmunological Laboratory (NIL), where animal experiments, molecular biology and cell culture immunology are carried out. In 2006, Ziemssen founded the MS Centre at the University Hospital in Dresden. Since the beginning of 2020, he has also been Scientific Director of the ‚Multiple Sclerosis Management' Master's degree programme.

The crucial question: What's the catch?

As always and so often in Germany, a lot of the data that we actually need for the ‚digital twin' is not yet being collected in the quality and standardisation required because there are, of course, insufficient financial resources to do so. However, at our centre we can show that digital biomarkers or standardised imaging is possible in a cohort of over 2,000 MS patients.

But what does real-life care currently look like in practice?

A patient sits with a neurologist for ten minutes and may also undergo a clinical examination. This results in a more or less informative free text without quantitative data. This means that only the neurological gut feeling can help with the comparison with later ideas.

What use is that?

Not much. If we really want to achieve a better quality of treatment and care, we have to learn to better describe diseases - and I don't just mean multiple sclerosis - in quantitative terms. To do this, we need to develop structures, tools and procedures and establish them in practice that enable the treating physicians - especially in the outpatient sector - to collect quantitative data from patients as easily as possible and without spending a lot of additional time, and feed it into their ‚digital twin'.

How do we get there?

Certainly with the help of professional associations, but especially with public and media pressure. However, we need all the help we can get here, because we see ourselves as digital pioneers with a lot of passion. But as a doctor providing care, I can't and don't want to develop a business concept on my own.

My aim is to show conceptually that such digital concepts can bring many benefits if you think fundamentally about what you actually want with data: mere data collection or meaningful data utilisation for doctors and patients?

It would be great if Gematik were to set up a pilot programme.

If it's not Gematik but the Bundesdruckerei, as has now been agreed, I can't complain. We're going down the modular route anyway, so we can't complain. There is ERDF project funding for the basic architecture of the ‚digital twin', and we will also receive funding from the BMBF in the area of speech analysis in the future, as well as for the walking ability test. The pharmaceutical industry also has a veritable interest in these concepts, because high-quality data collections are being created that we didn't even have before. And this applies above all to the collection of safety data, which is currently still very suboptimal. We also want to enter into dialogue with the authorities in order to implement these concepts.

What about the health insurance companies? Are they interested?

Well, they are rather reluctant, as cost savings cannot be realised immediately, of course. But we are co-operating. For example, we have succeeded in ensuring that every patient who is insured with AOK Plus receives the ‚digital twin' combined with health insurance data in collaboration with the IPAM Institute in Wismar. We want to show that the ‚digital MS twin' can also map the economic component of the patient journey. For this reason, we have designed the concept in such a way that virtually every step a patient takes on their Patient Journey can be stored with an economic component, which in turn comes from health insurance billing data. This not only allows us to see and also predict in a simulation analysis what something will cost and when, but also to measure the quality of care: for example, how often an MRI has been carried out and reimbursed or how often physiotherapy or a neurological examination has been carried out. We are also currently analysing which therapy strategies cause which financial costs and also what consequential damage is caused by examinations that are not carried out or carried out too late or by changes in therapy.

Is there a study on the health economic effects of the ‚digital twin' concept?

We haven't got that far yet. Once we have launched the pilot project with enough modules, the Innovation Fund would be able to evaluate the value in practice, because at some point it will be our duty to make proven concepts available to all MS patients and not just those who come to us in Dresden.

What does the future hold for the ‚digital twin'?

It will not be alone in Germany. Together with two US universities, for example, we are developing the idea of making the databases of our twins interchangeable. To do this, we are entering the world of federated learning or swarm learning. To do this - cave German data protection - the data released by our patients for research does not even have to leave our centre. This means that our data is fed into models and calculated locally on our servers alone, which can be done in parallel with the same model but different data anywhere in the world. This approach would be able to really advance MS treatment and care - which would of course also be possible for many other disease entities. You just have to want it. And do it.

So how do we move from the patient-specific perspective to a public health level and thus to health services research?

Health services research is indispensable, for example, when it comes to describing, comparing and further developing patient journeys. Structures, processes and contexts, including all the ever-present complexities and interactions of healthcare reality and quality, can ultimately only be depicted by healthcare research, and the ‚digital twin' - understood and loved by patients and used by doctors - is also a blessing for healthcare research.

Mr Prof Ziemssen, thank you for the interview. <<

The interview was conducted by MVF editor-in-chief Peter Stegmaier.

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Literature:
1: https://genomemedicine.biomedcentral.com/articles/10.1186/s13073-019-0701-3
2: Hernandez-Boussard, T. et al. Digital twins for predictive oncology will be a paradigm shift for precision cancer care. Nat Med 27, 2065–2066 (2021).

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