

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 con-

tinuously 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.

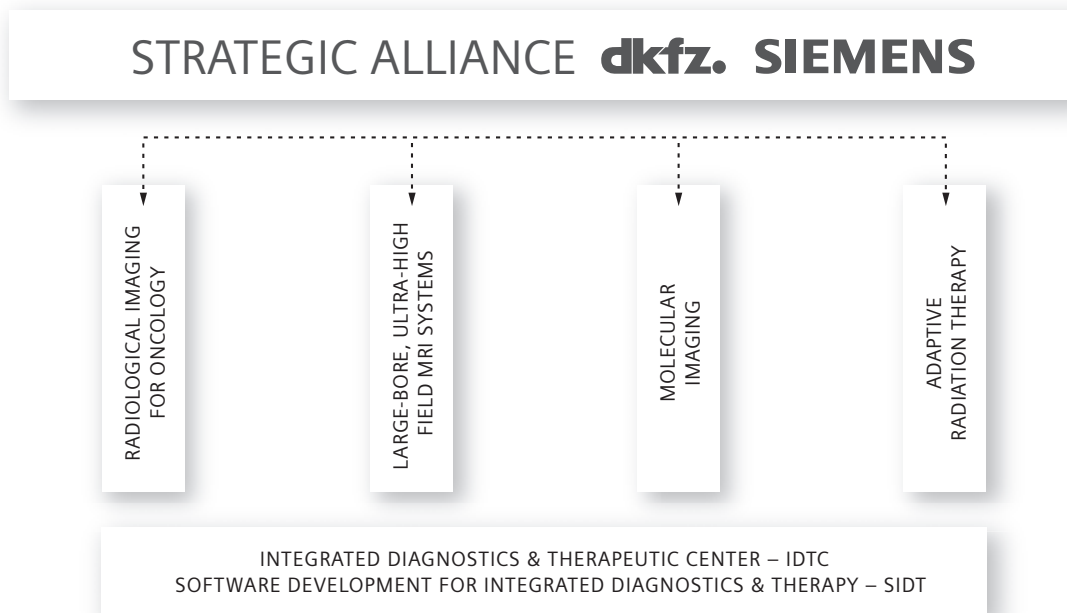
Hildegard Kaulen, PhD, is a molecular biologist. After positions at Rockefeller University in New York and the Harvard Medical School in Boston, Massachusetts, USA, she has worked since the mid-1990s as a freelance science journalist for leading newspapers and scientific journals.

Further Information

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Focused Expertise in Imaging and Radiation Oncology

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.

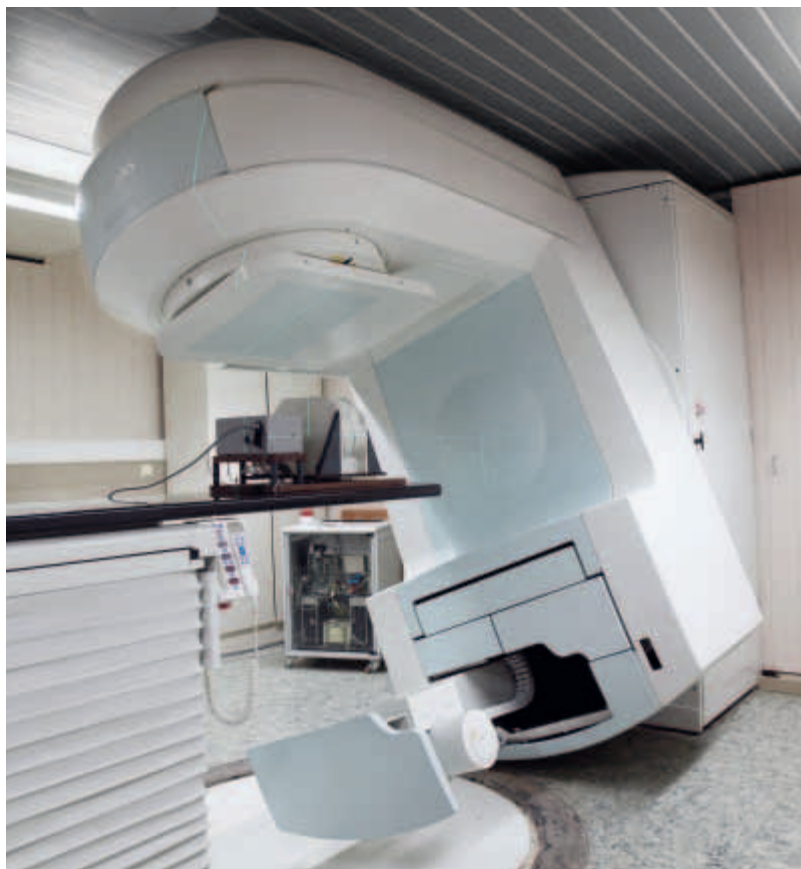
Linking Research and Clinical Application

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

Radiation therapy is always a balancing act, aiming to eliminate the cancer while sparing the surrounding tissue. In Intensity Modulated Radiation Therapy, multi-leaf 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 kilovoltage¹ 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.

"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

¹The 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 Tesla¹ (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 strengths up to 3T are clinically used.