

BIH Digital Health Accelerator Demo Day

May 19, 2021
Virtual Event



Welcome to BIH Digital Health Accelerator Demo Day 2021!

Tonight, ten innovation teams of researchers and clinicians of Charité – Universitätsmedizin Berlin and Berlin Institute of Health (BIH) will demonstrate the digital health solutions they have prototyped over the past six months in the BIH Digital Health Accelerator program stage 1, supported by expert mentoring, funding, free co-working space at BIH (most of the time virtual due to the pandemic), and access to our pool of talents and partners.

Innovation teams selected to advance to the BIH Digital Health Accelerator stage 2 will continue to receive end-to-end support to realize their visions of developing and translating digital health products into medical applications via industry cooperation, licensing, or spin-off company formation.

Each of these Charité and BIH innovation teams has been working extremely hard on top of their day jobs in clinic and research. To help their innovations become reality, partnerships are key. Whether you are a potential advisor or co-founder, validation partner or health insurance representative, industry partner or investor – innovation in medicine is a team effort. Together, let's collaborate to improve patients' lives.



The Berlin Institute of Health (BIH) The mission of the Berlin Institute of Health (BIH) is medical translation: transferring biomedical research findings into novel approaches to personalized prediction, prevention, diagnostics, and therapy and, conversely, using clinical observations to develop new research ideas. The aim is to deliver relevant medical benefits to patients and the population at large. The BIH is also committed to establishing a comprehensive translational ecosystem as a translational research area at Charité – one that places emphasis on a system-wide understanding of health and disease and that promotes change in the biomedical research culture. The BIH is funded 90 percent by the Federal Ministry of Education and Research (BMBF) and 10 percent by the State of Berlin. The two founding institutions, Charité – Universitätsmedizin Berlin and Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC), were independent member entities within the BIH until 2020. As of 2021, the BIH has been integrated into Charité as the so-called third pillar; the MDC is a privileged partner of the BIH.

BIH Innovation is the joint technology transfer office of BIH and Charité. BIH drives translational medicine by supporting the community of researchers and clinicians at BIH and Charité in discovering, developing, and commercializing assets such as new technologies and products via industry cooperation, licensing, and spin-off company formation. BIH

Innovation also serves as a single point of access for partners to facilitate cooperations. BIH Innovation offers four service areas: Digital Labs with Digital Health Accelerator, Validation Fund/Spark-BIH, Patenting and Licensing, and Strategic Cooperations.

BIH Digital Health Accelerator (DHA) is operated by BIH Digital Labs. The BIH Digital Health Accelerator program supports all employees of Charité, including BIH, in research and clinical practice, in developing digital health solutions from their innovative approaches and transferring them to patients in medical applications or the market. Participating teams go through a structured process with support from funding, mentoring by high-profile experts, access to networks, and interdisciplinary collaboration in the BIH Digital Labs Co-working Space. The goal is the generation of innovative digital health solutions and transfers to patients and our society.

The DHA program supports innovators at Charité and BIH to develop digital health solutions aiming at step-change improvements in patient outcomes and healthcare system performance. Initiated in 2017, 28 teams have participated in DHA program to date. Four teams that started in 2017 or 2018 founded spin-offs in 2020. Five teams that started in 2018 and 2019 are currently targeting commercialization. To fuel growth, BIH DHA is open to partnerships with leading life science/technology companies, industry and investors.

Agenda

6:30 pm

Welcome and Opening Remarks

6:30 – 6:35 pm

Introduction

Dr. Laura Johnson

6:35 – 6:40 pm

Welcome

Prof. Dr. Christopher Baum

Chairman of the Board of Directors of Berlin Institute of Health and Chief Translational Research Officer of Charité – Universitätsmedizin Berlin

6:40 – 7:00 pm

Keynote

From Bench to Startup: An Entrepreneur Story into Startup

Anh Hoang-Lindsay, PhD

Founder, CSO, Sofregen Medical

7:00 – 8:40 pm

BIH Digital Health Accelerator Pitches

TimeTeller: Circadian Clock Profiling for Cancer Treatment Timing

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Recovery Cat: Keeping Patients With Chronic Mental Disorders Safe

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MetaboKin: A Virtual Cell for Modeling Liver Metabolism

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rAldiance: AI-Based Radiology Solution to Improve ICU Care

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MutationSearch: A Full-Service Platform Solution for Whole Exome Sequencing

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Aurelia: Monitoring Brain Perfusion During Anesthesia and Improving Perioperative Outcomes

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DAGI: Keeping Your Child With Congenital Heart Disease Safe at Home

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PerMitra: Optimization Tool for Heart Valve Surgery

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WePath: A Platform-Based Global Network for Pathology Expertise

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MyaLink: A Monitoring Platform Solution for Orphan Diseases in Neurology

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Closing Remarks

Prof. Dr. Axel Radlach Pries

Dean, Charité – Universitätsmedizin Berlin

Breakout Sessions / Networking and QA with DHA Teams

Agenda

8:40 – 8:45 pm

8:45 – 9:30 pm



TimeTeller: Circadian Clock Profiling for Cancer Treatment Timing

The circadian clock is an internal time-generating system that rules our sleep-wake cycles and molecular processes, such as metabolism and cell division. Each of us has our own individual circadian clock, which means that molecular processes occur at different times of the day for different people. If one's circadian rhythm is disrupted, molecular processes are altered. This is the reason you e.g. experience jet lag, a temporary alteration of the circadian system. Circadian rhythm disruption is also associated with various diseases: cancer, obesity, depression, Alzheimer's, and Parkinson's Disease.

More than 50% of FDA-approved drugs on the market target 24h-rhythmic genes, but clinical care has yet to take circadian rhythms into consideration. In oncology, the side effects and efficacy of cancer treatments vary significantly from patient to patient. The timing of treatment can reduce side effects by up to 60% and increase the length of survival.

The TimeTeller team developed a method to profile the personal circadian clock and predict optimal time windows for a given drug and patient. TimeTeller has created a non-invasive at-home testing kit, and a patient biomarker monitoring tool. The team is currently developing a decision support tool for clinicians. First, the patient collects his/her saliva at home and sends them to the lab. Then, RNA from the samples undergoes molecular analysis of core-clock and clock-controlled genes. Mathematical modeling is used to profile the individual's circadian rhythms and to determine which time windows are more or less toxic for a certain drug treatment. TimeTeller's analysis also provides recommendations for the timing of daily activities—sleep, light exposure, meals, exercise—to reduce circadian dysregulation and maintain a healthy clock. Ultimately, this can further reduce side effects and support treatment.

The TimeTeller platform is applicable across various therapeutic areas, ranging from cancer to neurodegenerative diseases, diabetes, and more. Currently, the team is involved in clinical studies on ovarian and colon cancer. Studies on pediatric leukemia and Parkinson's Disease will begin later this year.

TimeTeller is powered by the expertise of systems- and molecular biologists, computational scientists, a clinical trials assistant, and a product developer. If you would like to learn more, check out the introductory video: sysbio-relogio.com/timeteller-video/

ASK

- Cooperation with the pharmaceutical industry for further development and testing of a companion diagnostic solution
- National and international clinical partners to further develop and test TimeTeller in clinical trials
- Cooperation with CROs to further develop and test TimeTeller in clinical trials
- Partnership with Pharma or technology industry for co-development projects
- Team members: business lead and regulatory

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KEYWORDS

Circadian Clock, Oncology, Computational Biology, Decision Support Tool

NETWORKING AND QA 8:45 PM

ZOOM



Recovery Cat: Keeping Patients With Chronic Mental Disorders Safe

In Germany, there are eight million people with severe mental illness. This large, underserved population is frequently hospitalized, and one-third of patients are readmitted to the hospital within three months. This reflects the shortcomings of the current standard of psychiatric outpatient care.

Effective medical treatment is critical to stabilize these patients, but it can be difficult to find the right drug for the right patient, especially when outpatients only have 15 minutes with their psychiatrist every six weeks. In just 15 minutes, a psychiatrist is expected to understand the events, symptoms, side effects, and medication adherence from a patient's previous six weeks and make an informed clinical decision to continue, stop, or change the dose of the medication. Unfortunately, many psychiatric drugs are only effective for a small group of patients, making this process even harder.

Recovery Cat is a personalized decision support tool for psychiatrists and outpatients with severe mental disorders (schizophrenia, bipolar disorder, and recurrent depression). Recovery Cat aims to be the first digital tool directly integrated into psychiatric care that supports collaborative, data-driven clinical decisions and patient adherence to the therapy plan. The tool tracks drug intake, target symptoms, and side effects to detect risk and non-response early, which can help physicians find the right medication faster. Recovery Cat wants to empower patients to feel more confident about their treatment and to better understand the relationship between their symptoms and medication.

In the future, Recovery Cat aims to build a digital assessment tool for subjective psychiatric outcomes, which could serve as a robust basis for treatment decisions. This tool could facilitate N-of-1 trials—in which the patient functions as his/her own control—to better estimate a treatment's causal effects with time series analysis. The team's long-term vision is to build algorithms on a data-secure federated learning platform and derive robust models for outcome prediction in psychiatric care. The team is inspired by this larger vision to reimagine the future of evidence generation for routine psychiatric care.

Recovery Cat is powered by a highly interdisciplinary and experienced team of psychiatrists, psychotherapists, product and tech developers as well as UX/UI designers.

ASK

- Cooperation with insurance companies for clinical trials and reimbursement strategy testing
- Partnerships with national and international hospitals and psychiatric outpatient centers for feasibility studies and clinical trials
- Cooperation with hospitals and psychiatric outpatient centers for co-development
- Collaboration with other start-ups in the (severe) mental health space
- Advisors from industry for market access

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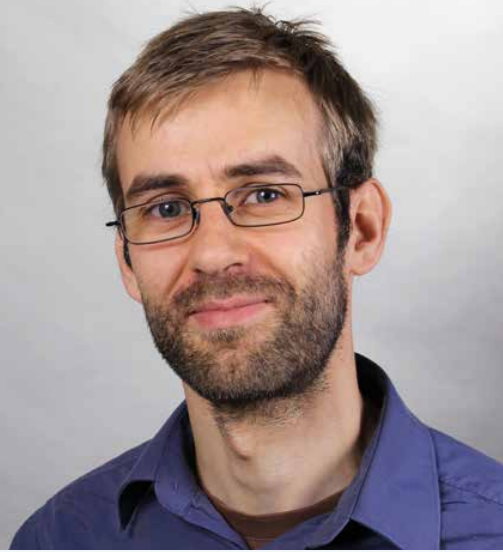
RECOVERYCAT

KEYWORDS

Psychiatry, Remote Monitoring, Mental Health, Chronic Mental Illness, Decision Support Tool, Digital Therapy, Adherence

NETWORKING AND QA 8:45 PM

ZOOM



MetaboKin: A Virtual Cell for Modeling Liver Metabolism

Non-alcoholic fatty liver disease (NAFLD) affects more than 25% of the world's population. Metabolic syndrome manifests in the liver as NAFLD and develops into more severe disorders like non-alcoholic steatohepatitis (NASH). Despite pharmaceutical companies' significant efforts in recent decades, there is still no available drug treatment for NASH. It is critical to improve our understanding of the underlying metabolic changes and to develop new treatment options for NASH; however, it is rather difficult to pursue this, both experimentally and clinically.

Team MetaboKin has developed virtual cells that simulate central metabolism with kinetic properties from approximately 400 metabolic enzymes and transporters. Over the last four decades, biochemists gathered kinetic data which, today, enables realistic in silico representations of organ metabolism. The major advantage of these deterministic virtual cells is that they do not need further data for training or application. These virtual cells also enable the simulation of organ metabolism without direct measurement.

MetaboKin is the ideal tool to characterize metabolic changes in NASH, improve drug target identification, further differentiate between mechanisms of action, and support patient stratification. The tool analyzes proteomics data from tissue samples and provides functional insights into central metabolic pathways, which enables the comparison between clinical and pre-clinical samples. MetaboKin works for animal and human samples, makes R&D development processes leaner, and maximizes the value of proteomics data.

Currently, MetaboKin characterizes metabolism for the liver, brain, and heart. Its applications are not disease-specific: MetaboKin can be used to evaluate metabolism under various physiological and pathological conditions, including diabetes and cancer types. The team is in the process of developing virtual cells for other organs: kidney, fatty tissue, and muscle tissue.

In the future, the team envisions that it will be standard in the drug development process to incorporate metabolic changes, just like PBPK modeling became a standard 30 years ago. The MetaboKin team aims as long-term goal to create a clinical application with virtual cells as a decision-support tool for diagnosis, treatment, and prognosis.

ASK

- Partnership with pharmaceutical companies for pilot projects
- Cooperation with proteomics facilities to test solution
- Cooperation with physicians to co-develop clinical applications
- Team member (Business, Product Development)

rAldiance: AI-Based Radiology Solution to Improve ICU Care

X-rays are extremely important to answer specific diagnostic questions in medicine. For patients in the intensive care unit (ICU), doctors may order a new x-ray every day, and correct interpretation is critical. It would be ideal if a radiologist could immediately assess every image, but this is simply not possible in many hospitals: in Germany 60% of hospitals do not have a radiologist on-call to assess x-rays at night or on the weekends. As a result, the medical staff on-site must interpret the images themselves, and if expertise is lacking, the error rate is subsequently high. These errors can delay diagnosis, lengthen hospital stays, or lead to suboptimal therapy, which can additionally burden patients and the healthcare system.

Team rAldiance aims to support physicians in the ICU make better, more confident decisions when analyzing images without a present radiologist. The rAldiance solution is based on an AI technology and highlights important image areas and quantifies findings to improve the speed and accuracy of image interpretation. This tool is especially important for the ICU, as ICU images are more difficult to interpret, and ICU physicians rely more on fast, accurate diagnoses for effective treatment. The tool is also designed for seamless integration into existing diagnostic systems, which minimizes IT overhead costs for hospitals and PACS providers alike.

rAldiance is powered by an interdisciplinary team with many years of experience in radiology and AI. The team also works closely with PACS vendors and expert advisors in software development, regulatory affairs, and market access.

ASK

- Partnerships with national and international clinical institutions to test the solution
- Cooperation with technology industry partners to optimize API
- Team members: regulatory affairs, data scientist



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rAldiance

KEYWORDS

Radiology, AI, Decision Support Tool, ICU, ER, Medtech

NETWORKING AND QA 8:45 PM

ZOOM

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MetaboKin

KEYWORDS

Biosimilars, Proteomics, Metabolism, Kinetic Models, Simulation, NASH, Pharma R&D

NETWORKING AND QA 8:45 PM

ZOOM



MutationSearch: A Full-Service Platform Solution for Whole Exome Sequencing

Although most of the 6,000+ single-gene disorders are rare, more than 200 million humans suffer from any one of them. Due to their rarity, most single-gene disorders are difficult to diagnose. Many patients and their families live in uncertainty about the name of the disease and its cause for years.

High-throughput sequencing technologies, such as Whole Exome or Genome Sequencing (WES/WGS), allow for the identification of disease-causing DNA mutations with a single assay. As the cost of these approaches continues to decline, WES/WGS will soon become routine diagnostic procedures. Currently, WES/WGS are only performed in dedicated labs without access to detailed patient information. Most of these labs are using software without CE certification, which will be legally required beginning 05/2022.

MutationSearch aims to bring WES/WGS to the clinic as a full-service platform solution to discover the molecular causes of genetic disorders. The software analyses raw data from DNA sequencers, detects variations from the reference genome (~40,000/patient in WES, ~4,000,000/patient in WGS), and predicts their pathogenicity, even without a clinical diagnosis. Medical doctors can add relevant information about the patient's phenotype, which allows the software to focus on variants in genes likely to cause the disorder. MutationSearch will automatically print a report with all information necessary for physicians for a molecular diagnosis.

MutationSearch is powered by an interdisciplinary team of experts in bioinformatics, computer science, molecular medicine, biochemistry, business, and machine learning. They have many years of experience developing scientific software for the elucidation of genetic diseases and disorders. Their software for pathogenicity prediction, MutationTaster, has more than 4,000 citations in the scientific literature.

ASK

- Co-development and/or cooperation with diagnostic labs for testing of MutationSearch
- Partnerships with sequencer manufacturing companies to test and integrate MutationSearch into existing pipelines
- Collaboration with geneticists/physicians to incorporate special needs into diagnostic sequencing
- Collaboration with patient organizations to create meaningful reports
- Venture capital and angel investors to discuss seed funding for a high-growth target market
- Venture capital and angel investors

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KEYWORDS

Whole Exome or Genome Sequencing (WES/WGS),
Bioinformatics, Translational Genetics

NETWORKING AND QA 8:45 PM



Aurelia: Monitoring Brain Perfusion During Anesthesia and Improving Perioperative Outcomes

During surgery, the anesthesiologist is the guardian of patient safety and protects physiological homeostasis. Currently, this is done via various invasive and non-invasive devices that monitor physiological biosignals. Unfortunately, millions of patients undergoing mid to high-risk surgery experience perioperative complications, which only emerge later after the anesthesia wears off. These perioperative complications can have severe consequences on the brain (postoperative delirium, postoperative cognitive dysfunction, intraoperative stroke), on the spinal cord (perioperative nerve damage), on the heart (perioperative cardiac ischemia), on the kidneys (perioperative acute renal failure), and on the intestines (perioperative intestinal ischemia). These complications dramatically increase the risk of postoperative morbidity and mortality and related health care costs. There is one common cause: episodic critical disruptions in brain perfusion during anesthesia, which lead to neural network damage and affect the brain and multiple other organ systems.

Although the anesthesiologist is equipped with multiple monitors, no system currently exists to track global brain perfusion non-invasively and effectively. Charité Anesthesiology and their technology partner SectorCon have developed Aurelia, a prototype sensor-based system that non-invasively tracks brain perfusion. This system can provide vital information and be a powerful asset for the everyday anesthesiologist, enabling them to implement personalized hemodynamic strategies, maintain adequate brain perfusion, and ensure optimal physiological homeostasis. The elusive biosignal of brain perfusion would finally be unlocked, which could improve perioperative outcomes for all patients undergoing anesthesia.

Project Aurelia is powered by an interdisciplinary team of anaesthesiologists (Prof. Sascha Trekatsch, Dr. Michael Nordine) and technical experts (SectorCon's Roland Kopetsch, Philipp Käferstein) that are pioneering the development of non-invasive anesthesia monitoring for the digital age. Aurelia aims to be the go-to solution in every operating room to reduce perioperative complications.

ASK

- Team members
- Business/venture development
- Product development
- Data scientist
- Cooperation partners for clinical testing



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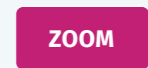


AURELIA

KEYWORDS

Anesthesiology, Perioperative Monitoring, MedTech

NETWORKING AND QA 8:45 PM





DAGI: Keeping Your Child With Congenital Heart Disease Safe at Home

Congenital heart disease is the most common birth defect in humans, affecting 1 in 100 newborns. In Germany, over 4200, children undergo lifesaving open-heart surgery each year, of which over 60% need surgery in the first year of life. Advances in cardiovascular medicine and surgery have led to a steep decline in mortality in Western Europe in the past three decades. Improved survival brings new challenges: Children with the most severe heart defects need close medical surveillance and, therefore, stay in hospital for several weeks, months, or even years. Long periods of hospitalization are associated with significant costs and cause an emotional burden for children and their families. To improve care for these vulnerable patients, the team has developed a remote patient monitoring solution, DAGI, to facilitate earlier discharge and conduct medical surveillance at home. The DAGI app is tailored to the specific needs of patients with congenital heart disease and combines daily monitoring of vital parameters, medication adherence, information, and a chat function with a state-of-the-art interface for health professionals.

Team aims to improve medical care and quality of life for children with congenital heart disease. In the future, they would like to create a companion solution for all patients with congenital heart disease to develop, validate, and monitor new therapies.

Dagi's team combines a passion for medical innovation with world-leading clinical and scientific expertise. The team is supported by advisors in legal affairs, marketing, as well as research methodology and statistics.

- ASK
- Cooperation with insurance companies for feasibility study
 - Cooperation with clinical institutions for clinical validation
 - Partnership with technology industry for co-development

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DAGI

KEYWORDS
Pediatric Cardiology, Congenital
Heart Disease, Remote Monitoring

NETWORKING AND QA 8:45 PM

ZOOM



PerMitra: Optimization Tool for Heart Valve Surgery

In Europe, mitral valve regurgitation is a heart condition that affects 2.4% of adults over age 40. As the heart contracts, blood flows into the systemic circulation, but for those with this condition, blood also problematically flows backward into the atrium because the valve can no longer close. As the condition progresses, heart failure and dyspnea are the consequences. The standard therapy is surgery. Here, annuloplasty rings can be used to reduce the valve's diameter to allow the valve leaflets to close again.

PerMitra was developed to support surgeons' choice of the optimal ring model/size, streamline clinical decision-making, and improve patients' outcomes post-procedure. PerMitra combines image-based models of a patient's unique heart structure with digital models from commercially available annuloplasty rings. The key technology is a fast geometric simulation that shows how a particular ring model would change the anatomy of a patient's heart. This tool allows surgeons to simulate personalized strategies before surgery and to visually demonstrate them for discussion, both with the team and with the patient.

In the future, Team PerMitra plans to expand the scope of their modeling and simulation approach to other cardiac surgical and interventional techniques and devices. The long term vision is to support complex, whole-heart interventions through the adaptation of patient-specific anatomical models.

PerMitra is powered by a team of cardiac surgeons and AI experts with complementary core competencies and a shared understanding of how to improve cardiac interventions. The team has a broad network of international research partnerships with industry, academia and hospitals

- ASK
- Original equipment manufacturers (OEMs) for distribution cooperation
 - Cooperation with clinicians interested to support a feasibility study
 - Cooperation with cardiac surgery units for clinical trials and further product development
 - Team members: business, regulatory, product development

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KEYWORDS
Heart Valve Surgery, Artificial
Intelligence, Therapy Simulation,
Decision Support Tool

NETWORKING AND QA 8:45 PM

ZOOM



WePath: A Platform-Based Global Network for Pathology Expertise

Pathology is the study of human disease and is central to medicine. In recent years, pathologists' workload has steadily increased, and their work has also become more complex with precision diagnostics and personalized therapies. The number of oncology studies that require histopathological expertise continues to rise. At the same time, there is a decreasing number of pathologists worldwide due to a wave of retirements and an insufficient number of trainees. As a result, the recruitment of suitable pathologists can be difficult for preclinical and clinical trials as well as for the healthcare system.

Pathology is going digital, which offers various new opportunities for routine diagnostic work. The WePath platform aims to help the pathology community take advantage of these new opportunities by providing access to a global network of experts. WePath takes collaboration to a new level by integrating incoming and outgoing cases in real-time and making other pathologists available at your fingertips.

The WePath community creates new high-potential opportunities to conduct preclinical and clinical trials and to clinically validate AI solutions. For digital clinical studies, the platform can manage cases, specimens, and the generated data together in one place to streamline organizational processes and assure regulatory compliance. Pharmaceutical and AI software companies can also gain access to the clinical expertise of human diagnostic pathologists for all subspecialties, regardless of workload and time constraints.

In the interdisciplinary WePath team, pathologists, mathematicians, biochemists, and computer scientists are working together to build the WePath platform. The team brings together colleagues with many years of experience in digital pathology at Charité, in North America and Southern Europe as well as highly motivated young computer scientists. Their expertise includes pathology, digital pathology, image processing, AI and software architecture.

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KEYWORDS

Digital Pathology, Second Opinion,
Platform, Digital Clinical Trials, R&D

NETWORKING AND QA 8:45 PM

ZOOM

ASK

- Cooperation Industry for feasibility study
- Cooperation CRUs for clinical trials
- National and international pathologists platform experts
- Team members: business/venture and product development

MyaLink: A Monitoring Platform Solution for Orphan Diseases in Neurology

Team MyaLink has developed a solution to provide better care for patients with neurological orphan diseases. MyaLink believes that every patient—no matter the rarity of disease—should have access to a specialist when they need one. Physicians should be able to monitor patients over time and react to acute events when necessary.

The team has developed a platform solution for neurological orphan diseases that remotely monitors patients' vital parameters and tracks their condition daily. Over time, physicians can get a better overview of disease progression, rather than a quick snapshot during an in-person visit. MyaLink can help prevent expensive crises and ICU stays through the early detection of severe situations. The real-world data can also be very valuable for novel orphan drug development and post-market surveillance.

MyaLink's first use case is myasthenia gravis (MG), a chronic orphan disease that causes muscle weakness and affects people of all ages. MG frequently fluctuates and affects the respiratory muscles, sometimes leading to life-threatening crises or death. Monitoring with MyaLink provides patients with support from a specialist when they feel unsafe and have urgent questions. If a patient's vital parameters indicate an impending crisis, the physician can remotely adjust the dosage of immunosuppressive medication. This can prevent a severe crisis, reduce the cost and burden of disease, and empower patients to cope with and manage their chronic condition.

MyaLink is powered by a team of neurologists and researchers and is part of the largest nationally certified integrated myasthenic center in Germany. MyaLink works with their tech partner, Qurasoft, and the German Myasthenia Association.

ASK

- Partnership with insurance companies for feasibility study and clinical trials to validate solution
- Co-development with industry partners to explore further disease areas and therapy development
- Team members: market access, business, product, regulatory affairs



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KEYWORDS

Remote Monitoring, Telemedicine,
Digital Platform Solution,
Myasthenia Gravis, Orphan Disease;
Empowerment

NETWORKING AND QA 8:45 PM

ZOOM

NEXT CALL FALL 2021!

Keep Updated Here:

www.bihealth.org/de/digital-labs

After the keynote and pitches, meet each project team in individual breakout rooms and network with the Berlin digital health ecosystem.

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