Stratetic Alliance in Radiological Diagnostics and Therapy

Hildegard Kaulen

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Strategic Alliance in Radiological Diagnostics and Therapy

For three years now, Siemens and the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have been applying their knowledge and expertise in the field of oncologic radiology in a strategic alliance. Otmar Wiestler, MD, Professor and Chairman of the Board at DKFZ, discusses the partnership's topics and goals.

By Hildegard Kaulen, PhD

Professor Wiestler, what are the aims of the strategic alliance between the DKFZ and Siemens?
WIESTLER: We want to continuously improve imaging methods and link them to create a new level of imaging quality. This information can then be used for highly precise radiation therapy planning as well as monitoring therapy progress. We have agreed on various projects with these aims in mind. In fact, the alliance between us is extremely multifaceted. For example, Siemens and the DKFZ will work together to sound out the potential of high field strengths in magnetic resonance imaging [MRI] in cancer diagnosis. Siemens is providing a 7 Tesla system. The DKFZ commissioned a new building with complex steel cladding and a special foundation to house the unit's 32-ton magnet. The two partners are also cooperating in radiation therapy. In this field, Siemens is supplying the jointly developed ARTISTE® radiation therapy solution, which takes 3D cone beam computed tomography images just before and during the radiation therapy session to assess tumor position. Then, the therapist can adjust the therapeutic radiation to the specific tumor size and location. Soon, we will probably also try to combine an MRI unit with a source of radiation. And, in our third project, we are cooperating in the area of molecular imaging. To help treating physicians plan the radiation therapy more precisely, Siemens and the DKFZ are additionally developing a software platform that reconciles clinical images and methods into a single, coherent, big picture. Another part of our strategic alliance is the creation of the Integrated Diagnostics and Therapy Center, which will function as a link to the hospital. Here, all of the modern imaging data will converge for inclusion in cancer therapy.

What brought the two partners together?
WIESTLER: Our strategic alliance is based on a longstanding cooperation in imaging and radiation therapy between the DKFZ and Siemens. The 160 MLC multileaf collimator that is used to shape the radiation field in the ARTISTE solution, is, for example, a joint development. Our future plans include forming a strategic alliance with the University Hospital Heidelberg as a third partner. The DKFZ is already in close contact with this hospital – for example, via clinical cooperation units and the National Center for Tumor Diseases.

In a strategic alliance, partners with shared interests and goals work


“The two partners are an ideal fit.”

Otmar Wiestler, MD, Chief Executive Officer, Chief Scientific Officer, German Cancer Research Center, Heidelberg, Germany

together. What makes this alliance so attractive to both sides?
WIESTLER: Cancer research and medical technology are predestined for strategic alliances. Both fields are interested in how technical developments can make diagnostics and therapy even more precise and more tolerable for patients. Because of the short development cycles, the business risk in this field is also easier to assess than, say, in the pharmaceutical industry, where ten to 15 years pass before a new product comes to market. During the same time span, medical technology makes swift advances, as past developments have shown us. In addition, the two partners are an ideal fit. The DKFZ provides Siemens with its large body of scientific expertise in cancer research. In return, the scientists at the DKFZ receive access to the latest generation of Siemens equipment and the opportunity to be involved in the further development of the hardware and software components. Clinical evaluation is tremendously facilitated through our close connection with the National Center for Tumor Diseases. The latest prototypes have to be tested on patients quickly, which is one reason why cooperation arrangements with clinical partners are so important. It doesn’t work without the patient.

Are these kinds of alliances also politically desirable? After all, one of the aims of the European Union is to become the most dynamic, most competitive, knowledge-based economic area in the world.
WIESTLER: It certainly makes sense to have political support. But whether a strategic alliance works doesn’t depend on politics. The strategic alliance between the DKFZ and Siemens is based on what the two partners bring to the table and how they live out the alliance. It’s all about complementary strengths in oncologic radiology and about dealing with each other in a true spirit of partnership. The outcome is a direct win-win situation for both partners.
And, by the way, the idea for this cooperation came up during a meeting with Professor Erich Reinhardt, who, at the time, was the head of Siemens Healthcare. There was a desire to pool our efforts and develop intelligent new products that reach the patient quickly. That’s why we are working together on high-field magnetic resonance imaging, Adaptive Radiation Therapy, and molecular imaging. These ideas are also in line with the new role of imaging, which is increasingly becoming an instrument of holistic disease management, from the initial

findings through to monitoring the course of therapy.

You mentioned the inclusion of patients. How does the strategic alliance benefit patients?
WIESTLER: The patients are included right from the start through clinical studies. One of the alliance's stated goals is to ensure that these promising new methods are put into clinical use quickly. We want to make lasting improvements in the quality of cancer care provided. And that definitely is something that benefits the patient.

Which types of cancer is the strategic alliance examining?
That depends on the individual projects. We are currently using the 7 Tesla MRI unit to scan patients with brain tumors. Our colleagues in that project are building on data collected using a conventional 3 Tesla MRI scanner. They are checking whether additional information can be gained from a scan at a higher field strength and if so, what that information entails. Alongside much improved anatomical resolution, these new units can also be used to depict molecular spectra in the smallest possible space. This permits highly precise tumor characterization. Plus, this unit is still in the prototype stage. Both partners are putting a lot of work into the further development of this new technology.

What are the plans for other kinds of cancer?
WIESTLER: In the area of lung cancer, we are working closely with the chest clinic here. We believe further development of Adaptive Radiation Therapy will particularly benefit lung cancer patients, whose tumors move with every breath. These tumor movements should be taken into account during radiation therapy in order to spare as much healthy tissue as possible. The aim, in this case, is to arrive at a radiation therapy that adapts to movement. Colon carcinomas and prostate cancer are similarly affected by changes in position, because they are shifted by the contents of the intestine and the bladder. Just like in lung cancer, radiation therapy is a key component in prostate cancer treatment. Because the organ is surrounded by sensitive structures, radiation should be applied as precisely as possible. Prostate cancer is currently the most frequently diagnosed type of cancer in men.

What about molecular imaging? Have there already been tangible results in this area?
WIESTLER: Molecular imaging provides information on the molecular composition and functional characteristics of the tumor. The requirements that apply to new tracers, however, are very strict. They have to be tumor-specific and it must be possible to make them visible. They have to be distributed throughout the body and find their target molecule. In addition, it is important for them to remain within the body long enough to supply a good positron emission tomography [PET] image. But, they also can't be eliminated too slowly in order to avoid placing unnecessary strain on the patient. That's a challenging profile, and one that isn't easy to fulfill. It's no coincidence that marked glucose still remains the most frequently used PET tracer. But in our strong alliance with Siemens, I am really confident that we will master this challenge.

Should there be more strategic alliances like the one between the DKFZ and Siemens? Does this cooperation serve as a model for others?
WIESTLER: In Germany, we have strong research institutions and a thriving medical technology sector. We just have to get the results into the value chain faster. The connection between these two worlds carries a great deal of potential for the rapid transfer of innovative research into clinical applications. We need cooperative arrangements to achieve this, and they have to meet certain conditions in order to succeed. The alliance must be based on strong partners, as is the case between

Summary

Challenge:
- New developments in medical physics, medical technology, and radiation therapy should reach patients faster than before.
- Strategic alliances need strong partners with complementary expertise that ensures a win-win situation for them.

Solution:
- The strategic alliance between Siemens and the DKFZ is based on longstanding cooperation with shared product developments.
- Both partners established the prerequisites for the strategic alliance themselves, making them independent of short-term sponsoring programs.
- There are plans to bring the University Hospital Heidelberg into the strategic alliance as a third partner.
- The cooperation between the partners encompasses diagnosis and therapy for brain tumors, lung cancer, and prostate cancer, among others. The alliance aims to achieve better tumor characterization and integrate all image data into a shared data set that can then be used for a highly precise radiation therapy plan.
- Initially, the alliance will address the entire value chain for cancer: calculating the risk of disease, identifying cancer earlier and characterizing it precisely, planning and applying radiation therapy or other therapies optimally, and measuring therapeutic success.

Result:
- The strategic alliance aims to improve the quality of cancer care.

the DKFZ and Siemens, that complement each other in terms of their subject expertise. And, they have to bring a lot of tenacity to the table. Both DKFZ and Siemens are at the international cutting edge of their respective fields. Many political initiatives fizzle out because they are originally designed to run for just a few years, and when their time is up they can't find subsequent financing. The special thing about the strategic alliance between Siemens and the DKFZ is that both partners have created the conditions for it on their own, not through an aid program. At the same time, raising funds from outside sources, as we have now done with DOT-MOBI, a sponsoring program run by the Federal Ministry of Research, is an important goal for the alliance.

What will the future hold in terms of content?

WIESTLER: Our next goal will be to cover the entire value chain. That means calculating the risk of disease, identifying cancer earlier and characterizing it more exactly, planning and implementing radiation therapy and other treatments very precisely, as well as measuring therapeutic success. That's how we will continuously become more successful in the fight against cancer. That is, after all, the big goal both partners had in mind when they entered into this arrangement.

__Hildegard Kaulen,__ PhD, is a molecular biologist. After positions at Rockefeller University in New York and the Harvard Medical School in Boston, Massachusetts, USA, she has worked since the mid-1990s as a freelance science journalist for leading newspapers and scientific journals.

Further Information

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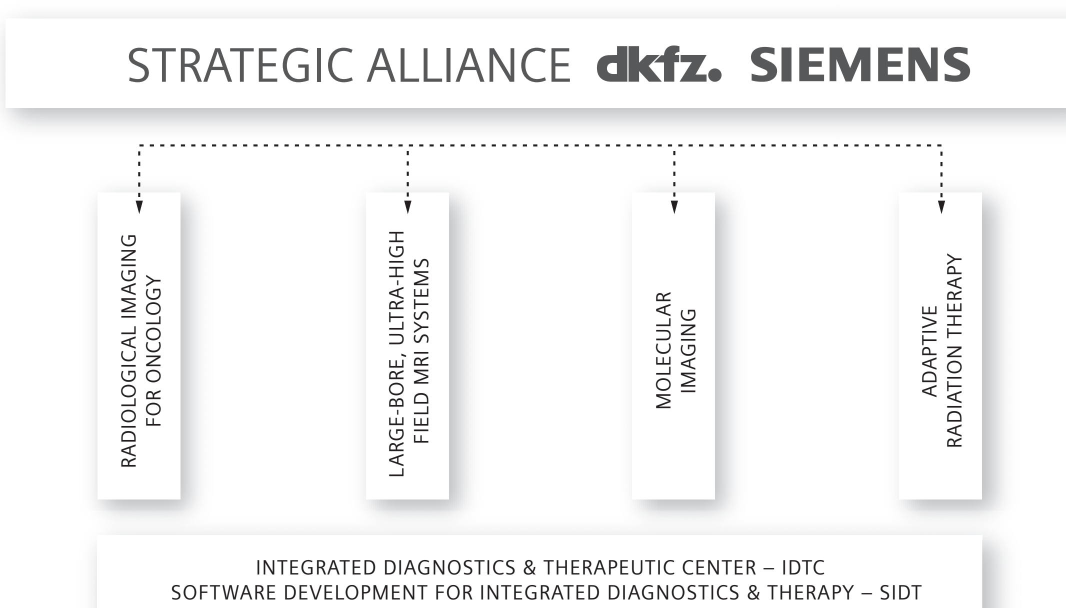
The German Cancer Research Center and Siemens are breaking new grounds with the cooperation between a national research center and a commercial enterprise.



The four pillars of the strategic alliance between the German Cancer Research Center and Siemens rest on a solid base.

Linking Research and Clinical Application

With a special role in the strategic alliance, the Integrated Diagnostics and Therapeutic Center (IDTC) coordinates and aligns all the clinical processes, from diagnosis to tumor characterization and radiation therapy planning, to monitoring therapy. Christian Thieke, MD, PhD, who heads the center, is both a physician and a physicist. He is on the staff of the DKFZ and the University Hospital Heidelberg. This dual role helps him in his duties as the head of the IDTC.
Thieke and his colleagues design the clinical studies that are necessary to transfer the results of the strategic alliance into clinical applications. They work together with the project partners to determine which of the newly developed methods should be considered for clinical trials and for which patients these methods promise the greatest success. They are involved in the clinical analysis of the imaging data and radiation therapy. That's why the development of the software platform DIROlab (Diagnostic Imaging and Radiooncology) also falls within the IDTC realm. This is where the paths needed for the combined analysis of diagnostics and therapeutic data converge. The IDTC also brings new clinical issues to light. Working with additional partners, the Center is now involved in DOT-MOBI, a collaborative research project funded by the Federal Ministry of Education and Research, which aims to optimize radiological diagnostics and radiation therapy for cancer using molecular imaging.

"The Integrated Diagnostics and Therapeutic Center (IDTC) stands for the transfer of fundamental developments into clinical application."
Christian Thieke, MD, PhD, Project Manager, Integrated Diagnostics and Therapeutic Center, German Cancer Research Center, Heidelberg, Germany

Modern architecture houses a 7 Tesla MRI system (top). The ARTISTE linear accelerator solution (bottom) is used for joint developments of DKFZ and Siemens.

Everything in One Sweep

Computed tomography, magnetic resonance imaging, positron emission tomography: When a patient has cancer, various imaging methods are used, but the results are not always consistent. In addition, some data sets can currently only be evaluated using certain workstations, as is the case with magnetic resonance spectroscopy. The DKFZ group run by Oliver Nix, PhD, colleagues from the Bremen-based research institute Fraunhofer-MEVIS, and from Siemens are therefore working on developing a software platform that can be used to quickly and effectively bring together all information. This can then serve as the basis for precise radiation therapy planning, but therapy monitoring and analysis of the radiation treatment's effectiveness also take on a new quality.
A differential image of the tumor and normal tissue can be used to generate a radiation therapy plan that is highly precise and fine-tuned to the patient. The software program is called DIROlab, for Diagnostic Imaging and Radiooncology. Because the system speeds up reporting as well as planning and analysis of radiation therapy, it also improves workflows. Nowadays, no physician can afford to spend hours of meticulous work putting together all findings, analyzing them by hand, and transferring them into the radiation therapy planning programs.
In addition, a doctor shouldn't have to have a degree in computer science to be able to use the software. Thus, DIROlab also aims to be an easy-to-understand computer assistant.

"With DIROlab, complex diagnostic information and radiation therapy can be combined to enable highly precise radiation planning."
Oliver Nix, PhD, Project Manager, Software Development for Integrated Diagnostics and Therapy, German Cancer Research Center, Heidelberg, Germany

More Targeted Radiation Therapy


Professor Wolfgang Schlegel, PhD

"We are connected through our long-standing cooperation with Siemens. Motion-adaptive radiation therapy is the logical next step."
Professor Wolfgang Schlegel, PhD, Department Head, Medical Physics in Radiation Therapy, German Cancer Research Center, Heidelberg, Germany

Radiation therapy is always a balancing act, aiming to eliminate the cancer while sparing the surrounding tissue. In Intensity Modulated Radiation Therapy, multileaf collimators shape the radiation field so the spatial distribution of the dose is closely adjusted to the target volume.
At the same time, irregular overlapping subfields spare healthy tissue, affecting only the tumor. But because the tumor can shift over the course of several weeks of therapy, its position should be checked before every treatment session. To accomplish this, the DKFZ uses the ARTISTE® radiation therapy solution, in which the conical treatment beam also generates a computed tomography image.
To further increase treatment efficacy and spare healthy tissue, Professor Wolfgang Schlegel, PhD, and his colleagues are working together with Siemens to develop motion-adaptive radiation therapy. This method aims to check the position of the tumor several times per second to ensure that the beam can be adjusted to the tumor's delicate back-and-forth shifts. To this end, the verification image will no longer be generated with a megavoltage cone beam, but rather with a kilovoltage[1] cone beam mounted at a 180-degree angle to the megavoltage radiation source. Imaging with a kilovoltage cone beam yields higher-contrast diagnostic images than a highly charged treatment beam. The appropriate flat-image detector for this configuration is still under development. In their clinical work, the project partners are focusing on tumors in the lungs, the prostate, and the spinal cord area. In the case of the lungs, tumor mass is especially prone to shifting due to breathing; in the prostate, the same is true due to the contents of the bladder or the intestine.

[1] The information about this feature is preliminary. The feature is under development and not commercially available in the U.S., and its future availability cannot be ensured.

What a PET Scan Tells Us About a Tumor's Biology

A positron emission tomography (PET) scan measures the local concentration of a radiopharmaceutical and captures – for instance, using the glucose-analog F-18 deoxyglucose (FDG) – the metabolic activity in the body. Using mathematical methods, the raw data can be dissected into individual steps that give researchers a better window into the biological processes taking place within the tumor. If FDG accumulates in the tumor, three processes are involved: good blood flow to the tumor, uptake of the tracer into the cancer cell, and metabolism within the cell.

Thanks to new software tools, Professor Ludwig Strauss, MD, and his team can separate these three processes from each other and correlate PET data with the activity of the molecules involved. By doing so, they are able to depict the dynamics of disease-specific molecular processes and gain an overview of vascular density, membrane transport, and intracellular metabolism. This is called parametric imaging. Within the strategic alliance, researchers are also examining the extent to which this information, together with the morphological data from other imaging processes, can be used for radiation therapy planning. Strauss and his colleagues are also interested in new tumor-specific molecules that can be used as tracers.

Currently, there are three tracers in use: FDG, F-18 misonidazole, and F-18-fluoro-3'-deoxy-3'-L-fluorothymidine (FLT). F-18 misonidazole is used to measure the tumor's oxygen content, and FLT to measure the unchecked growth of the tumor cells.

"With mathematical processing of the PET scan, we add a wealth of new data on the disease-specific processes taking place within the tumor. This information can be used for precise, individualized radiation therapy planning."

Professor Ludwig Strauss, MD

Professor Ludwig Strauss, MD, Project Manager, Molecular Imaging, Nuclear Medicine Clinical Cooperation Unit, German Cancer Research Center, Heidelberg, Germany

Some of the biomarkers referenced in this article are not currently recognized by the US Food and Drug Administration (FDA) as being safe and effective, and Siemens does not make any claims regarding their use.

High Magnetic Fields for Cancer Research

The strategic alliance also brought a MAGNETOM® 7 Tesla[1] (7T) magnetic resonance imaging (MRI) system to the DKFZ. This system can visualize anatomical structures that are considerably smaller than one millimeter. For brain imaging, the quality of the 7T MR images is thus almost comparable to anatomic cross sections, which allows assessing cancer lesions in all their heterogeneity. The ultra-high field strength also helps to measure the tumor's functional characteristics, such as blood flow or diffusion. With MR spectroscopy, it is even possible to detect tumor-specific metabolites, which can then be quantified to examine the metabolic activity.

All this information serves to optimize, for example, radiation therapy or to monitor the success of a chemotherapy. Together with their clinical partners, Professor Wolfhard Semmler and Michael Bock, PhD, of the DKFZ are also evaluating which cancer patients benefit from a 7T MRI scan, as the high field strength does not necessarily improve the diagnostic quality for all patients. At present, patients with brain tumors and metastatic brain cancer are the primary groups participating in the 7T MRI studies. In the future, there are plans to extend the studies to patients with prostate cancer and other types of cancer. For all patients, the 7T MRI images are compared with conventional 1.5T or 3T images to quantify how much additional information can be found in the high-field images. The University Hospital Heidelberg and the universities of Würzburg and Freiburg are also involved in this cooperative project.

"Our aim is to bring 7T MRI up to the same technical maturity that is common today for clinical oncologic applications at 1.5T and 3T."

Michael Bock, PhD, 7T MRI Project Manager, Department of Medical Physics in Radiology, German Cancer Research Center, Heidelberg, Germany

[1] The information about this product is preliminary. The product is under development and not commercially available in the U.S., and its future availability cannot be ensured. Only field strenghts up to 3T are clinically used.

Global Siemens Headquarters

Siemens AG
Wittelsbacherplatz 2
D-80333 Munich
Germany

Global Siemens Healthcare Headquarters

Siemens AG
Healthcare Sector
Henkestrasse 127
D-91052 Erlangen
Germany
Telephone: +49 9131 84-0
www.siemens.com/healthcare

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Local Contact Information

Asia/Pacific:
Siemens Medical Solutions
Asia Pacific Headquarters
The Siemens Center
60 MacPherson Road
Singapore 348615
Telephone: +65 9622-2026

Canada:
Siemens Canada Limited
Healthcare Sector
2185 Derry Road West
Mississauga ON L5N 7A6
Canada
Telephone: +1 905 819-5800

Europe/Africa/Middle East:
Siemens AG, Healthcare Sector
Henkestr. 127,
91052 Erlangen
Germany
Telephone: +49 9131 84-0

Latin America:
Siemens S.A., Medical Solutions
Avenida de Pte. Julio A. Roca No 516,
Piso 7
C1067ABN Buenos Aires
Argentina
Telephone: +54 11 4340-8400

USA:
Siemens Medical Solutions U.S.A., Inc.
51 Valley Stream Parkway
Malvern, PA 19355-1406
USA
Telephone: +1 888 826-9702