DRCMR

DANISH RESEARCH CENTRE FOR MAGNETIC RESONANCE

40 YEARS

REGION H Amager og Hvidovre Hospital

DANISH RESEARCH CENTRE FOR MAGNETIC RESONANCE

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THANK YOU

CELEBRATING 40 YEARS OF SCIENTIFIC DISCOVERY

What began in the spring of 1985 with a visionary donation from flamboyant travel magnate Simon Spies, enabling the installation of Denmark's very first human-use MRI scanner, has matured into a national cornerstone of biomedical research.

Over four decades, DRCMR has attracted a remarkable constellation of researchers and clinicians, whose combined efforts have forged a dynamic, world-class research environment. It is this intellectual vibrancy and scientific rigour that have ensured DRCMR's enduring position at the forefront of magnetic resonance imaging in Denmark. That status was formally recognised in 2014 when the Capital Region of Denmark honoured the centre with the prestigious Center of Global Excellence in Health award.

There is no shortage of stories to tell — of breakthroughs, collaborations, and quiet revolutions in imaging science. Which is why the leadership at DRCMR has chosen to mark this milestone with a commemorative publication: a curated selection of some of the most defining moments from 40 years of pioneering MR research. This volume does not claim to be exhaustive. Rather, it is a prelude — an invitation to explore further. For readers seeking more detail or eager to delve deeper into the centre's work, we warmly refer them to DRCMR's website and annual reports.

At heart, this jubilee publication is also a thank you — a heartfelt salute to the many individuals who have shaped DRCMR into the success story it is today.

It is with deep gratitude that we also extend thanks to:

- the regional leadership and hospital management, for their unwavering support through the years;
- the public and private foundations whose generous funding has powered DRCMR's scientific ambitions; and
- our many research partners, without whom world-class collaboration would not have been possible.

Here's to the past 40 years — and the many discoveries yet to come.

Hartwig R. Siebner
Professor, Head of Research DRCMR
Department of Radiology and Nuclear Medicine

Karam Sidaros
Head of section / Researchcoordinator DRCMR
Department of Radiology and Nuclear Medicine

A GIFT THAT CHANGED EVERYTHING

In the final chapters of his life, the terminally ill Simon Spies — Denmark's eccentric travel magnate — was admitted to Hvidovre Hospital on several occasions. So deeply moved was he by the care and compassion shown to him that, during one meeting with the hospital's chief physician, he swept his arms wide in a typically theatrical flourish — a "whatever you wish for, you shall have" gesture. Spies kept his word. This is the story of the time leading up to a quiet medical revolution: the installation of Denmark's very first MRI scanner in May 1985.

A TRANSFORMATIVE DONATION

In 1983, a curious sight caught the attention of patients and staff at Hvidovre Hospital. Simon Spies, the nation's flamboyant "travel magnate", was seen pacing the corridors, clutching his own down duvet. Though the once iconic beard and wild hair were long gone, and the neon wardrobe of the 1970s had been replaced by more subdued attire, the force of his presence remained unmistakable. Wherever he went, people noticed. Doctors, nurses, fellow patients — all felt the ripple of Spies' magnetism.

Spies had been admitted to Hvidovre with incurable liver disease, undergoing several stays between 1983 and his death in April 1984. The tests were plentiful and painful - liver biopsies among them - but by all accounts he remained deeply appreciative of the care he received. So much so, in fact, that he made a bold promise to the hospital's head physician, Einar Krag: he would leave them a gift. Not a token of thanks, but a transformative donation — one that would ease the suffering of future patients, sparing them, if possible, from the invasive procedures he had endured. It would be a gift that could truly make a difference.

Jørgen Funder from the Copenhagen Hospital Sector and Janni Spies. Excerpt from the magazine fra B.T. on the 28th of june 1984.

THINK BIG

Today, private donations are the financial lifeblood of innovation in public healthcare. But in early 1980s Denmark, the idea was practically unheard of. True, Rigshospitalet had recently received a generous contribution from the Mærsk family — but such gifts were rare, and the culture around them hesitant. Perhaps that's why Krag and his colleagues initially responded with caution when Spies made his offer.

Some sources say Krag requested a laboratory technician's salary. Others recall a proposal to fund an ultrasound machine. But all agree on one thing: Spies wasn't impressed. "Think bigger," he told them. Eventually, Krag returned with a more ambitious idea. A revolutionary piece of technology — still in its experimental

infancy – that might not replace liver biopsies, but could hold enormous promise across diagnostics more broadly. It was, of course, the magnetic resonance imaging scanner. An MRI.

A VISIONARY LEAP

On Spies' initiative, a delegation was formed. Erik Juhl, Einar Krag, and senior consultants Anders Uhrenholdt and Kjeld Winkler travelled abroad to investigate the few hospitals in the world already trialling MR scanners. They returned persuaded: the technology, though new, was mature enough to justify the investment. Simon Spies agreed.

"It was with joy that Simon gave the large sum of money to the hospital..."

"We were quite alert when we had to make the decision to invest in the MR scanner in 1983" recalls Erik Juhl, then senior consultant at Hvidovre and later director of the Capital Region's hospital services. "It would be the first scanner of its kind in Denmark. Internationally, the technology was still very new and relatively untested, and a private donation of 20 million kroner - that was very unusual, and above all, it was a lot of money. Was an MR scanner really the right investment for the patients and for research? We believed in it, but to be honest, we were also a bit unsure.

"It was a very modern and forward-thinking choice of equipment. And it was an expensive choice. But it was with joy that Simon gave the large sum of money to the hospital to ease the situation for other patients. It is interesting to think about how he was ahead of his time in that way as well.." says Janni Spies in 2015.

A GIFT REJECTED

In a twist that borders on the farcical, the initial response from Copenhagen's Hospital Directorate was: no, thank you. The reasoning? Installing an MRI scanner would require significant construction at Hvidovre – in the end, a dedicated 450-square-metre wing was built. The running costs, to be borne by the hospital, would be high. More sensitive still, the idea of a private citizen funding a public hospital's technological leap was politically fraught. Spies wasn't just donating equipment – he was, in a sense, intruding into the business of state healthcare. But the rejection didn't faze the irrepressible tycoon. With characteristic wit, he penned a sharply worded letter, calling the decision "short-sighted and foolish", urging the Directorate to reconsider. Eventually, they did. The donation was accepted.

A RESEARCH REVOLUTION

In June 1984 – just two months after Simon Spies passed away – Janni Spies handed over the donation in a modest, official ceremony. At the time, Einar Krag told the newspaper BT that the gift marked a "giant leap forward": only five scanners of equivalent quality existed worldwide. Four were in the United States. The fifth was operating experimentally in West Germany. Installation of the 1.5 Tesla scanner followed in May 1985, nearly a year later. Under the terms of the donation, the machine was to be used 75% for research, and 25% for clinical diagnostics during its first three years. While Spies had insisted on real patient benefit for the general danish public, it was clear that such a pioneering technology would require rigorous research and development.

Indhejsning af den første MR-skanner den 11. december 1984. Skanneren var 3 meter lang og vejede over 7 tons. Kilde: Polfoto.

With the donation came not just machinery, but a mandate for scientific progress. As a result, Hvidovre Hospital didn't just receive one of the most advanced diagnostic tools in the world — it founded a research centre that would go on to become a global leader in MRI innovation.

THE SIEMENS PARTNERSHIP

Following field studies abroad and preliminary negotiations with the handful of MR scanner suppliers available at the time, Siemens was ultimately chosen as the provider of what soon became widely known across the country as the "Spies Scanner." Siemens was eager to gain not just a contract, but a partner in the development of new clinical applications for MR technology; according to the terms of the agreement, the scanner was to be used primarily for research and the advancement of what was still a nascent and evolving field. It marked the beginning of a fruitful and close-knit collaboration between DRCMR and Siemens —

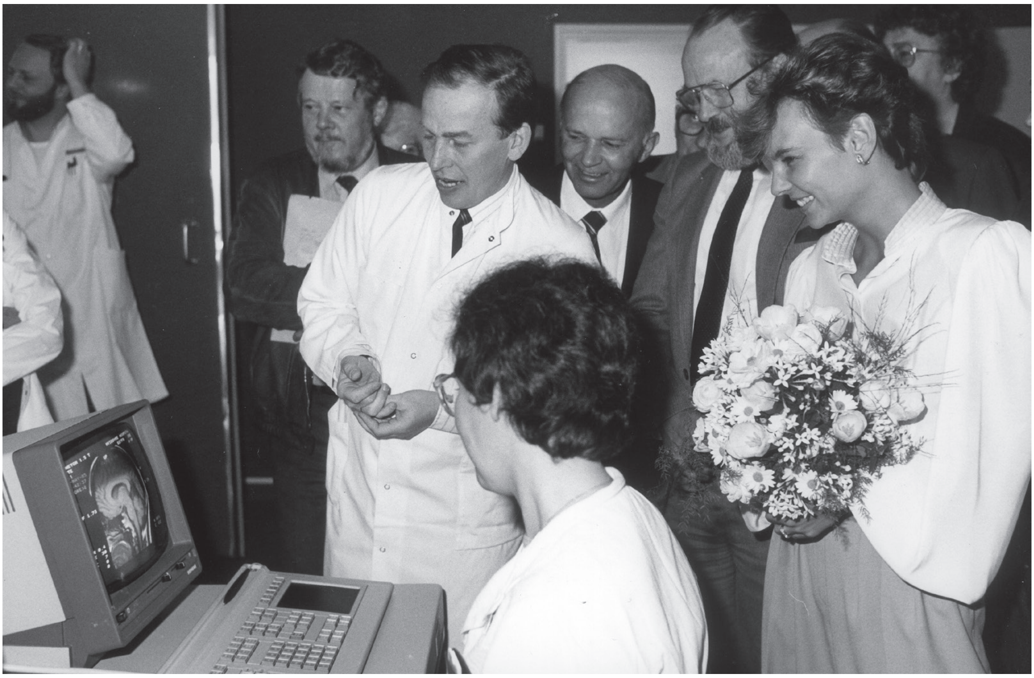
Photo: Hanne Juul/Aller/MEGA

BETTER EXAMINATIONS AND TREATMENTS

During her husband's illness in 1983-84, Janni Spies was by his side during hospital stays and meetings with the hospital's senior consultants. Since then, she has carried forward his thoughts and wishes in her role as chair of the Simon Spies Foundation, and today she takes great pride in the results that the first – and later several other – donations from the Spies Foundation to DRCMR have made possible:

"It is with great pride that I can reflect on the fact that the seed for an entire MRI department, a research centre, and a highly specialised field was planted by Simon. I take joy in the knowledge that so many Danes have received better examinations with greater detail and improved treatment as a result of Simon's desire to bring joy and benefit to others. The MRI scanner was the first major donation from the Spies Foundation, and a donation that held great personal significance for Simon himself. That is why DRCMR has since received special attention from the Spies Foundation: It has been natural for us to carry forward the ideas and wishes that Simon himself had the opportunity to express.."

Janni Spies, chair of Simon Spies Fonden

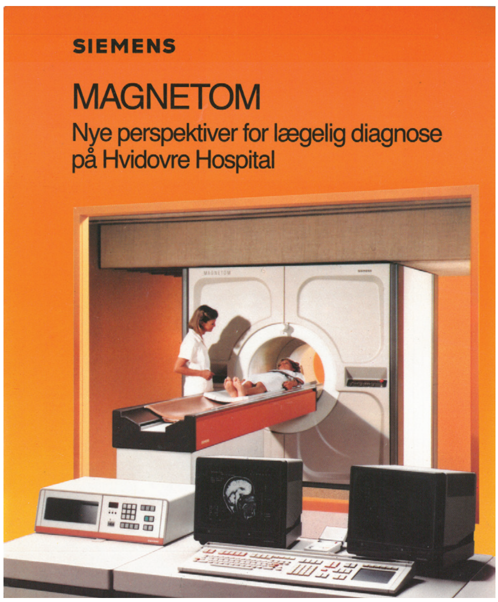


Head of Department Ole Henriksen and Jannie Spies at the inauguration of the Spies-scannere on the 8th of may 1985. Kilde: Polfoto

one that would prove instrumental in propelling the centre to the forefront of MR imaging innovation, both at home and on the international stage. No less significant in those formative years was the internal alliance with the Department of Clinical Physiology, which lent staff to the fledgling MR unit and acted as a vital support arm to its next-door neighbour.

It was from that very department that DRCMR's first director was drawn. Hvidovre Hospital's executive board appointed senior consultant Ole Henriksen to lead the new unit, valuing his firm grounding in clinical science and his ability to steer both patient care and pioneering research.

The decision paid dividends: it was, to a considerable extent, Ole Henriksen who shaped DRCMR's identity during its trailblazing early years.



THE HISTORY OF MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) originated from Isidor Isaac Rabi's Nobel-winning 1937 discovery and has since evolved into a cornerstone of modern diagnostic medicine. Key breakthroughs by Falix Bloch, Edward Purcell, Paul Lauterbur and Sir Peter Mansfield - all Nobel laureates - transformed MRI into a practical and powerful clinical tool. The technology's impact is reflected in the multiple Nobel Prizes awarded for its development, underscoring its status as one of the most significant medical advances of the 20th century..

THE STORY BEHIND THE SCANNER

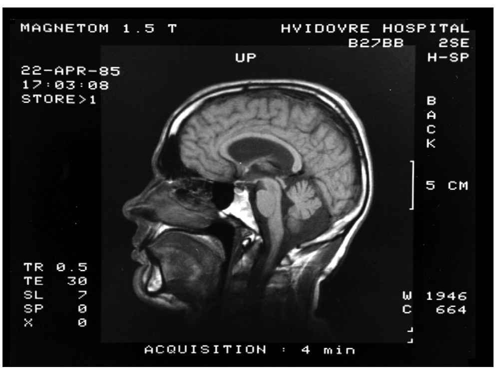
It is, in many ways, the paradox of magnetic resonance imaging: a technology born nearly a century ago, yet still young in the grand theatre of clinical medicine. The concept first emerged from the blackboards of physics in 1937, when American physicist Isidor Isaac Rabi demonstrated that the nuclei of atoms could be coaxed into motion by radio waves. It was an esoteric discovery at the time — but one that would, decades later, allow us to see the human brain in breathtaking detail without ever lifting a scalpel.

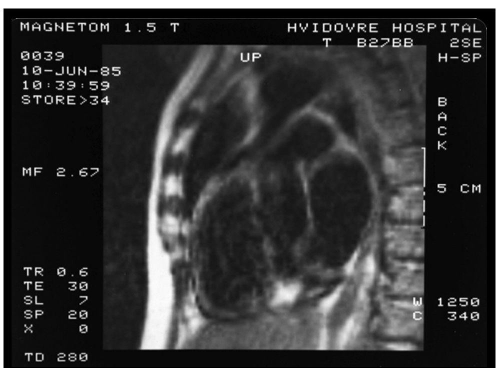
For this revelation, Rabi was awarded the Nobel Prize in Physics in 1944. But it would take the better part of the 20th century for magnetic resonance to escape the lecture hall and enter the hospital ward.

It wasn't until the early 1950s that Rabi's intellectual heirs, Felix Bloch and Edward Purcell, brought the theory into the tangible world. Working independently, they refined the method, liberating it from the vacuum chambers of particle physics and applying it to liquids and solids — a leap akin to transforming an idea into an instrument. Suddenly, researchers could peer into the molecular make-up of a substance without laying a finger on it.

THE FIRST IMAGES

Progress was slow but steady. Then, in 1971, a bold claim was made by another American physicist, Raymond Damadian. He published a study suggesting that magnetic resonance technology could distinguish between healthy tissue and cancer. Though his method proved impractical for clinical use, it laid a crucial foundation.





Examples of some of the first MR images captured with the Spies scanner: brain (left) and heart (right).

Source: Polfoto

Later that same year, the breakthrough finally came. Paul Lauterbur, a chemist by training, succeeded in producing the first images using magnetic resonance. His work opened a new frontier in diagnostic medicine and earned him the Nobel Prize in 2003 – shared with the British physicist Sir Peter Mansfield.

Mansfield's contribution was transformative: he developed techniques that drastically accelerated scan times, with some measurements taking less than a second. It was a feat of precision engineering that made MRI viable as a real-world diagnostic tool.

In 1977, Mansfield unveiled the first MRI image of a human body part – a finger. Just three years later, the University of Aberdeen in Scotland installed the first full-body MRI scanner. Its very first clinical use revealed a tumour in a woman's breast that had already metastasised to the bones – a harrowing diagnosis, but proof of concept beyond doubt.

A YOUNG GIANT

And so, when Danish travel magnate Simon Spies decided in 1983 to fund Denmark's first MRI scanner, the technology was still in its clinical infancy – promising, yes, but largely unproven. The scanner was inaugurated in 1985 at what would become the Danish Research Centre for Magnetic Resonance. It marked the start of Denmark's journey into one of the most powerful diagnostic tools in the world. From that first installation, the technology has matured rapidly. Today's MRI machines are capable of producing astonishingly detailed, high-resolution images of the body's internal organs, joints, and tissues – all without a single incision.

Indeed, the technology is rightly hailed as one of the most epoch-making breakthroughs in 20th-century medical science. Its significance is underscored by many Nobel Prizes awarded to research directly tied to the development of MR imaging – most recently, in the field of medicine, in 2003.

The completed Indomitable (the world's first MR scanner)

From left toright: Drs. Raymond V. Damadian, Lawrence Minkoff and Michael Goldsmith

(Courtesy of FONAR Corporation)

MAGNETIC RESONANCE EXPLAINED

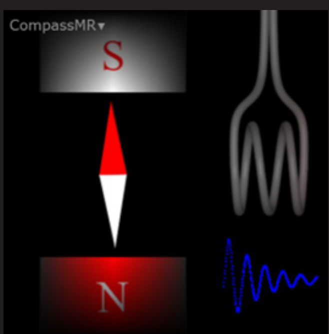
When you lie inside the strong magnetic field of an MR scanner, something extraordinary happens: Your own body becomes slightly magnetic. It is this subtle magnetism that allows the machine to "see" the inside of your body. The phenomenon is rooted in physics: The nuclei of the hydrogen atoms in your body act like tiny magnets, each with a north and south pole. Under the influence of the scanner's powerful magnetic field, these nuclei align, much like compass needles in Earth's magnetic field.

The principle of magneitc resonance is best understood with a simple analogy: Imagine a compass needle suspended within a strong magnetic field. In the drawing below on the left, the field is caused by two magnetic poles (north and south), each attracting an end of the needle.

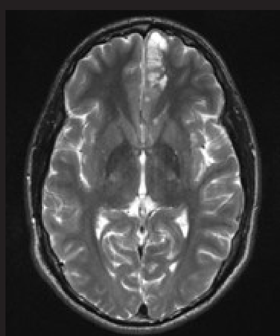
At rest, the needle aligns itself neatly with the field that is vertical in the drawing, but given a push, it will vibrate in the field before it comes to rest again. During this period, the vibration will cause a small oscillating voltage in a nearby coil made of conductive wire. To make the needle or the tissue magnetization vibrate, a current is instead sent through the nearby coil.

This makes the coil magnetic as illustrated by its coloring in the figure below on the right: The north end of the coil will push the needles north end, and attract the south end, so it is rotated slightly out of equilibrium.

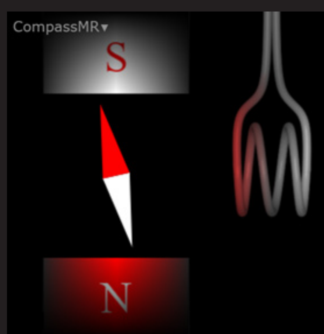
Making the nuclei vibrate is not as simple as flipping a switch, however, since the magnetic pushes are tiny. The coil must repeatedly push the needle in just the right rhythm — tiny pulses, carefully timed — to build up a resonance. It's much like pushing a child on a swing: Push them in sync with the swing's natural motion, and even the gentlest push can send them soaring. Mistime the push, however, and the



When given a push, a compass needle in a magnetic field will vibrate before it comes to rest. This can induce an oscillating voltage (blue) in a nearby coil. In MRI, the tissue magnetization vibrates similarly, and it is the measured strength of the oscillation that is visualized.



Some tissues may cause strong signals that are shown bright, whereas others cause weaker signals colored darker as shown in the MRI of a slice of a living person's brain.

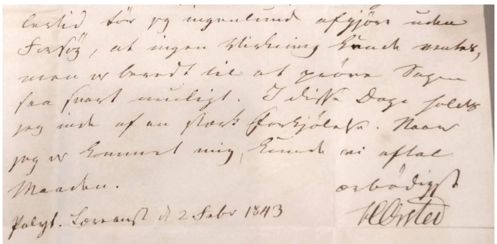


Passing an electric current through a coil will make the coil magnetic as illustrated by its coloring above. It can therefore push and pull other magnets such as the hydrogen nuclei. This is the mechanism through which the tissue magnetization is set in motion during MRI.

swinging will not be impressive – and the child will protest. Afterwards, when the needle still swings back and forth, the movement induces a small voltage in the coil. This is measured and translated into the familiar grey-scale color of an MRI scan. In essence, each point in an MR image reflects how strongly the magnetization of the tissue is vibrating. This elegant dance of physics is illustrated in a locally produced YouTube video, which has now been viewed over 100,000 times – a testament to the fascination that continues to surround the quiet marvels of modern medical imaging. In the video, the MR phenomenon is explored interactively using the online simulator CompassMR found on the DRCMR web page.

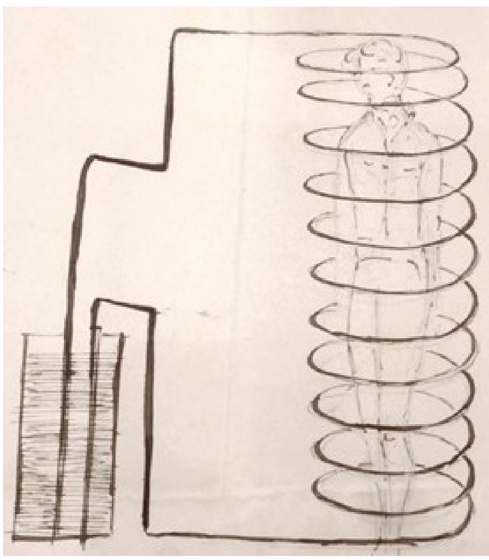
EXTRAORDINARY DRAWING PREDATING MRI BY 130 YEARS

In 2004, a collection of 300 newly discovered letters were acquired by The Royal Danish Library. It included writing from notabilities such as Hans Christian Ørsted, the discoverer of electromagnetism in 1820, and Hans Christian Andersen, the author of fairy-tales, to Just Mathias Thiele, author, professor, and secretary for the Danish King.



An exerpt from a letter from H.C. Ørsted to J. M. Thiele from a collection of 300 newly discovered letters were acquired by The Royal Danish Library.

This illustration from around 1843 was found together with a letter from H. C. Ørsted to J. M. Thiele. It shows a main component of a scanner, the coil magnetizing the body, but it predates MRI by 130 years. Obviously MRI was not anticipated by Ørsted: Electromagnetism and Faraday induction were known since 1820 and 1831, repectively, and basic magnetic resonance (MR) is conceptually simple, but in 1843 there was no anticipation of magnetic particles oscillating in the body like compass needles (responsible for the MR signal). Of course, a magnet is not a scanner, and the technology needed a century of maturation before nuclear MR even became possible.



A drawing possibly by H. C. Ørsted discovered among the letters.

The story behind the drawing together with the full letter from Hans Christian Ørsted, can be found at the DRCMR web page: www.drcmr.dk/oersted

1985-1995
A SOARING START

New Discoveries by the Day - During the first decade of DRCMR's existence, research was very much at the heart of its mission. The centre's director, consultant physician Ole Henriksen, was above all a man of science, and doctors and physicists from across the globe made their way to Hvidovre to learn from their Danish counterparts. At the same time, patients still had to be scanned—using a piece of technology with which no one had any real experience. It was a case of laying down the tracks even as the train was already moving forward.

INTO THE UNKNOWN

When the so-called Spies scanner — Denmark's first MRI machine — was switched on in 1985, it marked not just the arrival of a powerful diagnostic tool, but the birth of an institution. In those early years, the newly minted MR department and its affiliated research centre — now known as the Danish Research Centre for Magnetic Resonance (DRCMR) — were fuelled by a sense of pioneering spirit and unabashed scientific curiosity. What the researchers and clinicians had in their hands was, by all accounts, a technological marvel, scarcely tested, barely understood, and capable of extraordinary things. The 1.5 tesla Siemens scanner was one of only a handful in Europe. "DDRCMR was a very exciting place to be in the mid-80s." recalls Dr Margrethe Herning, who worked at the centre from its inception until 2006, the final 17 years as a senior consultant. "But it was also a difficult place; I think there were only two other scanners in Europe at that time. And very few in the US and the rest of the world. There were no textbooks on MR

"DRCMR was a truly exciting place to be in the mid-1980s."

diagnostics and hardly any articles. So we had to create our own foundation of experience. It grew day by day, but there were no answer keys."

A STORY OF RAPID ASCENT

Herning played a crucial role in establishing the centre's diagnostic capabilities. Though DRCMR was set up with a strong emphasis on research, clinical diagnostics soon followed. The images produced by the Spies scanner were of unprecedented diagnostic quality – just as flamboyant travel tycoon Simon Spies had envisioned when he donated it. The scanner quickly proved indispensable, transforming care for patients from across Denmark.

"In those first years, we had visitors from across the globe..."

Indeed, its success would ultimately embarrass the original sceptics in the Copenhagen Hospital Authority, who had initially declined Spies' gift out of concern for ongoing costs. In a sharp reversal, the scanner became a net asset – its use by patients from other counties generated revenue that directly funded DRCMR's growth.

This influx allowed for rapid expansion, new hires, and greater academic freedom. The centre's reputation blossomed accordingly. "The MR scanner held a special position." recalls Professor Jens Henriksen of Hvidovre Hospital's Department of Clinical Physiology. "It was physically located at Hvidovre Hospital, but

THE MOST IMPORTANT MILESTONE OF MY CAREER

From its very beginning in 1985, DRCMR has been an international workplace that, with its progressive and highly qualified professional environment, attracts young researchers from both Denmark and abroad. Professor of MR Physics at Lund University (1999-2019) and Head of Lund University Bioimaging Center (2008-2018), Freddy Ståhlberg, was the first foreigner at DRCMR. He worked at the center from 1985 to 1994 and continued living in his home in Lund the entire time – resulting in a staggering 5-hour daily commute! Still, he never once doubted his choice of workplace:

"The early years at DRCMR were a time marked by enormous enthusiasm from everyone working at the center. There was a true pioneering spirit, with people working evenings and nights to develop the right codings so we could create new images with the machine. We were working with Denmark's first truly large magnet – and with the most powerful MR scanner in all of Scandinavia. We were a close and relatively small group of physicists and doctors – and that time will always stand out as a golden moment in my entire career. It is the most important milestone in my professional life, where I was propelled forward, and where I formed friendships and professional ties for life."

Freddy Ståhlberg, Professor Emeritus Lund University, Employed at DRCMR 1985-94
Head of Lund University Bioimaging Centre 2008-2018
Professor of MR-Physics, Lund University 1999-2019

administratively, in the first years, it fell directly under the Copenhagen Municipal Hospital Directorate. And from being something the directorate was somewhat hesitant about, the entire department quickly became an example that was consistently highlighted: This was another way of doing things. Completely different from what people were used to – but clearly successful."

THE VISIONARY AT THE HELM

Much of DRCMR's early success is indelibly linked to its first director, Ole Henriksen. Poached from the Department of Clinical Physiology, Henriksen was not without his critics – no strong leader ever is – but his intellect and ambition were widely admired. "Ole was razor-sharp," says retired engineer Poul Ring, who was responsible for the centre's computing infrastructure.

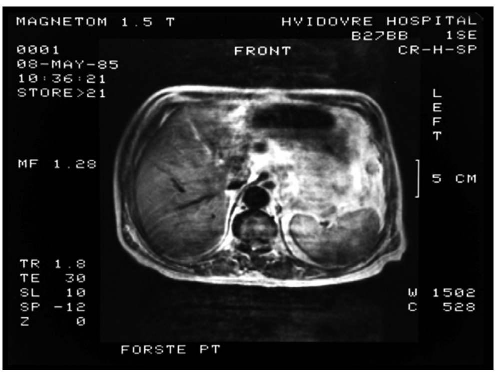
"He was a trained doctor, but as an engineer with responsibility for the installation and operation of the computers in the department, I had a good back-and-forth with him. As a leader, he may have been a bit autocratic, but he was innovative and had great ambitions for the department. And he succeeded with his ambitions: A great deal of very good research was conducted under his leadership."

”...We were in the process of building something entirely new

GLOBAL INTEREST

From the outset, DRCMR was uniquely positioned to make a global impact. At a time when most of the world's MRI scanners were being used for clinical diagnosis – particularly in the US – Denmark was developing a dedicated research hub around its scanner. This was virtually unheard of.

"Especially in the early years, we had visitors from across the globe to observe and learn from this very special department at a small Danish hospital that was conducting research in MRI." recalls Pia Olsen, a radiographer at the DRCMR from 1985 to 2014. "In that way, it was a very exciting place to work: there was great attention on what we were doing – and at the same time, we were in the process of building something entirely new.."



Cross-section MRI imgae of the body through the liver, of the first patient scanned at Hvidovre Hospital, the 8th of may 1985.

Staff left to right: Carsten Thomsen, Helle Simonsen, Margrethe Herning, Hernik Larsson, Anne-Marie Vind, og Pia Olsen.

TROUBLE ON THE HORIZON

For nearly a decade, everything pointed upward, and steeply so. But by 1993, cracks began to form. Financial and structural problems emerged, and the centre faced its first real crisis. More hospitals across Denmark were acquiring their own MRI machines, drying up the stream of referred patients that had previously funded DRCMR.

Head of Department Ole Henriksen, Mayor Jørgen Frederiksen, Peter Christoffersen and hospital director Jørgen Funder at the inauguration of DRCMR's second MRI scanner in 1989.

In 1994, a major reorganisation saw the formation of the Capital Region Hospital Partnership. Despite Henriksen's appeals, no special considerations were made for DRCMR. The centre received no additional funding to offset the loss of income from external patients.

The following year, matters took a darker turn. While jogging around Copenhagen's Damhussøen lake, Henriksen suffered a cardiac arrest. Though resuscitated, he was left with such severe complications that he could no longer continue in his role. The man who had so resolutely steered the centre through its formative years was, in an instant, gone from the helm. Thus, DRCMR was in a position to welcome its next head – Professor Olaf Paulsen from Rigshospitalet.

INCREASINGLY FINE CROSS-SECTIONS OF THE BRAIN

DRCMR has had a long-standing collaboration with the paediatric neurologists at Rigshospitalet: Since the early 1990s, Rigshospitalet has referred children and adolescents with epilepsy, who are to undergo surgery for their condition, to MR scanning at Hvidovre Hospital. This is a highly specialised treatment, with approximately 20 children per year being sent for MR scans before and after surgery; the scanning programme itself is also highly specialised and extensive. It takes about 1½ hours to interpret the scan results afterwards.

"Our collaboration with the neuroradiologists from DRCMR centres around the epilepsy surgery conferences. Here, the radiologists from Hvidovre come to Rigshospitalet and present their images, which are absolutely crucial in determining whether the children can undergo surgery. Many studies have shown that a standard MR scan detects significantly fewer lesions than a highly specialised department. Without these findings, we are not able to operate, and over the years, the neuroradiologists have become increasingly skilled at performing the scans. As scanners improve, we're able to produce increasingly thinner cross-sections of the brain – and detect even more lesions"

Peter Uldall
Chief physician, professor, dr. med., BørneUngeKlinikken, Rigshospitalet

Translated from DRCMR's 30th Anniversary Booklet

1995-2005
CONSOLIDATION

Close Ties to Rigshospitalet - Throughout the 1990s, DRCMR continued its growth. The centre's new director held a joint appointment at both DRCMR and Rigshospitalet, and it was largely thanks to his network and tireless work ethic that the centre was able to invest in new and more advanced scanners, attract an increasing number of highly qualified staff – and forge even closer ties with both researchers and clinicians at Rigshospitalet.

A SUDDEN CALL, A LASTING LEGACY

It was in the summer heat of August 1995 when an unassuming yet resolutely dedicated Professor Olaf Paulson received a phone call that would quietly reshape the course of Danish brain research. The call came not from a colleague, but from Erik Juhl, then the chief executive of the Capital Region Hospital Trust.

On the line, Juhl offered Paulson the directorship of DRCMR. With the sudden illness of the incumbent director, Ole Henriksen, it was an offer that demanded an answer in the here and now, recalls Paulson: "I said that it was a great honour to receive the offer – to which Erik Juhl replied: "Excellent. Can you start tomorrow?" That's how sudden it was. But there was also a need for some leadership, because Ole Henriksen had just received a major EU grant for the standardisation of MR methods with England, the Netherlands, France and several other countries. So I was thrown into it without warning.."

"...it was a great honour to receive the offer..."

A TEMPORARY TASK TURNS INTO A FIFTEEN-YEAR CHAPTER

Initially, Paulson's appointment was billed as a stopgap – a temporary arrangement while the future of the centre, located at Hvidovre Hospital, was decided. It was thus natural for him to juggle dual roles at both Hvidovre and his home institution, Rigshospitalet, but transition turned into tenure. For the next 15 years, Olaf Paulson stood at the helm of DRCMR, while also continuing to lead the Neurobiology Research Unit at Rigshospitalet.

"That meant that we gradually developed a very close collaboration with the researchers at Rigshospitalet. Olaf Paulson was a skilled and well-respected neurologist, and therefore a great deal of brain research was carried out during the years he was head of DRCMR. At the same time, he was good at securing funding – not only for new equipment, but also for research projects: In those years, many exciting projects came to DRCMR because of his network.," recalls retired radiographer Pia Olsen.

DENMARK'S FIRST 3 TESLA SCANNER

Early in his early tenure, Paulson began exploring avenues to equip DRCMR with new state-of-the-art technology. In 1997, he embarked on a mission to acquire a new whole-body scanner with twice the field strength of the original Spies-funded model – a 3 Tesla unit. Once again, the Spies Foundation stepped in, this time to mark what would have been Simon Spies' 80th birthday.

When the scanner was inaugurated in 2002, it was another first of its kind in Denmark. It opened the door to an entirely new discipline: functional MRI, which enabled scientists to map the brain's signals as they related to physical and cognitive function.

A HERCULEAN APPLICATION EFFORT

But scientific ambition rarely rests. By 2003, Paulson had already turned his gaze towards an even more powerful 7 Tesla scanner. In early 2005, a university-appointed committee determined that Copenhagen did indeed require such high-end imaging equipment.

Yet progress was anything but linear. The first funding application was rejected. Compounding the setback, administrative restructuring saw the dissolution of the Capital Region Hospital Trust in favour of a new regional system. Only in 2008 was Paulson permitted to reapply.

A year later, the Danish Agency for Science, Technology and Innovation agreed to cover 40% of the scanner's DKK 66 million price tag. The remainder was secured through a successful application to the John and Birthe Meyer Foundation, submitted jointly with Hvidovre Hospital's deputy director Torben Mogensen and Paulson's eventual successor, Hartwig Siebner.

"It is a very long process and an exceptionally large amount of work to secure funding for this type of investment. When I add it all up, I've put in the equivalent of a year and a half's full-time work into the application process to get the 7 Tesla scanner funded. It's completely monstrous to think about what else I could have done in that time." says Olaf Paulson

In 2002, DRCMR received Denmark's first 3-tesla MRI scanner, thanks to yet another donation from the Simon Spies Foundation.

THE RIGHT PLACEMENT

For 15 years – from 1995 to 2010 – Professor Olaf Paulson served as the head of DRCMR, but in fact, his affiliation with the centre did not formally end until Scandinavia's first 7 Tesla scanner was inaugurated in February 2015. It was largely thanks to Olaf Paulson's efforts that the necessary funding was secured and the scanner was acquired. Therefore, it was agreed that he would remain part of the centre until the scanner was in place.

"It is a great satisfaction that, after many years of groundwork and intensive effort, we are now able to put the 7 Tesla scanner into use. It is a national project with participants from several regions, and the application phase was marked by national consensus on locating the 7 Tesla scanner in the Copenhagen area, just as there was support for placing a so-called MEG scanner in Aarhus."

Olaf B. Paulson
Professor of neurology at the Neurocenter, Rigshospitalet og leader of the DRCMR 1995-2010.

CRISIS AND RECONSTRUCTION

Juggling two demanding posts and a relentless stream of funding bids took its toll. Paul Ring, who managed DRCMR's IT systems for many years, remembers Paulson as more administrator than hands-on scientist – a stark contrast to his predecessor. Yet it was Paulson's stewardship that allowed the centre to expand.

The cost of growth, however, was significant. In 2006, a wave of resignations from doctors at the clinical wing of DRCMR left the institute in a bind. A full-scale administrative rebuild was required, and Paulson gave himself six months to achieve it.

"a great deal of internationally recognized research was carried out."

"Fortunately, I was given free rein to recruit new doctors – also internationally. And that meant, among other things, that I was able to hire Per Åkeson, who, together with others, came to play a crucial role in getting the clinic back up and running again in record time.." Olaf Paulson recalls.

Åkeson would later help acquire a hyperpolariser – a device capable of boosting MR signals by a factor of 10,000. Donated by the Spies Foundation in 2008, the machine made possible intricate metabolic studies, such as analysing breast cancer in mice and assessing changes in cardiac metabolism.

ACADEMIC COLLABORATION AT A HIGH LEVEL

At the Center for Clinical Intervention and Neuropsychiatric Schizophrenia Research (CINS), work is being done to classify schizophrenia disorders based on their neurobiological and functional background. The aim is to contribute new knowledge that can lead to new treatment strategies targeted at the disturbances in the individual patient. In the work of understanding the neurobiology of patients with schizophrenia, the researchers describe, among other things, changes in the brain's structure, function, and neurochemistry in the affected individuals, and how these relate to clinical symptoms, cognitive abilities, treatment response, and disease progression. In this context, CINS has had a long-standing and close collaboration with DRCMR.

There are many different competencies gathered at CINS and at DRCMR, and it is precisely this multidisciplinary approach to research that is crucial for creating new results. Together, for example, we have demonstrated the importance of substance abuse for certain of the brain changes seen in patients with first-episode schizophrenia. Among other important findings is that, based on certain functional disturbances (measured with MR scans), one can predict the effect of treatment with antipsychotic medication on some of the severe symptoms associated with the disease. It is an academic collaboration in which the two parties truly cannot do without each other.

Birte Glenthøj
Professor Emeritus of neuropsychiatry at the University of Copenhagen.
Former head of the Center for Neuropsychiatric Schizophrenia Research (CNSR)
& Center for Clinical Intervention and Neuropsychiatric Schizophrenia Research (CINS)

A SHIFT IN FOCUS

In its first decade, DRCMR was a research juggernaut. At one point, it boasted more accepted papers at the world's premier MR conference than any other group on the globe. Yet as the 1990s progressed, research output started to dip.

”It was a very inspiring time.”

In its place came deeper integration with Rigshospitalet, both clinically and academically. The new equipment opened fresh frontiers, including investigations into behaviour and the serotonergic neurotransmitter system – one of the brain's key communication channels. These studies, conducted under the auspices of the Centre for Integrated Molecular Brain Imaging (Cimbi), were led by Professor Gitte Moos Knudsen and funded by the Lundbeck Foundation.

LOOKING TO THE FUTURE

During this period, DRCMR also launched an ambitious longitudinal study of childhood brain development, beginning with a cohort of seven-year-olds who continue to be followed to this day. The project is run in partnership with Professor Terry Jernigan from the University of California, San Diego.

It is, perhaps, a fitting epilogue to Olaf Paulson's tenure: what began with a sudden phone call became a chapter marked by resilience, innovation, and vision. In the quietly humming halls of DRCMR, the echoes of that legacy still reverberate.

”We also began a collaboration with CBS on neuroeconomics, investigating the mechanisms behind gambling addiction. A major dementia project was launched, led by Professor Gunhild Waldemar and colleagues at Rigshospitalet. Research projects on multiple sclerosis were initiated in collaboration with Senior Consultant Morten Blinkenberg, Professor Per Soelberg Sørensen, and Professor Finn Sellebjerg from Rigshospitalet.

In addition, studies on brain plasticity in blindness were conducted in partnership with Professor Maurice Ptito from Canada and Professor Ron Kupers from the Faculty of Health Sciences." says Olaf Paulson. .”Psychiatry also gained an increasingly prominent role. Research was conducted on schizophrenia in collaboration with Professor Birte Glenthøj from the Psychiatric Center Glostrup, and on affective disorders in collaboration with Professor Lars Kessing and psychologist Kamilla Miskowiack from the Psychiatric Center Copenhagen. So a great deal of internationally recognized research was carried out – also in collaboration with Professor Jens Bo Nielsen and his colleague Mark Schram Christensen from the University of Copenhagen, who worked on motor control.”

Paulson is backed by Karam Sidaros, who arrived at DRCMR as a young Master's student in 1997: “It was a welcoming environment to enter. There was serious, hardcore research being done, but the approach was very exploratory; it was playful and less formal. There was a kind of free space, where everyone knew everyone, and the structure was a bit looser than it is today. It was a very inspiring time.”

So inspiring, in fact, that he never truly left DRCMR again. Instead, Karam Sidaros became one of the key figures carrying the centre's development forward: Today, as section head and research coordinator under DRCMR's third director, Professor Hartwig Siebner, he is a central figure in driving MR research forward at the centre.

2005-2015
LOCAL ROOTS, GLOBAL REACH

From the very beginning, the DRCMR cast its gaze outward in the world. But during the 2010s, the dynamic shifted. Increasingly, the world's leading MRI researchers began turning their eyes toward Denmark and the DRCMR too. In 2015, the centre stood as the most internationally diverse research institution in the Capital Region of Denmark. This was no accident. It was the result of a deliberate and ambitious strategy by a new generation of leadership – one that placed global partnerships, top-tier talent, and scientific excellence at the very heart of the centre's identity.

A DIAMOND IN THE ROUGH

As has so often been the case, Olaf Paulson's formidable network proved decisive when the time came to find his own successor at the helm of the Danish Research Centre for Magnetic Resonance (DRCMR). At a research congress in San Diego, a chance meeting between Hartwig Siebner and British neurologist James Rowe — himself a former DRCMR scientist — set the wheels in motion. Rowe, aware of Paulson's quiet search, also knew Siebner: a gifted researcher who had spent the past six years building a thriving research group in Kiel. He brought the two men together. The result? In autumn 2008, Hartwig Siebner moved to Denmark. Two years later, he would take charge of DRCMR.

"I saw enormous potential in DRCMR," says Siebner today, now professor and director of the centre. "It was a clinical environment that took research seriously — and there were challenges, too. It was a rough diamond. It needed shaping before it could truly shine. That's what convinced me to accept the role."

FROM SUPPORT UNIT TO INDEPENDENT FORCE

Siebner came with a plan. At the heart of it was the ambition to turn DRCMR from a supporting player in larger clinical studies into a self-driven research entity — one that would initiate and lead its own projects.

A formal structure followed. In 2010, Siebner introduced the role of principal investigators, appointing senior researchers to head their own groups. This empowered DRCMR to operate with greater independence while fostering dynamic collaborations — not as subordinates, but as equals.

> "I saw enormous potential in the DRCMR."

BUILDING A EUROPEAN POWERHOUSE

Another of Siebner's guiding principles has been targeted recruitment. "We've worked hard to attract the right people — and to make the centre attractive to top researchers across Europe," he explains. "The result is a highly interdisciplinary and international environment."

Today, with researchers from 19 countries, DRCMR is the most cosmopolitan research unit in the Capital Region of Denmark. Its reputation has begun to precede it: researchers from across the globe are increasingly approaching the centre with concrete project proposals, keen to collaborate.

"Hartwig Siebner has given DRCMR not only a new direction but new energy," says section research coordinator Karam Sidaros. "He's deeply invol-

ved in many of the projects and visibly committed to expanding our research profile. The impact has been clear."

WRITING THOUGHTS

Siebner's own research has flourished since relocating. In 2010, he secured a DKK 25 million grant from the Lundbeck Foundation to study how the brain controls movement — essentially mapping the journey from perception to action. Further grants followed. In late 2014, the Novo Nordisk Foundation awarded DRCMR DKK 15 million for a collaboration with the Technical University of Denmark (DTU), aimed at understanding how precise electrical stimulation might enhance brain function.

The centre invested in a state-of-the-art brain stimulation robot — a machine capable of sending electromagnetic pulses through the skull to specific regions of the brain. Combined with MRI imaging, this technology could shed light on treatments such as electroconvulsive therapy for depression.

"This grant marks a new chapter in our collaboration with DTU," says DTU professor Lars Kai Hansen. "You might say we're moving from reading thoughts to writing them. It's bold, it's difficult — and it's fascinating."

TECHNOLOGICAL AND BIOMEDICAL RESEARCH FOR THE BENEFIT OF PATIENTS

Research into MR imaging is a very interdisciplinary field which, in addition to various medical professionals, also involves physicists, engineers, computer scientists, mathematicians, and more. For that reason, the Technical University of Denmark (DTU) has consistently been a central and close partner of DRCMR. In 2000, associate professor Lars G. Hanson completed his PhD project at DRCMR - and today, he splits his working time between DRCMR and DTU where he is the Head of the Biomedical Engineering MSc education, offered in collaboration with the University of Copenhagen.

"MRI development thrives on advances from fields beyond its own, such as magnet and radio wave technology, computer hardware, and artificial intelligence, since MRI's primary constraints are technological rather than fundamental. For instance, nuclear alignment could theoretically be improved by a factor of 10,000 to 100,000, boosting the MR signal proportionally, but this is limited by current magnet technology. In this context, the collaboration between DRCMR and the Technical University of Denmark has proven invaluable. DTU researchers and students with a broad range of backgrounds develop and apply cutting-edge technologies for the benefit of patients and society. Conversely, the knowledge and needs from DRCMR and other hospital environments inspires common research and opens possibilities, , creating a mutually beneficial cycle. Examples are hyperpolarization techniques developed by DTU researchers. They offer the above-mentioned signal improvement factors for specific purposes by circumventing the limits of magnet technology. DRCMR researchers were instrumental in making hyperpolarization techniques clinically useful for human lung studies."

Lars G. Hanson
Associate Professor at DTU & senior researcher at the DRCMR.

THE FUEL BEHIND DISCOVERY

For Siebner, that sense of curiosity is vital. "Research should be fun — but it's not a game. Professionalism is key. Our scientists are world-class, and we owe it to them to provide the infrastructure that supports that level of work," he says. To that end, DRCMR has built a robust support system: a research coordinator, HR, an IT manager, and even a reader centre to handle contractual frameworks — including those involving the pharmaceutical industry.

INTERDISCIPLINARY BY DESIGN

A hospital-wide restructuring in 2011 moved DRCMR under the Function and Imaging Diagnostics Unit, separating its purely research remit from the clinical MR diagnostics, now housed within the radiology department. But Siebner saw the reorganisation as a gain, not a loss: "Our relationship with the radiologists remained strong. But the new structure opened up opportunities for internal, interdisciplinary projects," he explains.

Indeed, Siebner worked hard to ensure that DRCMR remained open to diverse disciplines — from neuroscience to linguistics, even musicology. "Anyone can contribute here — as long as they are good enough," he says. "The variety of perspectives brings a creative spark to our research. We learn a great deal from each other."

> ”Anyone can contribute here — as long as they are good enough."

A GLOBAL STANDARD

In 2014, the Capital Region of Denmark named DRCMR a Center of Global Excellence. And the centre has taken that mandate seriously. While embedded in Hvidovre Hospital, DRCMR's partnerships stretch across Denmark — from universities to industry, from local hospitals to its neighbours in Skåne. "We were building strong networks," says Siebner.

A NETWORK FOR AN ENTIRE CAREER

From 1995-99, Peter Born was employed at DRCMR, where he completed a PhD on functional MRI studies of infants. He experienced an inspiring research environment, where many different professional disciplines contributed their own perspectives on the issues – an environment that has since developed into a far-reaching network across various medical specialties:

”DRCMR was and is a high-profile research environment with a good research infrastructure, which makes room for PhD students. There is no doubt that it is beneficial for a young doctor's career to complete a PhD at DRCMR, and my PhD has also opened doors for my further career. I still have many contacts that I draw on from my time at the center – both among neurologists and radiologists. Most recently, I have resumed collaboration with DRCMR through a PhD student from our department, who is doing a project at the center.""

Peter Born
Consultant pediatric neurologist, Copenhagen University Hospital

"Not just here in the region, but nationwide – and with companies, too. For instance, we had a Philips employee working on site with us, helping develop our methodologies."

A CLEAR ROADMAP

The centre had a clear roadmap for the future. Chief among its goals: enhancing academic profiles and ensuring researchers remain at the forefront of technological progress. "We needed more than one professor," said Sidaros. "We had many excellent senior researchers, but they needed stronger university affiliations – that's how we secure more grants and support more PhD students. Our first step was working to get more of them appointed as university lecturers.".

COMPLETING THE CIRCLE

That 7T scanner marked a return to the centre's origins. DRCMR began with the donation of the pioneering Spies scanner – once the only one of its kind in Denmark, serving patients nationwide. In 2015, once again, DRCMR found itself at the heart of a national enterprise.

"The 7T project is about national collaboration," says Siebner. "We want it to go beyond the steering group. And we don't want to limit it to brain research. With 7T, you can see microstructures in cartilage – ideal for studying the musculoskeletal system."

A RADICAL CHANGE OF CAREERS

As far back as the 1980s, a young Terry Jernigan reached out to DRCMR's then head, Ole Henriksen, eager to learn from the internationally renowned Danish research center. She returned to the center in the mid-90s-and again for a five-year period in the 2000s, during which she was also affiliated as a professor at the University of Copenhagen. Particularly, this last appointment at DRCMR was a pivotal period in her career: here, she laid the foundation for the research field she continues to work in today - both in collaboration with researchers from DRCMR and with colleagues across the United States.

"I helped start the HUBU cohort (Brain Development in Children and Adolescents), where the brain's structure and development are studied in a group of healthy children. They entered the study at school age, and we followed them for 12 years through the teenage years. This has given us entirely new insights into the development of the healthy brain, and we have published surprising and groundbreaking results based on the HUBU findings. It was an important career shift for me, having previously worked mostly with adult populations of patients with neuropsychiatric and neurodegenerative disorders, and after returning to the US, I have continued in the same direction. I still work closely with colleagues from DRCMR, and we have now reached a point where we can combine and compare the Danish results with our studies from the US. It is very rewarding and highly promising to study brain development alongside youth behavior and social development."

Terry Jernigan
Distinguished Professor of Cognitive Science, Psychiatry, and Radiology, UCSD
Director of Center for Human Development, UCSD.

2015-2025

NEW AVENUES

In February 2015, years of dedicated work were concluded to bring the most powerful human MRI scanner ever seen in Denmark to Hvidovre Hospital. The 7-tesla scanner now forms the foundation for a wide array of research projects from across the country — while also opening the door to new and far-reaching international collaborations. This is also the decade where the Capital Region of Denmark awarded the "Center of Global Excellence" prize in recognition of the centre's outstanding international standards.

DENMARK'S MOST POWERFUL MR SCANNER ARRIVES

Tuesday, 24 February 2015 marked a historic leap forward for medical imaging in Denmark. On that day, Regional Council Chair Sophie Hæstorp Andersen of the Capital Region officially inaugurated Scandinavia's most powerful magnetic resonance scanner for human use. After more than a decade of planning, years of fundraising, structural renovations at Hvidovre Hospital, and the careful installation of a 44-tonne magnet,

Denmark's new 7-tesla MRI scanner was finally ready to enter service.

The high-vis jackets stepped aside; the lab coats stepped in. "This is a landmark moment for Danish research," declared Sophie Hæstorp Andersen at the opening. "The 7-tesla scanner is a national collaboration—uniting universities, the government, and hospital-based research environments—and it promises to benefit patients across the country for years to come. But we must also remember that today's achievement builds on the work of the researchers who laid the foundations for a strong research envirenoment here at Hvidovre Hospital."

"It was a big day for danish research."

UNLOCKING HIDDEN DETAIL

With a magnetic field 140,000 times stronger than Earth's, the 7-tesla scanner delivers more than double the imaging power of conventional clinical MR machines in Denmark. The implications are profound. Researchers can now produce images of extraordinary resolution and detail, revealing fine structures in organs that were previously invisible.

"We hope to have the opportunity to combine the scanner's high-resolution imaging with functional examinations of individual areas in the organs." said Professor Jørgen Frøkiær of Aarhus University in 2015 when the magnet was installed. "Initially, this will probably be

From right: Regional Council Chair Sophie Hæstorp Andersen, Søren Drost-Nissen from The John and Birthe Meyer Foundation, and Hospital Director Torben Ø. Pedersen at the inauguration of the 7 Tesla scanner on February 24, 2015.

primarily the brain and the musculoskeletal system, but we have a clear ambition to extend the scanner's capabilities to various disease areas and other organs. For example, there is great potential in the area of the heart."

Jørgen Frøkiær is the chairman of the Steering Committee for the National 7 Tesla Project, which includes partners from research environments at hospitals and universities in both the Capital Region and the Central Denmark Region. He emphasizes that – beyond getting started with the research, which everyone was looking forward to – there was a major task ahead in creating a collaboration model that ensures all relevant research environments in Denmark gain access to the scanner.

The national project spans hospitals and universities in both the Capital and Central Denmark regions. But with such a powerful and in-demand tool, equitable access is critical. "It is important that we create a sustainable process for how researchers from across the country can gain access to utilize the facilities. It will be absolutely essential that there is transparency in the way we evaluate the projects that researchers wish to conduct using the 7 Tesla scanner. And that we develop very precise guidelines for how the researchers should describe their projects. Likewise, we must also ensure that we achieve a good balance between projects from already established, high-profile research environments and new, emerging ones." said Frøkiær in 2015.

A SCANNER FOR ALL OF DENMARK

That spirit of openness is central to the vision at DRCMR, where the scanner is housed. Professor Hartwig Siebner, echoed the commitment to collaboration: "We had a clear ambition for the 7 Tesla project to truly become a nationwide collaboration. A collaboration that extended beyond the units represented in the steering committee, and one that opened up for research not solely centered on the brain."

PUBLIC-PRIVATE PROJECT

The inauguration of the 7 Tesla scanner at DRCMR is a successful example of public-private financing of major investments in the healthcare system, which is a hallmark of the Danish healthcare model. The state, through the Danish Agency for Science and Innovation, has paid 40 percent of the scanner's purchase price, while a generous donation of no less than DKK 38.6 million from The John and Birthe Meyer Foundation covers the remaining 60 percent.

"The 7 Tesla project is a very fine example of how public-private financing can lead to an exceptional infrastructure in research. With the new scanner, we are now able to reach new heights in research by digging deeper into the fundamental knowledge of the world of cells."

Jørgen Frøkiær
Head of Departmentof Clinical Medicine & Clinical Professor, Århus University
Chair of the Steering Committee for the National 7 Tesla Project 2012-2024

”It was important that we were able to accommodate a diversity of projects. This was Denmark's scanner – and we owed it to patients across the country to take that into account.” said Siebner. ”Still today, we look forward to new, inspiring collaborations and are opening the doors to partners from all over the country.”

OPENING DOORS TO THE WORLD

The scanner's impact did not stop at Denmark's borders. Just across the Øresund, Lund University Hospital in Sweden also installed an identical 7-tesla machine just a few months after the DRCMR scanner. According to Siebner, this opened the door to unprecedented collaboration between the two institutions.

“Having matching scanners on both sides of the strait gave us a tremendous advantage. We could exchange PhD students, host joint workshops, share physics expertise, and collaborate closely on technical development,” he said. “We were also applying, in partnership with other 7-tesla groups across Europe, to establish a training network focused on clinical applications of this cutting-edge technology.”

”We ended up working even more closely with our colleagues in Lund after the installation of two identical scanners with very high magnetic strength. There was the possibility of exchanging PhD students, benefiting from increased interaction between our physicists, holding joint workshops, and generally working together on method development for the new machines. At the same time, we also had an application in collaboration with other European 7 Tesla groups to create a training network, where we focused on the clinical development of 7 Tesla technology. There were truly many opportunities to expand our international collaborations with the new scanner.” Sibner emphasized.

”There were truly many opportunities to expand our international collaborations ..”

HVIDOVRE HOSPITAL ON THE MAP

Torben Mogensen was, as Deputy Director at Hvidovre Hospital between 2003-2015, an important collaborator for DRCMR. Among other things, he was a co-signatory on the application to The John and Birthe Meyer Foundation, which secured the funds for the purchase of the 7 tesla scanner, which was inaugurated in 2015. Over all the years, he was able to observe a research center in constant growth and with an increasing degree of internationalization. And that has helped give the hospital as a whole a special place on the map:

”Being a leader in MR – both diagnostically and in terms of research – has meant a lot for Hvidovre Hospital. It means that we have been able to provide services of a very special caliber both internally at the hospital and for our partners. And it has greatly benefited both the patients and the research. Looking ahead, I see it as a core task for the center that they manage to broaden their research efforts so that, to a greater extent than before, they also include other organs than the brain – for example, the heart and the gastrointestinal system.” said Torben Mogensen in 2015.

Torben Mogensen
Deputy Director in the years 2003-2015, Hvidovre Hospital

Translated from DRCMR's 30th Anniversary Booklet

EXPANDING THE 7T CAPABILITIES

The first preclinical MRI scanner at DRCMR was installed in 1989 – a 4.7 Tesla Oxford Magnet. The magnet was unshielded, meaning the magnetic field spread several meters beyond the magnet itself. In fact, the field was so strong that forks could hang on the wall – it almost became a tourist attraction for visiting researchers.

"Back then, the preclinical facilities were pretty basic. They could host a few rodents and support simple surgical procedures for experiments." says Tim Dyrby, senior researcher at DRCMR and Professor at the Technical University of Denmark. At the time, some of the emerging research areas included diffusion MRI-based microstructure imaging and hyperpolaried carbon-13 techniques.

In 2016, DRCMR's preclinical research took a major strategic turn toward using cell-specific targeting tools in genetically modified rodents to explore and manipulate specific brain networks. The goal was to become more precise in investigating diseases and ultimately translate that knowledge into clinical applications. We aimed to explore both structural and functional MRI, brain stimulation, and behavior.

"To support this shift, we built a new animal facility, a virus lab, and a modern wet lab. The old MRI scanner was replaced with a shielded preclinical 7T Bruker BioSpec MRI scanner – so no more forks on the wall." says Dyrby. Today, DRCMR's preclinical research uses genetic rodent models to develop new MRI-based imaging technologies. These are linked to 3D microscopic imaging through AI-driven analysis tools, and are used to target and manipulate cell-type-specific neuron populations in the brain.

A STRONG LINK BETWEEN PRECLINICAL AND CLINICAL DOMAINS

Ulrik Gether from Department of Neuroscience, University of Copenhagen has a long-lasting collaboration with DRCMR. His team has a strong expertise in studying the dopamine system with focus on the molecular, cellular and physiological function of dopamine receptors and transporters in health and disease. The expertise includes use of state-of-the-art genetic and viral-based tools in mice to dissect neural circuits and their relation to behavior and how they are altered in diseases such as parkinsonism. Moreover, by targeted expression of fluorescent biosensors, the team can in combination with fiber photometric techniques assess in-detail neural activity and release dynamics of dopamine and other neurotransmitters.

"Our collaboration with DRCMR provides an important and strong link between preclinical and clinical domains by framing an interdisciplinary research environment that bridges rodent investigations with human studies. Indeed, I believe that our collaboration will have great potential for dissecting precise mechanisms for how transcranial brain stimulations are able to engage cortico-basal ganglia circuits and thus potentially create a translational framework that might transfer transcranial brain stimulation from basic science into the clinical realm

Ulrik Gether
Professor, Department of Neuroscience, University of Copenhagen

A NEW TRANSCRANIAL STIMULATION UNIT AT HVIDOVRE HOSPITAL

One of the most notable advancements in the more recent years was the launch of investigational studies utilizing transcranial magnetic stimulation (TMS) as a therapeutic tool. Building on a decade of brain stimulation research, this initiative represents a natural progression towards clinical translation. While TMS is an approved therapy for conditions such as major depressive disorder, the standard one-size-fits-all approach is only effective for some patients and effect size is usually modest. Adopting a precision medicine approach, our goal is to enhance the efficacy of TMS by tailoring therapeutic TMS protocols to each patient's unique brain anatomy and function. Currently, the focus is on Transcranial Magnetic Stimulation (TMS) therapies whereas other brain stimulation modalities such as transcranial focused ultrasound and electrical stimulation will be added later. Thanks to generous support by Hvidovre Hospital, we were able to establish a unit for precision brain stimulation in Center E of Hvidovre Hospital. This unit became functional in 2023 and includes three labs dedicated to therapeutic brain stimulation studies and two offices. To ensure that patients feel welcomed and comfortable between treatments, the center also includes a receiving area along with rest areas where patients can relax between treatments. The treatment labs are equipped with top-shelf brain stimulation equipment, including custom-made high-performance magnetic stimulators, suspension systems for weightless neuronavigated coil control, and a new generation Cobot, enabling robotic precision stimulation. Even with robotic support, precision brain stimulation calls for a group effort. The human infrastructure includes PhD students, research assistants, postdocs, and a clinical neurophysiology assistant that work together to manage ongoing therapeutic trials. The new treatment facility enabled us to initiate three clinical TMS trials in collaboration with clinical partners in RegionH. The therapeutic TMS studies are led by Prof. Hartwig Siebner and test the use of personalized TMS for patients with Parkinson's Disease, multiple sclerosis, and treatment-resistant major depressive disorder.

Neurodiagnostic technologiest Aino L. Jensen and PhD Student Sofus A. D. Nygaard from DRCMR in the new unit for TMS.

DRCMR Postdoc Armita Faghani Jadidi.

GLOBAL EXCELLENCE IN HEALTH

Back in 2014, DRCMR received the "Global Excellence in Health" award by the Capital Region of Denmark. This was renewed in 2017 until the end of 2020. The Capital Region of Denmark decided to discontinue the Global Excellence programme after 2020.

The award was a large asset for the DRCMR to facilitate scientific interactions and initiate research collaborations within and beyond the Capital Region of Denmark, boosting the DRCMR's regional, national, and global reputation.

"We are grateful to the Capital Region for this recognition."

"We are grateful to the Capital Region for this recognition – a recognition that fueled our efforts to pursue translational neuroimaging research at the highest quality and to further develop our center as key infrastructure for interdisciplinary and diverse brain imaging in the Capital Region." says Siebner.

"Although the reward was discontinued in 2020, it certainly has not stopped us from striving to further enhance our status as a centre of global academic excellence" says Siebner, who maintains the same high standards as always.

In 2014, DRCMR received the Capital Region of Denmark's award "Center of Global Excellence" in recognition of the center's high international standard. Regional Council Chair Sophie Hæstorp Andersen, Regional Council Member Lars Gaardhøj, and Hartwig Siebner at the award ceremony. Photo: Joachim Rohde.

PARTNERSHIPS WITH ACADEMIA

Over the last decade, we have deepened our ties with the University of Copenhagen (KU) and the Technical University of Denmark (DTU), hosting more than 66 joint master's and 72 PhD projects. This tight integration with KU and DTU has reinforced DRCMR's academic excellence and collaborative culture. Faculty positions at both universities expanded significantly, with new professorships and associate professorships at KU and DTUI strengthening our academic presence. For example, Axel Thielscher was appointed as Full Professor at the Technical University of Denmark. Since 2022, he is Head of the Section for Magnetic Resonance at the Department of Health Technology of DTU. He maintains a part-time position as Senior Researcher at DRCMR, contributing to the traditionally strong collaborative environment between DTU and DRCMR.

While some colleagues with faculty positions moved to partner institutes in Greater Copenhagen, they remain close collaborators. Recognizing the need for greater diversity, we also launched REFRESH. This initiative is supported by Lundbeckfonden and addresses the gender imbalance at the senior researcher level.

TECHNICAL UNIVERSITY HOSPITAL

Technical University Hospital of greater Copenhagen, TUH, is a partnership between the Capital Region of Denmark and the Technical University of Denmark. Its mission is as ambitious as it is timely: to become a powerhouse of health technology, where medical science and engineering converge in a seamless union. The goal? To spark innovations that aren't confined to

FORTY YEARS AND STILL GOING STRONG!

Perhaps even stronger now than ever before. Undoubtedly, DRCMR has been instrumental in developing neuropsychiatric psychosis research in the Capital Region- and even in Denmark. A hallmark of DRCMR is the dedicated research team, who are deeply engaged in advanced MRI methodologies, but at the same time respect the important aspects of flexibility and empathy when running imaging trials in vulnerable clinical populations. With the clear and deeply engaged lead of Hartwig Siebner, DRCMR has created a unique environment for conducting world-class clinical neuropsychiatric psychosis research for the benefit not only Danish academic but for patients struggling with psychotic disorders and schizophrenia.

Photo: Markus Redvall

"Personally, I consider myself as one of the first medical doctors with an interest in psychiatry, who completed at PhD as co-affiliated with DRCMR. From 2005-2009 we investigated brain structural changes in never-medicated patients with first-episode schizophrenia before and after their initial antipsychotic treatment. We were so fortunate to do this on a highly advanced 3 Tesla scanner, and while the project was underway, my supervisor William Baaré paved the way for including functional- and diffusion sequences to investigate working memory and white matter tracts. In 2025, two decades down the line, we have the privilege of continuing our collaboration, but we are now using the 7 Tesla scanner and apply spectroscopy sequences focusing on the cerebral glutamate system in patients with psychosis."

Bjørn Ebdrup
Leader of the Center for Neuropsychiatric Schizophrenia Research
Professor of Psychiatry at the University of Copenhagen & Consultant Psychiatrist

laboratories, but instead deliver real, tangible healthcare solutions.In April 2024, a strategic partnership was established between the Technical University of Denmark (DTU) and the Capital Region hospitals (RegionH). The goal is to strengthen and better integrate technological expertise with patient treatment, diagnosis, education, and research—ultimately improving care for patients, supporting innovation in the healthcare system, and creating value for industry. One important ambition of TUH is to create a clear academic career path for the many skilled researchers working in hospitals—similar to the path that already exists for medical doctors through the Faculty of Health and Medical Sciences at the University of Copenhagen. At the same time, TUH aims to position Greater Copenhagen on the international stage as an attractive hub for future generations of researchers. The foundation for TUH was laid already in 2015, when an agreement made it possible for a limited number of senior hospital researchers to hold shared academic positions at DTU. At the Danish Research Centre for Magnetic Resonance (DRCMR), this led to the appointment of four senior researchers—Axel Thielscher, Kristoffer Madsen, Esben Thade Petersen and Tim Dyrby—as associate professors at DTU Health Tech and DTU Compute. Three are now full professors and they play key roles in realizing TUH's mission. At DRCMR, the TUH partnership has already proven a great success. It has made it significantly easier for new researchers to become affiliated with DTU, helping foster a stronger bridge between technological innovation and clinical application.

Today, DRCMR proudly hosts two full professors, one associate professor, and one additional candidate currently under evaluation for a DTU affiliation. We are especially proud that Tim Dyrby has been appointed Coordinating Professor between Amager & Hvidovre Hospital and DTU—further strengthening the connection between research, technology, and patient care.

A STRONG LINK BETWEEN CAMBRIDGE AND COPENHAGEN

James Rowe from the University of Cambridge has a close affiliation with DRCMR over 25 years. In 2000, during his PhD, he delivered a series of lectures on brain imaging analysis methods. In 2004-5 he moved to Denmark, as a researcher at DRCMR and as 1. Reservelaege (senior registrar) in neurology at Rigshospitalet. He has maintained and expanded the connection between the two research environments, and was appointed adjunct professor at the University of Copenhagen in 2015, renewed in 2025. The strong collaboration includes support for PhD students, advice for ADAPT-PD programs, and new joint research projects in advancing 7T MRI and Parkinson's disease research.

"There is a very strong bond connection between the translational neuroscience undertaken in Cambridge and Copenhagen. I am especially grateful to the LundbeckFonden for supporting my visits to DRCMR during my sabbatical 2024-25, and to the team at DRCMR for being so welcoming. The research and innovation here is of the highest caliber, and we share the commitment to research with real impact on human health"

James Rowe
Adjunct Professor in Clinical Neuroscience at the University of Copenhagen &
Professor of Cognitive Neurology at the University of Cambridge

HIGHLIGHTS FROM 2015-2025

Over the past decade, DRCMR has strengthened its position as an internationally recognized hub for MRI-based brain imaging and translational research. Bringing together scientists and clinicians across fields and borders, we have advanced technological and computational innovations in brain MRI and translated them into novel tools for precision imaging. This success has been driven by strong synergistic ties, linking engineering, computation, preclinical science, and clinical medicine across hospitals and universities.

MRI-based precision brain mapping has emerged as the central theme. This is reflected in large longitudinal studies that follow well-characterized groups of healthy individuals and patients over months or years. Some projects have used state-of-the-art multimodal MRI to evaluate how treatments affect the brain, while others track cohorts across critical life stages to reveal how brain structure and function evolve over time. These studies have identified "brain substrates" that signal risk for developing brain disorders or, conversely, resilience factors that support lifelong brain health. In parallel, several projects have combined advanced MRI techniques with non-invasive brain stimulation, opening new possibilities for tailoring diagnostics and therapies.

UNIQUE RESEARCH HARDWARE

Since 2015 the DRCMR is home to Denmark's only ultra-high field (7T) MRI scanner, a national facility that has brought researchers together from Denmark and abroad to push the frontiers of brain science. Expert physicists have ensured its success, and a special tribute goes to Associate Professor Esben Petersen, whose vision and leadership shaped the program until his passing in 2023.

Beyond the 7T MRI scanner, there have been major investments in modern infrastructure, including three renewed clinical MRI scanners, an upgraded preclinical facility for experimental research enabling the combination of cell-type-specific stimulation and MRI, a high-performance computing cluster for advanced data analysis, a dedicated MRI Reader Centre, and a new precision brain stimulation unit. Together, these resources have enabled groundbreaking studies, strengthened collaborations across Denmark and worldwide, and advanced the development of precision medicine.

INTERNATIONAL RECOGNITION

International recognition included renewal of the Global Excellence Award (2017–2020) and flourishing collaborations through EU Horizon projects, NIH partnerships, and national initiatives such as the VIA and DANNORMS study. Prestigious visiting professorships, awarded to Ray Dolan (UCL), James Rowe (Cambridge), and John Rothwell (UCL), further enriched our scientific environment.

Our researchers secured highly competitive grants from major funding bodies, including the European Research Council, NIH, Novo Nordisk Foundation, and the Lundbeck Foundation. These resources supported projects on neurodevelopment, brain disorders, stimulation techniques, computational modelling, AI, and advanced imaging, leading to several major new initiatives.

PUBLIC ENGAGEMENT

In an age where science unfolds in closed research laboratories and is published in specialised journals, outreach emerges not as a luxury, but as a moral and societal imperative. It is through deliberate engagement—lectures, exhibitions, media, and school visits—that researchers demystify their work, rendering the abstract tangible and the complex comprehensible.

”... outreach reconnects you with the wonder that drew you to science in the first place”

”Outreach breathes life into science, forging a vital bridge between the lab bench and the living room. It cultivates public trust, inspires the next generation of thinkers, and ensures that discoveries made with public funds return value to the public good. For science to flourish, it must not only speak for itself—it must speak to us all.” says Prof. Hartwig Siebner, head of the DRCMR.

And indeed, as the DRCMR has grown and public financing has increased, so too has the engagement with the public. In the last decade, DRCMR researchers have been interviewed by the national radio, national television, and newspapers on everything from smart choices, homeground advantage in football, white lies, and how to maintain a healthy brain, to name a few.

”Outreach is fun because it brings science to life outside the lab, sparking curiosity in unexpected places. It’s deeply rewarding to see complex ideas click in someone’s mind.” says research fellow David Meder from DRCMR. ”Engaging with different audiences challenges you to think creatively and communicate with clarity and passion. Best of all, outreach reconnects you with the wonder that drew you to science in the first place.”

Research fellow David Meder and journalist Lars Igum Rasmussen, and the cover of the newspaper Politiken’s article on the effects of 69 units of alcohol in three days on our brains. Published in October 2019

COMMUNITY BUILT AROUND COMMON VALUES

Behind every scanner and discovery stands a team of people. At DRCMR, our strength lies not only in bringing together experts in physics, engineering, computing, medicine, and psychiatry, but in how we work together. We ground our research culture in transparency, inclusive and centralised decision-making, and rigorous data governance—values that ensure clarity, fairness, and trust across projects. Collaboration is not an add-on, but the foundation. Our multidisciplinary approach integrates diverse expertise under shared principles, supported by a culture of education and career mentorship that enables everyone to grow. A hallmark of our centre is that all members are encouraged to understand, and where possible give feedback on, the work of others—an ethos made possible by our exceptionally broad educational program. This openness ensures that new ideas and perspectives can circulate freely, regardless of background or seniority.

Perhaps the greatest achievement of the past decade is not a single technology or project, but the community itself. We have welcomed outstanding researchers and young talents from Denmark and abroad, who—guided by our values—have driven innovation, secured major funding, and deepened our understanding of the brain.

In 2020, the Covid-19 pandemic put this community to the test. While research activities were disrupted, our shared principles ensured resilience: inclusive dialogue, transparent communication, coordinated decisions, and a commitment to open science. The result was a record number of publications, including important Covid-related studies. Even in difficult times, DRCMR grew stronger, expanded recruitment, and reaffirmed its dedication to working openly, collaboratively, and across disciplines.

SMARTER MRI

Professor Tim B. Dyrby completed his PhD in 2008 at DRCMR, initiating diffusion MRI research at DRCMR under the broad topic of validiation of microstructural MRI techniques. He founded his research group in 2010 and been PI in European projects such as CONNECT FET-Open (2009-2012) and TRABIT ITN (2017-2021) and ERCcog CoM-BraiN (2022-2027). His current MRI research combines such as X-Ray Holographic Nano-Tomography to visualise microstructures (axons, myelin, somas, blood vessels) using AI. In 2023 he became full Professor at DTU and in 2024, with the founding of the Technical University Hospital of Greater Copenhagen (TUH), he became Coordinating Professor at Hvidovre Hospital.

"My research is about making MRI smarter, more precise, and more insightful. My dream is to unlock the hidden potential of MRI and turn it into a powerful diagnostic tool that lets doctors see disease changes at the microstructural level — cells, axons, and myelin. While MRI has limits in resolution, other 3D imaging techniques like XNH and Light-Sheet Microscopy can reveal what MRI alone cannot. The challenge is bridging these methods across scales, and with AI we are now closer than ever to making the invisible visible. This mission is also about the future - training the next generation of researchers to carry it forward."

Tim Dyrby, Professor at the Technical University of Denmark, Senior Researcher at the DRCMR

FIVE

WAYS WE HAVE MOVED THE FIELD FORWARD IN 2015-2025

Over the past ten years, our research has grown in many directions, but five areas stand out as the pillars of our work. These achievements have been made possible by a rare blend of state-of-the-art scanners and the people who know how to use them.

1

DEVELOPING NEW WAYS OF LOOKING INTO THE BRAIN

Using powerful MRI scanners, including scanners working at ultra-high field strength (7 tesla) and advanced imaging methods such as diffusion MRI, quantitative MRI, and MR spectroscopy, we can now capture the brain's structure, metabolism, and functional activity in much greater detail than ever before.

2

LINKING MRI TO BIOLOGY AND COGNITION

We have pursued translational studies across species and tissues to validate MRI as a tool to study the brain´s microstructure. By combining animal studies, tissue analyses, and advanced microscopic 3D imaging techniques, MRI has become a reliable window into the living brain. By combining cogntive science and neuroimaging we provide insight into understanding the brains cognitve functions and dysfunctions.

3

BRINGING MRI INTO THE CLINIC

New MRI-based markers have been tested from newborns to the elderly and applied to patients to capture key mechanisms and monitor clinical conditions such as multiple sclerosis, Parkinson's disease, hearing loss, and psychiatric disorders.

4

UNLOCKING INSIGHTS FROM LARGE DATA SETS AND AI

With today's vast amount of brain data, artificial intelligence and data science has become a central part of our workkey tool. We now use advanced modelling and statistical techniques to detect hidden patterns in the data, test theories, reduce bias, and make personalized predictions about health and disease.

5

PUTTING PATIENTS FIRST

Technology only matters if it works for people. Therefore, our research strongly considers patient safety and comfort. One highlight is our ability to scan newborn babies without the need for sedation, offering new possibilities for understanding early brain development.

2025-2035
THE NEXT DECADE

For four decades, the DRCMR has been at the forefront of biomedical research in MRI, with a strong focus on advancing brain imaging. As DRCMR enters its fifth decade in 2025, the DRCMR stands ready to lead the next wave of breakthroughs in precision brain imaging that can guide and validate novel personalized therapies, driven by an outstanding team and a strong spirit of collaboration. Looking ahead, the next ten years will bring both new opportunities and challenges — and we are well positioned to meet them.

STRONGER CLINICAL INTEGRATION

Our hospital will undergo major changes. Large psychiatric centers in Glostrup, Hvidovre, and Amager, along with the planned establishment of a new neurology department at Hvidovre, will result in a major shift in clinical focus towards treating citizens with diseases that affect the brain.

These developments will open unprecedented possibilities for collaboration and transla-tional research. Patients with psychiatric and neurological disorders will directly benefit from the integration of clinical expertise with our advanced neuroscience infrastructure and expertise in advanced MRI-based brain imaging. Our unique translational platform for MRI-informed precision brain stimulation, including a dedicated treatment unit with several ongoing clinical trials, provides a solid foundation for developing next-generation therapies in close partnership with psychiatrists and neurologists.

BRAIN-BODY INTERACTIONS

A second research frontier will focus on the interplay between the brain and the body. Brain-body interactions are central to health and disease, yet they remain poorly understood. Using multimodal, multi-organ imaging, we will investigate how syste-

BRIDGING DISCIPLINES: FROM BRAIN-BODY INTERACTION TO CLINICAL TRANSLATION

Hartwig Siebner is board-certified neurologist and clinical professor at the University of Copenhagen and has led DRCMR since 2010 as Head of Research. With a career spanning neuroimaging, non-invasive brain stimulation, and clinical neurology, he has advanced understanding of causal brain dynamics in conditions such as Parkinson's disease, multiple sclerosis, dystonia, and psychiatric disorders..

"The coming years bring unprecedented opportunities for DRCMR, as new psychiatry and neurology departments will join our hospital. This expansion will enable truly integrated research across neurology, psychiatry, and internal medicine, creating fertile ground for discoveries that benefit patients with both brain and systemic disorders.
Understanding how the brain interacts with the body, how neural circuits shape, and are shaped by, metabolic and organ health, will be a key frontier. To seize this potential, we must maintain world-class research infrastructure and continue to attract and nurture the next generation of international talent. Together, these elements will allow us to drive innovation at the interface of brain, body, and medicine"

Hartwig Roman Siebner
Professor and head of research, DRCMR

mic metabolic disturbances, such as those arising from endocrinological diseases, obesity, or dysfunction of organs like the gut, liver or heart, affect brain function. Conversely, we will explore, how the brain and its signals send out to the body - via neuronal and chemical signals - maintain metabolic balance and physical health. These efforts will build on close collaborations with local and regional experts in endocrinology, hepatology, gastroenterology, and cardiology.

TRACING HOW THE BRAIN CHANGES DURING CRITICAL PERIODS OF HUMAN LIFE

A third focus will be the study of brain development and aging. We aim to extend brain map-ping into the earliest phases of life, including prenatal imaging and postnatal mapping of infants, to better understand how maternal and early-life factors shape mental development. We will also expand our longitudinal studies in childhood, adolescence, and late life, capturing how individual brains change structurally, functionally, and metabolically over 5–10 years.

These studies will be integrated with genetic, metabolic, socioeconomic, and behavioral data, providing a comprehensive picture of risk and resilience across the most dynamic periods of human life. Our participation in large international collaborations will ensure that these efforts contribute to global progress in understanding brain health and disease.

LONGITUDINAL COHORTS: UNLOCKING THE ROOTS OF MENTAL HEALTH

With a keen interest to apply her biomedical engineering background to drive innovation in mental health, Melissa Larsen joined the DRCMR in 2012 for her doctoral degree. After completing her PhD, she continued her research journey with a postdoctoral fellowship in Australia working with leading experts in the field of neuroimaging and psychiatry. Now a senior researcher at DRCMR, Melissa leads the Developmental Psychiatry group. Together with her team, Melissa has contributed to pioneering studies exploring brain structure and function in mental health disorders, such as the uniquely rich Danish High Risk and Resilience Study -VIA. By combining technical innovation with a strong clinical focus, her work reflects a commitment to bridging engineering, neuroscience, and clinical research, and to fostering collaborations that advance both methodology and patient care.

"Our long-term collaborative cohort studies offer extraordinary potential for psychiatry. Most mental health conditions have its root in neurodevelopment. Having access to decades of imaging and clinical data allows us to trace early brain changes that precede symptoms and clinical manifestation. At DRCMR, we are uniquely positioned to integrate multimodal neuroimaging data with psychiatric assessments, genetics, and environmental information, enabling a more complete understanding of the biological pathways underlying disorders like depression, schizophrenia, and bipolar disorder. By following individuals across key life stages, we can identify both risk and resilience factors – knowledge that is crucial for early intervention and prevention. As DRCMR celebrates 40 years, I'm inspired by how these cohorts will continue to transform psychiatric research and, ultimately, patient outcomes."

Melissa Larsen
Senior Researcher, DRCMR

PUSHING THE FRONTIERS OF MAGNETIC RESONANCE TECHNOLOGY

We will continue to advance MR technology in both imaging and image processing. In particu-lar, the advances in machine learning and artificial intelligence offer new opportunities that we will pursue in close collaboration with DTU Health Technology and DTU Compute under the framework of the Technical University Hospital. These advances will not only enhance image acquisition and analysis, but also support the mathematical modeling of cognitive and physiological processes — linking abstract parameters such as learning rates or decision-making tendencies directly to brain function and structure.

CLINICAL TRANSLATION AND BIOMARKER DEVELOPMENT

The development and validation of MRI-based biomarkers will remain a strategic priority. Our efforts will range from mapping small but critical structures, such as brainstem nuclei, to characterizing large-scale network organization and connectivity ("connectomics"). At the microscopic level, we aim to resolve fine features of brain architecture, including cortical layers and the microstructure of distinct fiber bundles. We will also pioneer novel MR methods to advance clinical imaging, for example by detecting disease-related changes in neurofluid dynamics (e.g., the glymphatic system) or alterations in specific metabolic pathways of the hu-man brain.

A further major direction will be to link individual patients' symptoms with alterations in brain structure, function, and metabolism. Building on our success in multiple sclerosis, we will expand biomarker research across a broader spectrum of neurological and psychiatric disor-ders. These efforts will be closely integrated with our translational work on precision brain

ADVANCING BRAIN STIMULATION: FROM CIRCUITS TO THERAPIES

Attracted by the center's pioneering integration of brain stimulation and neuroimaging, , Lasse Christiansen joined the DRCMR in 2019 after an extended international postdoctoral journey. He is now heading the "Transcranial Stimulation" methods and the "Control of Movement" research groups. He is a key contributor to our joint effort to push non-invasive brain stimulation towards clinical translation. Exploiting the DRCMR's unique infrastructure and collaborative culture, his work explores how brain stimulation can be harnessed to both understand and modulate the human nervous system in health and disease..

"The brain stimulation field is evolving rapidly, and our collaborative approach gives us a distinct advantage. The next decade will be about combining brain stimulation with neuroimaging and computational modeling to reveal how different modalities act on intact and compromised brain circuits. By linking stimulation effects across time and brain states, we aim to bring cellular-level specificity to human brain stimulation. This precision will allow us to target pathological network dynamics with unprecedented efficacy. The future holds great promise for therapeutic brain stimulation."

Lasse Christiansen
Senior Researcher, DRCMR

stimulation and circuit-based therapies, strengthening the bridge from advanced imaging science to individualized treatment.

SUSTAINING EXCELLENCE THROUGH EXCELLENT INFRASTRUCTURE AND RESEARCH TALENT

Realizing these ambitions will require continuous investment in our MR infrastructure at high and ultra-high field strengths, ensuring that we remain at the international forefront of biomedical imaging. This will depend on close collaboration between our hospital, the healthcare region, and public and private funding partners — support that has been vital to our achieve-ments to date and will be equally crucial in the decade ahead.Equally important will be our commitment to attracting outstanding Danish and international talent. We will continue to provide an environment that fosters personal and professional development through intramural training, mentoring, and collaborative opportunities. Maintaining our flexible, matrix-based research structure, with no "walls" between groups, will remain a cornerstone of our success, allowing us to bring together complementary expertise across disciplines to generate innovative, high-impact research.

CHARTING BRAIN DEVELOPMENT: INDIVIDUAL TRAJECTORIES FROM EARLY LIFE

Kathrine's journey with the DRCMR began in 2005, when she started her master's thesis on the animal scanner. A rat allergy led her to human imaging, and she completed her PhD at DRCMR in 2011 as part of the Cimbi project. In 2007, she helped Terry Jernigan start the HUBU project (Brain Development in Children and Adolescents), a longitudinal study tracking children's brain and behavioral development - a focus that remains central to her research today. From 2012 to 2015, Kathrine held a postdoctoral grant from the DFF. This allowed her to split her time between DRCMR and UCSD, working closely with Terry on longitudinal neuroimaging studies of brain and behavioral development. This experience provided a strong foundation for exploring developmental trajectories in even younger populations. In recent years, she has extended her work to also include studies of infants.

"My work has always focused on understanding why children's brains and behaviors develop so differently, in both typical and at-risk populations. At DRCMR, we have a unique opportunity to scan children repeatedly over many years. In HUBU, for example, children had up to 12 scans between the ages of 7 to 21 years, revealing that many brain differences are established much earlier in life. Recently, I therefore extended my work to study infants. Within the next decade, I aim to expand our longitudinal studies to include prenatal assessments, to capture brain development from its earliest stages in the womb. Prenatal imaging lets us observe these formative stages and investigate how maternal biology and early environmental factors shape the brain. Postnatal follow-up is equally important, as early life is a critical period when biology and experience interact to shape the developing brain. By combining pre- and postnatal measurements, we can map individual differences in developmental trajectories from the earliest stages. This approach will help identify biological and environmental factors that shape healthy and at-risk pathways for psychiatric and neurological disorders."

Kathrine Skak Madsen
Senior Researcher, DRCMR

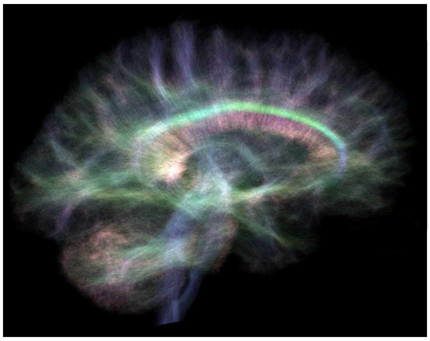
RESEARCH AREAS AT DRCMR TODAY

The matrix structure at DRCMR - not commonly seen in research institutions - encourages interdisciplinary research by connecting researchers across departments and specialties, breaking down traditional silos. It allows our researchers to contribute their expertise to multiple projects simultaneously, fostering collaboration and knowledge sharing. This framework ensures that ideas flow freely between disciplines, sparking innovation at the intersections. As a result, at DRCMR, complex problems can be addressed from multiple perspectives, leading to more impactful solutions.

ADVANCED BIOMEDICAL MRI

MAGNETIC RESONANCE METHODS

While the research at DRCMR is multidisiplinary and involves a number of different techniques, MR-based methods are at the core of most projects. The continuous development of new methods enables new research questions to be raised. We take active part in the forefront of methods research and follow the achievements of the MR community closely to reach new goals in neuroscientific and clinical research. MR methods range from high resolution anatomical imaging to studying brain anatomy in better detail, quantitative imaging and spectroscopic techniques reflecting different microstructural molecular features of tissue to dynamic imaging methods tracing neuronal activation and physiology. Increasing interest is also put into body imaging, e.g. the heart and the liver.



Tractography reconstruction of white matter bundles based in diffusion weighted MRI

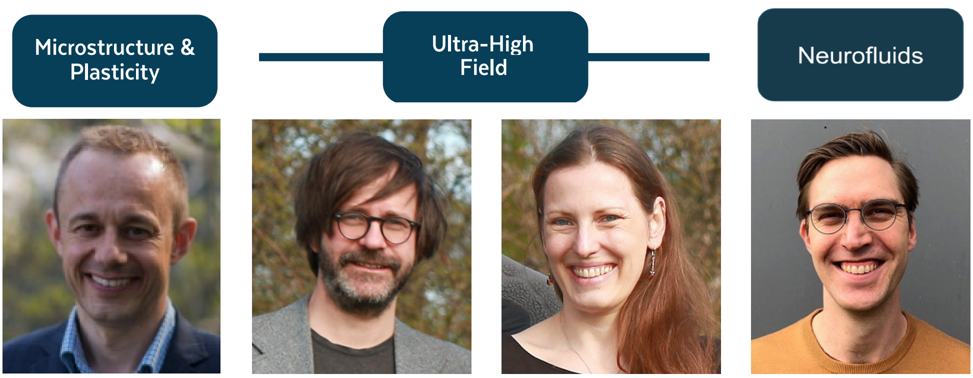
ULTRA-HIGH FIELD MRI

In our work, ultra-high field MRI is crucial for innovation in experimental and clinical research as well as the integration of multimodal approaches during the scanning session. Translation of experimental methods in preclinical and ultra-high field settings to clinically feasible routines is also at the heart of our work. This requires efforts in the construction of new hardware, scanner sequences and not at least computational methods to analyse new types of data.

We have a particular interest in spectroscopy, diffusion, perfusion and functional MRI but are also extending to combined approaches, e.g. using MRI and transcranial magnetic stimulation.

UNLEASHING NEW METHODS

To unleash the powers of new methods, we coordinate our work with other research areas at the department as well as external collaborators in Denmark and internationally. This ensures the synergy needed to span from basic research to clinical work. The MR Physics and Analysis research area is coordinated by Senior Researcher Henrik Lundell.



PRECISION BRAIN STIMULATION

TOWARDS CAUSAL NEUROSCIENCE

Non-invasive Transcranial Brain Stimulation (TBS) techniques directly interact with intrinsic brain activity and can induce long-lasting effects on human brain function. These features make them unique complements to neuroimaging techniques such as MRI that are correlative in nature, with limited possibilities to determine whether the measured brain activity patterns play critical roles in the observed behavior. In contrast, combining TBS with neuroimaging in a perturb-and-measure approach can reveal causal insights into the function and dynamics of the complex brain networks that underlie our thoughts, feelings and actions. TBS can also shape and normalize dysfunctional brain activity patterns that underlie neuropsychiatric diseases, making it a promising therapeutic option.

Demonstration of TMS Therapy

MISSION AND VISION

We strive to advance TBS as a unique interventional tool to study causal brain dynamics and enhance cognitive, affective and motor function in health and disease. We aim to overcome current limitations with unprecedented spatial, temporal, and functional precision. Our goal is personalized TBS interventions that integrate neuroimaging-based phenotyping with computational dose control of the stimulation patterns in the brain to increase the specificity of the stimulation effects and minimize their inter- and intraindividual variability. We further work on establishing novel TBS modalities with complementary application profiles, such as ultrasound stimulation for spatially precise modulation of subcortical activity. We will exploit the potential of precision TBS, tailored to the individual brain, to uncover the causal dynamics of the human brain and translate these insights into powerful neuropsychiatric therapies for the 21st century.

A UNIQUE INFRASTRUCTURE

The DRCMR houses a unique infrastructure to support 'brain imaging informed' and '-controlled' TBS. This includes five state-of-the-art laboratories where all TBS modalities can be applied independently or combined. Brain activity can be continuously monitored with EEG, offering open- and closed-loop applications. Neuro-navigated TMS-fMRI and TES-fMRI on a state-of-the-art 3T MR system enable measurements of the immediate and lasting stimulation effects on brain activity. We have also established dedicated facilities for clinical trials that are equipped with a robotic system for automated and spatially highly precise TMS therapies. Finally, we support personalized computational modeling of stimulation fields and waves.

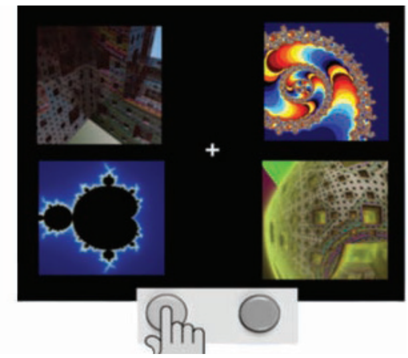
Brain Network Modulation

Neurophysics

COMPUTATIONAL & SYSTEMS NEUROSCIENCE

HOW DOES IT WORK, AND WHY?

The word cognitive refers to a focus on cognition, a wide spectrum of mental faculties that we all take for granted. Learning, decision-making, attention, reasoning, memory, language, and motor control are all examples of the faculties we rely on as part of our mental toolkit. Cognitive neuroscience, naturally, is the subfield of neurobiology charged with investigating the neurobiological underpinnings of these faculties. Computational Neuroscience, on the other hand, is a subfield in which mathematical tools are used to develop and test theories of brain function. Putting this all together, cognitive and computational neuroimaging thus studies the neural basis of cognition from a computational perspective, using neuroimaging as its primary technique.



Gambling task used to study the neuronal basis of risk-taking in the human brain.

Our research area's long-term vision is to pioneer new methods for bridging computational modelling of cognition and neuroimaging and to use this to understand the brain's functions and dysfunctions. Principal among these efforts is to develop advanced multi-modal methods for integrating computational models into the modelling of brain, cognition, and behaviour.

THE COMPUTATIONAL NEUROSCIENCE OF REWARD

We seek to build and test fundamental theories of reward value that are grounded in our physiology and evolutionary history. Our primary research interest concerns the brain's reward system. Put simply: how does it work, and why? We explore computational theories that constrain how it should work and then test the predictions of these theories against behavioural, economic, physiological, and neuroimaging data.

CONTROL OF MOVEMENT

We study how the central nervous system orchestrates movements. We combine neuroimaging, neuromodulation and computational modelling of sensorimotor networks. We adopt a triple-M approach to decipher the causal neurodynamics in sensorimotor brain networks by combining multimodal brain mapping with computational modelling and non-invasive modulation of sensorimotor networks. We focus on modelling and analysis of neuroimaging data based on machine learning methodology. The efforts within the group aim to improve sensitivity and interpretability of the vast amounts of data that are acquired with neuroimaging techniques through sophisticated modelling and analysis methods.

Computational Neuroscience of Reward

Control of Movement

BRAIN TRAJECTORIES & COHORTS

UNDERSTANDING THE DEVELOPING BRAIN

Lifespan imaging centres around understanding the development of brain structure, function and chemistry throughout the lifespan from birth to the end of life. We are interested in both typical and pathological development and in understanding the drivers, either biological or socio-environmental, of such development. Ultimately, we would like to predict whether individuals are at risk of negative development and provide recommendations for interventions that may alter such a trajectory for a particular person.

Figure of DRCMR researcher with Baby Arthur

A MULTI-DIMENSIONAL PROSPECTIVE APPROACH

We tackle these questions using a multi-dimensional prospective approach that combines state-of-the-art multimodal imaging techniques with advanced analysis methods and perform elaborative assessments of biological, physical, environmental and behavioural variables.

We believe that the key lies in longitudinal data, with following and examining the same individuals over time to accurately measure life span trajectories in (brain) health and disease. We also perform various intervention studies testing effects on brain health from e.g., physical exercise. In our studies, we have both healthy individuals and specific patient groups. We have established expertise and research infrastructures for detailed cross-sectional and longitudinal assessments of large cohorts and nurture active and elaborative regional, national and international collaborations. In the last couple of years, we have started up new projects in both the Brain Maturation and the Healthy Ageing research groups, which you can read more about in specific sections of this report.

OUR PASSION

In all our projects, we strive for high academic standards, interdisciplinary collaborations, innovative methods and techniques, and an ambitious, fun and diverse environment.

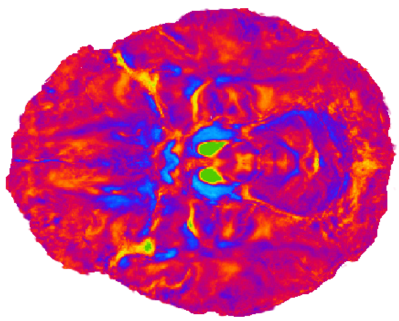
Healthy Ageing

Brain Maturation

IMAGING OF DISEASE & MECHANISMS

IMAGING OF BRAIN DISORDERS

Advancements in MRI are continuing to expand our possibilities for precision imaging of brain disorders, offering unprecedented insights into how a given brain disease affects the brain´s structure, function, and metabolism. The DRCMR is uniquely positioned to translate these innovations into clinical applications. Our location within a major University Hospital provides optimal conditions for clinical translation, and our preclinical MRI unit enables method validation in rodent models. This dynamic ecosystem makes DRCMR a critical hub for bench-to-bedside translational research, advancing MR-based Precision Medicine as a vital link between diagnostic radiology and clinical neuroscience.



Quantitative Susceptibility Map: MRI scan showing iron concentrations in the brain where green-blue is higher.

MISSION AND VISION

Our mission is to enhance MRI's role in clinical care, empowering neurologists, neurosurgeons, and psychiatrists to tailor treatments to individual patients. We strive to identify clinically relevant MR biomarkers that assess individual disease risk, prognosis, and treatment response. Additionally, we strive to develop MRI-based brain circuit biomarkers for disabling symptoms for the evaluation and monitoring of symptom-specific treatments. These objectives are pursued through longitudinal observational and interventional MRI studies in collaboration with our clinical partners. Integrating MRI, neuroscience, and clinical practice. Our neuroimaging research spans psychiatric and neurological disorders across all life stages. We develop and validate MR-based technologies to capture risk, resilience, and disease-related changes.

BRAIN-BODY INTERACTIONS

Recently, we have expanded MRI protocols to assess other organs, including muscle, heart, liver, and gut, examining physiological functions to strengthen brain-body MRI mapping. This integrated approach provides novel insights into abnormal brain-body interactions in neurological, psychiatric, and systemic metabolic disorders.

Movement Disorders	Neuroimaging in Multiple Sclerosis	Developmental Psychiatry	Brain Body Interaction




SIX CURRENT RESEARCH PROJECTS AT DRCMR

The research institute is currently involved in many groundbreaking projects aimed at advancing precision medicine and neuroimaging technologies, at understanding brain trajectories in children and adolescence as well as at elucidating the mechanisms of brain changes in diseases such as Multipe Sclerosis and Parkinson's disease. These initiatives bring together cross-disciplinary teams to develop innovative tools and therapies with real-world clinical impact. Listed in this section are five highlights of the currently ongoing projects at DRCMR.

KEY PROJECTS

DANNORMS

DANISH NON-INFERIORITY STUDY OF OCRELIZUMAB AND RITUXIMAB IN MULTIPLE SCLEROSIS

FUNDED BY: Danish Regions

Large cohort studies and clinical trials demand effective data management and even more specific and robust MRI techniques. The DRCMR Reader Centre has for the past two decades taken pride in supporting such studies from idea to quality-assured results. One of the main studies currently being supported by the Reader Centre is the DanNORMS study, which is short for Danish non-inferiority study of ocrelizumab and rituximab in Multiple Sclerosis. The study is a randomized, open-label, multi-centre, phase 3 non-inferiority clinical trial.

The primary aim of the study is to test whether rituximab treatment is non-inferior to ocrelizumab treatment in active forms of multiple sclerosis (MS). While ocrelizumab is the only approved therapy with phase 3 data on safety and efficacy, rituximab has demonstrated comparable efficacy in phase 1 and 2 studies and is often used off-label. If the study can demonstrate the non-inferiority of ritixumab, this would allow access to high-efficacy therapy for more persons with MS since ritixumab is significantly more cost-efficient.

The study is headed by the Danish Multiple Sclerosis Center at Rigshospitalet while the imaging part is coordinated by the DRCMR Reader Centre. The Reader Centre has set up a unified MR-protocol that is used at the 9 participating imaging sites across Denmark. All MR images are collected at DRCMR, where the Reader Centre staff performs quality assurance and data analyses of all the data. Several of the primary outcome measures of the study are MRI-related and the data analyses utilize a combination of the newest AI-driven automated anlyses methods and the expert knowledge of our experienced readers.

The study has succesfully recruited a total of 600 MS patients that will be scanned up to 7 times each over a period of 5 years. The primary outcomes of the study will be assessed after the first 24 months of treatment and are expected to be ready in autumn 2026.

7T-MS

CORTICAL LESIONS AND GREY MATTER DYSFUNCTION IN MULTIPLE SCLEROSIS

FUNDED BY: Lundbeckfonden, DFF, Gangstedfonden, Scleroseforeningen, Region Hovestaden & AHH

In multiple sclerosis (MS), cortical pathology contributes significantly to disability and has therefore attracted considerable interest in the last decade. However, we are yet to understand the impact of cortical damage on both the connectivity and functional integrity of the affected area and other parts of the central nervous system. Clinical magnetic resonance imaging (MRI) at 1.5 or 3 Tesla is indispensable to the diagnosis and monitoring of MS-related brain damage. However, common MRI features, such as atrophy and lesions, are insufficient predictors of disability in MS as they only partially reflect functional properties of affected brain networks. The greater sensitivity of 7 Tesla MRI is needed to assess cortical damage more comprehensively. 7T MRI doubles the number of detectable cortical lesions (Madsen et al. 2021), and allows for high-resolution myelin mapping of the cortex. This project exploits the increased resolution of 7T MRI to map cortical lesions and diffuse changes in cortical myelination using quantitative MRI in patients with MS. We also use transcranial magnetic stimulation (TMS) as a complementary tool, which allows investigations into functional cortical integrity and conduction properties of the corticospinal system. By using state-of-the art anatomical and quantitative MRI at 7T, supplemented by TMS, we aim to identify radiologically visible and invisible features of cortical grey matter damage that contribute to physical and cognitive impairment in MS. The ongoing project aims are:

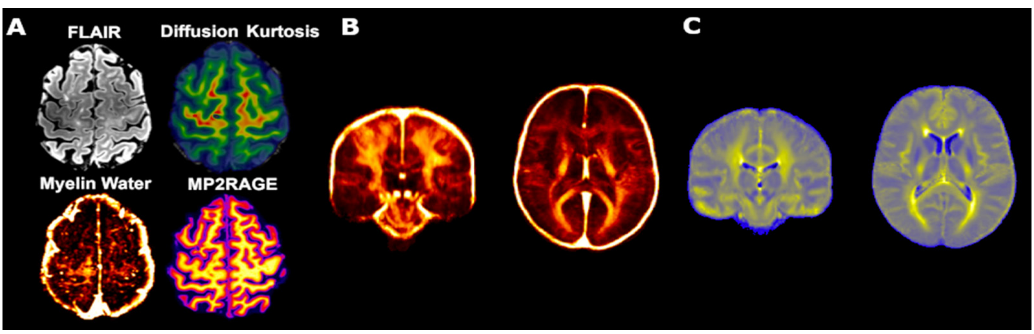
- To utilize submillimeter anatomical MRI to map the distribution of the different types of cortical lesions in relapsing remitting, secondary progressive and primary progressive MS patients.
- To characterize and compare cortical lesions, perilesional grey and white matter as well as

IMPACT

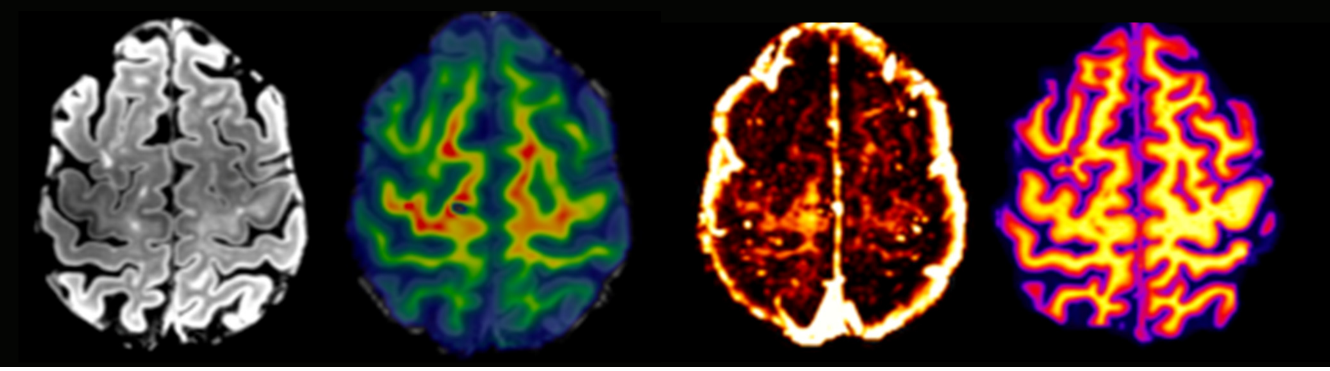
This project will reveal key insights into how cortical demyelination and damage, both regionally and globally, contribute to cognition and motor impairment in MS, two major disabling problems for patients. We will advance the possibilities of MRI to capture cortical involvement in Danish MS patients with the goal to improve individual stratification, monitoring of disease progression and capturing of the individual response to therapy.

FACTS

Project period:	01.01.2017 – 01.01.2026
PIs:	Hartwig Siebner & Vanessa Wiggermann
Collaboration:	Danish Multiple Sclerosis Center, Rigshospitalet Glostrup
Funding:	Scleroseforeningen, Independent Research Fund Denmark, Hvidovre Hospital, Gangsted fonden, The Lundbeck Foundation.



Exemplary advanced MRI metrics capture cortical myelin changes in a leukocortical lesion in a primary-progressive MS patient. Here shown: FLAIR for general MS pathology – Diffusion Kurtosis shows changes in tissue microstructure – Myelin Water detects specifically reductions in myelin – MP2RAGE for very high-resolution mapping of the cortex and cortical changes in T1 relaxation. (B) High-quality average templates of myelin water fraction and intra-extracellular T2 (C) can be created.



normal appearing grey matter using quantitative myelin-sensitive MRI sequences.

- To explore the relationship between MRI measures of focal and diffuse myelin injury with neurophysiological integrity of the corticospinal system and clinical disability in order to establish novel stratification tools and predictive biomarkers.

In close collaboration with the Danish Multiple Sclerosis Center at Rigshospitalet Glostrup, we are in the unique position to investigate these questions in MS patients at all stages of the disease. Starting from 2017, we developed and optimized high-resolution MR sequences for our 7T MRI system and set up a neurophysiological experimental protocol for measurements of sensorimotor conduction time and cortical integration, using TMS and electroencephalography (EEG). To date, we have collected data from 38 relapsing remitting patients, 12 patients with secondary progressive MS, 29 patients with primary progressive MS and 38 matched, non-neurological controls. Our results so far show that having a cortical lesion in the primary sensorimotor hand area is associated with a significant reduction in both manual dexterity and sensory acuity of the fingers. Additionally, our results demonstrate that TMS is sensitive to the disruption of cortical function due to cortical lesions, and that this disruption might be related to increased disability (Madsen et al. 2022). Digging even deeper into the pathology of cortical lesions, we showed that cortical lesions are associated with local changes in the concentration of excitatory and inhibitory neurotransmitters, using 7T MR-spectroscopy (Madsen et al. 2024).

TARGETED TREATMENT OF MULTIPLE SCLEROSIS

The Danish Multiple Sclerosis Center at Rigshospitalet is a European leader in research on the pathogenesis and treatment of multiple sclerosis (MS). MS research is crucially interlinked with MRI. Our long-standing collaboration with DRCMR highlights our combined strengths—bringing together excellence in patient management, fluid biomarker analysis and high-quality MRI data and analysis methods. In this close partnership, the MS Center uses DRCMR's equipment and expertise to conduct studies, and conversely, the center helps to recruit patients when researchers at DRCMR develop and test new MRI and brain stimulation methods. It is a fruitful collaboration that has contributed significantly to advancing our understanding and the treatment of MS over the past 25 years.

"Over the last 10 years, our collaboration has brought forward unique studies in primary-progressive MS, new frontier studies using 7T MRI to explore the role of cortical lesions in MS, as well as the to date largest national treatment trial for MS, answering the highly relevant question of treatment non-inferiority between two high efficacy therapies (DanNORMS). The DanNORMS trial is a key study on the European stage, that has challenged and advanced our collaborative strategies to new levels. These studies all contribute to improving our understanding of MS, to make reliable, earlier diagnoses and initiate treatments. Thereby, we are able to help many patients achieve a markedly better quality of life. MS treatment today is not just one thing—it encompasses many approaches—and we hope that in the future, with the help of MRI scanning, we will be able to predict the progression of the disease in each individual case, and thereby tailor treatment to the individual patient to an even greater extent than we do today."

Finn Sellebjerg
Professor, Copenhagen University & Head of the Danish Multiple Sclerosis Center, Copenhagen University Hospital

COM-BRAIN

UNDERSTANDING THE BRAIN'S INTRICATE COMMUNICATION NETWORKS

FUNDED BY: The European Research Council

The five-year project, titled "Non-invasive Conduction Mapping in Brain Networks: A Novel Imaging Framework for Axonal Fingerprinting of Brain Connections in Health and Disease" (CoM-BraiN), is hosted at the DRCMR, with co-hosting by the Technical University of Denmark.

The CoM-BraiN project focuses on understanding the brain's intricate communication networks, where countless axons—tiny "cables"—carry signals between different regions to power our thoughts, actions, and decisions. These axons, wrapped in a fatty substance called myelin, transmit signals at different speeds based on their size and the thickness of their myelin sheath. However, diseases like ALS and MS can damage these structures, disrupting communication in the brain and leading to severe functional and cognitive impairments.

Our goal in CoM-BraiN is to transform structural MRI into a kind of "in vivo microscope." As discussed at the kick-off meeting in Copenhagen (Figure below). This means making it possible to use MRI scans to examine these microscopic features inside living brains. By doing this, we can predict how structural changes in axons and myelin might affect the brain's ability to function. This kind of insight, which is typically only available by studying donated postmortem brains under a microscope, could revolutionize how doctors detect and treat brain diseases.

Although traditional structural MRI can only capture details at the millimeter scale, it is sensitive enough to reveal microstructural patterns beyond this resolution. Over the years, MRI methods have been developed to estimate axon diameters, but these methods often have biases that limit their reliability in real-world clinical settings. In CoM-BraiN, we are creating a new generation of MRI-based models that address these limitations, enabling higher precision in estimating axon diameters. Early in our work, we discovered that traditional ways of building models, based on assumptions about axon anatomy, are unstable when applied to more detailed data. These limitations stemmed from the fact that the MRI signals for some microstructural details were too similar to differentiate.

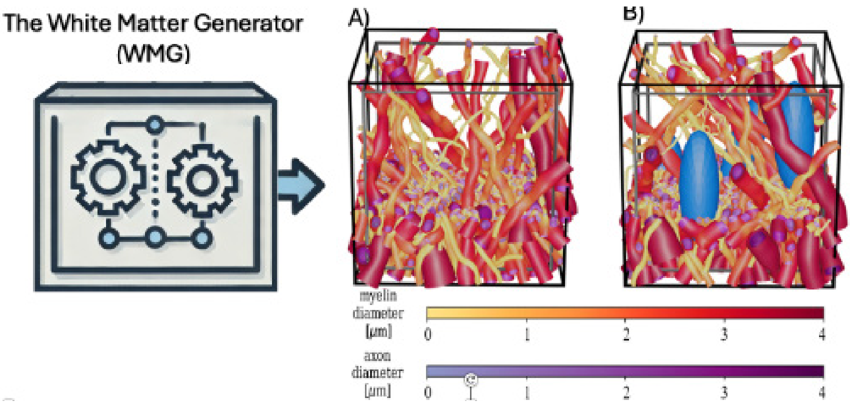
To solve this, we turned our focus to machine learning (ML) techniques, which are not limited by the same assumptions as traditional models. The ML methods showed exceptional results in controlled settings, but their performance declined significantly when tested on real MRI data. We are now testing novel data preprocessing approaches to address this challenge, and the preliminary results are promising. A key challenge in developing these models is the need for ground-truth data: how can we know what these axons and myelin look like in detail without directly seeing them? To overcome this, we used X-ray Nano Holotomography (XNH), a cutting-edge 3D imaging technique that allows us to visualize brain microstructures with astonishing detail—down to 75 nanometers. This technology requires access to synchrotron facilities like ESRF in Grenoble or MAXIV in Lund and produces massive datasets. To analyze these datasets, we developed an advanced image processing pipeline using deep learning. This pipeline takes sparse, manually labeled training data and uses it to accurately segment entire 3D images into tissue classes, including axons, myelin, blood vessels, and cells.

With this detailed understanding of brain microstructures, we developed a software tool called the White Matter Generator (WMG). This tool allows us to create synthetic 3D models of realistic brain environments,

representing both healthy and diseased states, such as axonal degeneration or myelin loss - Figure above. These models are used to train and test MRI methods, bridging the gap between the anatomical features seen in XNH images and the signals captured by MRI scans.

Myelin is a particularly important part of this story because it plays a crucial role in speeding up signal transmission in the brain. Changes in myelin are often linked to diseases, but current MRI methods cannot easily distinguish whether the myelin is being damaged or if it is in the process of repair—a vital clue for understanding disease progression and recovery. In CoM-BraiN, we have explored a new MRI-based approach that may reveal these dynamics. We tested this technique in animal models of demyelination (myelin loss) and remyelination (myelin repair), comparing the results with traditional microscopic analysis. The results were highly promising, showing that this new method could provide valuable insights into the state of brain diseases.

The CoM-BraiN project is paving the way for a deeper understanding of the brain while creating new possibilities for diagnosing and treating neurological disorders. So far, the project has achieved several promising results. We have developed a new generation of MRI-based axon diameter models and an innovative myelin metric, both of which offer doctors and neuroscientists more precise tools to detect early signs of brain disease and track disease progression. Additionally, our deep learning-based framework for analyzing massive XNH datasets, together with the WMG software, will be made publicly available. These resources will provide an invaluable foundation for future research, enabling scientists worldwide to advance their understanding of brain microstructures.



The White Matter Generator (WMG) is a software tool for creating realistic 3D meshes of White Matter microstructural features, including axons, myelin, and cells. Based on X-ray Nano Holotomography (XNH) imaging. Adapted from Winther et al., 2024, Front. Neuroinform.

VIA19 - BRAINMAP

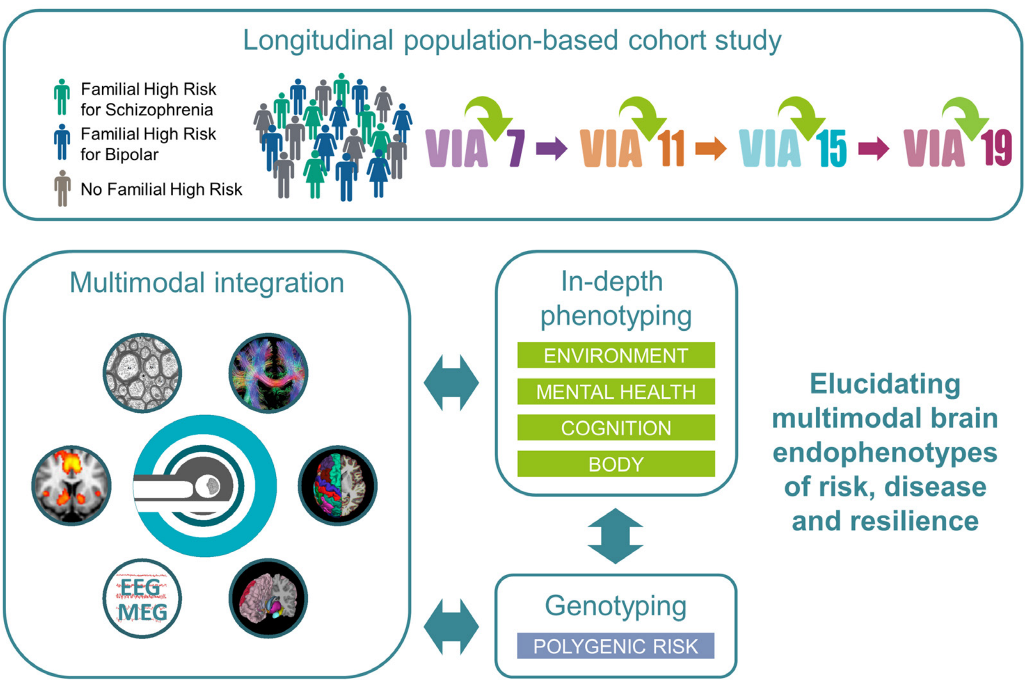
THE DANISH HIGH RISK AND RESILIENCE STUDY

FUNDED BY: Lundbeckfonden

Children of parents with schizophrenia and bipolar disorder are at high risk for developing mental illnesses. Studies of groups at high risk for schizophrenia and bipolar disorder provide opportunities to gain insight into the processes that contribute to or protect against the emergence of symptoms. The Danish High Risk and Resilience Study – VIA 19 includes 19-year-old adults whose parents have been treated for bipolar disorder, schizophrenia disorders or none of these disorders.

VIA 19 is the fourth follow-up study of a Danish cohort of 522 children who have already been studied at the age of seven (VIA7), eleven (VIA11), and fifteen (VIA15). When children took part in VIA 11 and VIA15, they underwent magnetic resonance imaging of the brain at the DRCMR or the Centre for Integrative Neuroscience (CFIN), Aarhus University. We are now re-scanning the children at the age of 19. Approximately half of the participants are additionally be examined with EEG at the DRCMR or with MEG at CFIN.

The design and scope of brain mapping in the VIA 19 study is unique on a global scale. Since brain imaging is performed repeatedly, before puberty (i.e., at the age of 11), during puberty (i.e., at the age of 15), and after puberty (i.e., at the age of 19) we have the opportunity to identify patterns of abnormal structural and functional brain development. We will particularly



focus on developmental changes of brain networks involved in social cognition, reward processing, and executive functions.

Furthermore, the brain imaging-based measures of brain network function and structure will be linked to the environmental, genetic, clinical, and neurocognitive data. This will enable us to elucidate underlying pathophysiological mechanisms and develop models predictive of risk, disease initiation and development, and resilience. We have now required funding to add 7T spectroscopy imaging in VIA19, which will allow us to relate neurochemical features to the functional read-out, allowing a mechanistic understanding of impairments.

FACTS

VIA 19 started in 2024 and is led by Prof. Merete Nordentoft from the Research Unit, Mental Health Center Copenhagen, University of Copenhagen. VIA 19 received funding from the Lundbeck Foundation, the Mental Health Services of the Capital Region of Denmark and the Novo Nordisk Foundation.

IMPACT

The combination of a multidimensional assessment of cognition, environment, and genetics with multimodal imaging in the VIA 19 Brainmap study allows to identify brain risk and resilience markers which may help to develop targeted treatments that prevent the transition to these disorders.

COMBINING CLINICAL PSYCHIATRY WITH WORLD-CLASS NEUROIMAGING

Professor Merete Nordentoft is a distinguished psychiatrist leading the CORE research unit at the Mental Health Centre Copenhagen, focusing on early intervention in psychosis, suicide prevention, and mental-health epidemiology. She is the founder of the Danish High Risk and Resilience Study (VIA), a landmark longitudinal cohort investigating children at familial risk of severe mental disorders. As a founder of VIA, Merete initiated the collaboration with DRCMR, to include imaging in this unique longitudinal cohort. To strengthen this work, she initiated a collaboration with the Danish Research Centre for Magnetic Resonance (DRCMR), integrating advanced neuroimaging into VIA. This partnership now pioneers the tracking of brain development from childhood into adulthood, offering unique insights into risk and resilience for mental disorders..

"Our collaboration with DRCMR allows us to combine clinical psychiatry with world-class neuroimaging. By integrating MRI and EEG into the VIA study, we can follow brain development over time and gain unprecedented insights into why some children at familial risk develop mental disorders while others show resilience. Looking ahead, we see great potential in expanding this partnership to explore new imaging methods and deepen our understanding of mental health across the lifespan."
Merete Nordentoft
Chief physician at the Mental Health Centre Copenhagen, Copenhagen University Hospital
Professor in Psychiatry at Copenhagen University

ADAPT-PD

UNDERSTANDING THE CORTICO-BASAL GANGLIA CIRCUIT DYNAMICS IN HEALTH & PARKINSON'S DISEASE

FUNDED BY: Lundbeckfonden

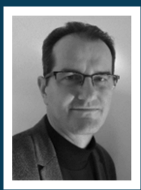
ADAPT-PD is a collaborative project that addresses a central question in neuroscience with enormous therapeutic implications: How can the dysfunction of brain circuits in Parkinson's disease be normalized with device-based neuromodulation? Parkinson's disease (PD) is a common and disabling, multi-system neurodegenerative disease which affects motor and non-motor brain networks. The symptoms of PD are motor symptoms like bradykinesia and tremor as well as non-motor symptoms such as autonomic dysfunction and cognitive decline. As of today, the main therapeutic approach is dopaminergic replacement therapy like levodopa. Unfortunately, most patients develop adverse effects with time. One common and disabling adverse effect is levodopa-induced dyskinesia (LID) which are involuntary movements coursed by the non-physiological fluctuations in dopamine concentrations and maladaptive plasticity at the cortico-striatal synapses. The project is led by Professor Hartwig Siebner at DRCMR, who is collaborating with Professor Andrea Kühn, Charité Universitätsmedizin in Berlin, Germany, and Professor Angela Cenci Nilsson, Lund University, Sweden. Each site focuses on different aspects of PD and by combining the different levels of analysis, this project can achieve a unique understanding of the disease and how to treat it.

We use an array of well-aligned methods to characterize how the cortex and its projections to the basal ganglia contribute to motor and non-motor disabilities in PD and LID. Invasive recordings and opto-/chemogenetic stimulation in rodent models of PD and LID yield novel insights into critical cortico-basal ganglia circuit features that constitute candidate targets for ADAPT. In humans, we use an array of neuroimaging techniques such

BOLDLY PAVING THE WAY FOR CIRCUIT-BASED NEUROMODULATION

Professor Angela Cenci Nilsson MD PhD leads the Basal Ganglia Pathophysiology Laboratory and the strategic research area MultiPark at Lund University (Lund, Sweden). By actively participating in multiple Scandinavian-German Joint Meetings on Parkinson´s disease, Angela has had the opportunity to know and interact with the movement disorder team at DRCMR over several years. These pleasant personal interactions and scientific discussions turned into concrete collaborations thanks to the project "ADAPT-PD", funded by the Lundbeck Foundation. As progress is made, new ideas and new technical solutions emerge, laying the ground for a continued fruitful collaboration in the future.

"Thanks to recent technological and scientific advances, remarkable progress is being made in understanding the structure and function of neuronal circuits and brain networks. As a consequence, we are witnessing a growing global interest in developing non-invasive methods of brain stimulation that can precisely target specific circuits to improve neuropsychiatric function. The collaborative project ADAPT-PD aims to take the lead in this exciting development. Using the motor features of Parkinson´s disease and L-DOPA-induced dyskinesia as a common model platform, we probe the possibility of controlling specific symptoms by modulating specific brain rhythms using TMS or DBS in human subjects, and optogenetic stimulation in rodent models. The project paves the way for the development of circuit-targeted neurostimulation approaches, with possible therapeutic applications beyond Parkinson's disease.
Angela Cenci Nilsson, Professor and leader of the group Basal Ganglia Pathophysiologyat Lund University



HARTWIG SIEBNER

DRCMR, AHH & Neurology, BHH

Transcranial brain stimulation and brain imaging

- Human Imaging & Stimulation
- Ex-Vivo Animal Recordings
- Chemogenetic Animal Stimulation

DANISH RESEARCH CENTRE FOR MAGNETIC RESONANCE

ANGELA CENCI NILSSON

Lund University

Basal ganglia circuits ain rodent PD models

- In-Vivo and Ex-Vivo Animal Recordings
- Optogenetic Animal Stimulation

LUND UNIVERSITY

ANDREA A. KUHN

Charite, Berlin

Interventional neurophysiology and deep brain stimulation (DBS)

- Human Deep-Brain Stimulation
- Human Direct Cortical Recordings
- Ex-Vivo Animal Recordings

CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN

as functional MRI, EEG & TMS to map the functional circuit changes dynamically over time as the brain goes from an unmedicated state to a medicated one. In our dedicated clinic for brain stimulation, we then apply this knowledge to test how non-invasive cortical stimulation can normalize the dysfunctional brain circuits. We develop novel brain stimulation therapies that primarily target the dysfunctional cortex.

ADAPT-PD will greatly advance the mechanistic understanding of cortico-basal ganglia circuit dynamics in health and PD and create a powerful hub for causal brain circuit discovery, paving the way for personalized device-based neurostimulation, with therapeutic implications beyond PD.

IMPACT

Using a multimodal and multiscale approach, we will investigate how the cortico-basal ganglia circuit is altered in Parkinson's disease as well as levodopa-induced dyskinesia. Based on this knowledge we will develop treatments with tailored non-invasive and invasive brain stimulation.

FACTS

Funding:	35 mill. DKK Lundbeck Foundation Collaborative Projects grant
Led by:	Professor Hartwig Siebner
Partners:	Professor Andrea Kühn, Charité Universitätsmedizin in Berlin, Germany Professor Angela Cenci Nilsson, Lund University, Sweden

PRECISION-BCT

A NEW PERSONALISED TREATMENT OF MAJOR DEPRESSIVE DISORDER WITH NON-INVASIVE TMS

FUNDED BY: Innovation Fund Denmark

The BASICS project (Biophysically Adjusted State-Informed Cortex Stimulation) launched a series of investigations into TMS at DRCMR. The BASICS project was an interdisciplinary research endeavor pursued jointly by DRCMR, DTU Compute and DTU Electro. The main goal was to synergistically combine non-invasive transcranial brain stimulation (NTBS), brain mapping, electric field modeling and machine learning to advance the potential of NTBS to shape human brain networks.
The vision of BASICS was to design efficient and novel brain stimulation applications through the synergistic combination of noninvasive brain stimulation, functional brain mapping, electrical field modeling, and machine learning.

Building on this work, PRECISION-BCT was started in order to further elucidate the mechanisms and benefits of TMS. In Precision-BCT, we combine leading clinical, technical, and methodological expertise of Danish and international partners to implement a new treatment of major depressive disorder (MDD), based on personalized non-invasive transcranial magnetic stimulation (TMS). Supported by a Grand Solutions grant from Innovation Fund Denmark, it is led by DRCMR and involves MagVenture A/S (Farum, Denmark), the Centre for Neuropsychiatric Depression Research of the Mental Health Centre Glostrup, DTU Health Tech, Localite GmbH (Bonn, Germany) and the Ludwig-Maximilians-University (Munich, Germany) as partners. Our aim is to improve and innovate on all aspects of TMS-based MDD treatments to boost their clinical efficacy.

MDD is among the most frequent brain disorders and severely affects the social life and relationships of the patients. It increases their risk for lowered financial income and unemployment and can result in somatic comorbidities and a lower life expectancy. MDD also poses a huge economic burden for society as a whole. However, not all patients respond to the available treatment options, including various antidepressants and different types of psychotherapy, even when these are given in combination. Repetitive TMS (rTMS) of prefrontal brain areas is currently developed as a promising and much-needed alternative treatment. It is approved as MDD treatment in the USA and EU, especially because it has been shown to be efficacious in many of the patients that are deemed resistant to standard thera-

pies. RTMS applies a series of strong electromagnetic field pulses to cause highly synchronized neural activity in the targeted brain area. It is safe, pain-free and non-invasive and can successfully restore normal activity in the dysfunctional brain networks and by that reduce the clinical symptoms of the disease. So far, rTMS is given as "one-size-fits-all" therapy that does not account for the substantial between-patient variability of the disease-related brain circuit alterations, which currently limits clinical efficacy. Precision-BCT aims to tackle this challenge by personalizing the treatment, with the aim to further increase its clinical value.

During the initial project period, we developed novel TMS stimulation and navigation equipment that enable precise spatial targeting and dose control, highly flexible stimulation patterns, and simultaneous stimulation of several brain regions. In addition, a personalization workflow that uses structural and functional brain imaging to identify the relevant individual brain circuit has been successfully tested in healthy participants. While the methodological research will continue, the project is now focused on translating the new findings and tools into clinical testing in a MDD patient cohort. We have received additional funding from The Independent Research Fond Denmark that will enable us to substantially increase the scope from methodological proof-of-concept testing towards a full clinical trial. Within the new COMPACT (Copenhagen Magnetic Personalized Accelerated Brain Circuit Therapy) trial, 70 MDD patients will undergo an intense one-week rTMS therapy based on the Precision-BCT approach. This will enable us to ensure the efficiency and maturity of our clinical workflow for personalized rTMS treatment of MDD that will be grounded in the underlying circuit-dysfunction and will pave the way for large-scale clinical studies aiming at a broad clinical adoption.

THE POWER OF RESEARCH/INDUSTRY COLLABORATION

As CEO of the Danish-based company MagVenture, the leading developer and manufacturer of transcranial magnetic stimulation (TMS) systems worldwide, I have had the privilege to work closely with DRCMR over many years. Our partnership is rooted in a shared commitment to scientific excellence and innovation in non-invasive brain stimulation. The PRECISION-BCT project is a testament to the power of cross-disciplinary collaboration between industry and academia bringing together engineering ingenuity, clinical expertise, and advanced neuroscience.

"The PRECISION-BCT project represents a paradigm shift in how we approach the treatment of depression. By combining real-time electric field modeling, individualized brain circuit mapping, and coordinated multi-site TMS, this initiative pioneers a personalized, circuit-based therapy. At MagVenture, we are proud to co-develop and commercialize this next-generation technology, which aligns seamlessly with our mission to improve mental health through non-invasive neuromodulation. Our collaboration with DRCMR continues to drive forward the frontier of precision medicine, ensuring that advanced TMS becomes more targeted, more effective, and more accessible to those in need."

Stig Wanding Andersen, M.Sc.E.E., CEO, MagVenture A/S

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