

RINCKSIDE

VOLUME 30 • 2019

SCIENCE
MEDICINE
IMAGING
ACADEMIA
PHILOSOPHY
ETHICS
SATIRE
ADVICE

ISSN 2364-3889

RINCKSIDE

ISSN 2364-3889 • VOLUME 30, 2019

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Radiologists: To see and not to be seen

Peter A. Rinck



I remember a day in the late 1960s when my father, the head of surgery and traumatology at a Berlin hospital, mentioned at our dinner table at home: “I guess I’ll hire a radiologist; we seem to need one.” And so it happened. Until that time the surgeons had performed and read their x-ray exams themselves. Still, the surgeons had the final say. The radiologist performed an “ancillary” service. (Incidentally, at one of my first Latin lessons at school I had learned that “ancilla” means housemaid.)

At the first meeting of an international society for the use of x-rays in medicine in London in 1925, Berkeley Moynihan gave a lecture, underlining that radiology is a supplement to surgery [1].

In those days, very few physicians were dedicated full-time to x-ray imaging and therapy, and complaints about the treatment of radiologists can be found in numerous contemporary papers in radiological journals. For instance, in an article about the business side of radiological practice in the U.S., published in *Radiology* in 1939, the author laments:

“There has been an unfortunate tendency for some hospitals ... to look upon the radiologist as a technician employed by the hospital.” [2]

The transition from radiologists being considered as mere technicians (with a certain medical background) to physicians of an independent discipline took many years. It was quite a long and uphill fight to final recognition, and the process varied in different countries.

At the German Congress of Roentgenology in May 1947, George Fedor Haenisch, a leading German radiologist in the first half of the 20th century, pointed out that roentgenologists still didn’t play on the main stage of medicine:

“The subject of roentgenology is officially recognized as a medical specialty, there is a specialist title, even a few professorships for radiology. Despite the official recognition, a general, so to speak ‘internal’, recognition still does not exist in

many places, both from different medical circles and from official authorities ... Since I delivered by invitation in Atlantic City in 1931 the Caldwell Lecture on this topic, the discipline of roentgenology has continued to prevail in the USA, while we have made relatively little progress in Germany, some of which has even been lost.” [3]

■ Twenty-five years ago, I wrote a column – “Do radiologists have a future?” – in which I mentioned that independent radiologists do not exist, patients do not come straight to them. Radiologists are always dependent on referrals from other physicians. [4] The profession of radiology developed from clinicians who used x-rays as only a part of their daily diagnostics to physicians who were occupied with performing the increasingly more complicated and time-consuming x-ray examinations for the referring clinician. But, because medicine was not so specialized as it is today, radiologists were still required to have a strong general clinical background – and had personal contact with the patient.

**A radiologist is both
the referring physician’s doctor
and also the patient’s doctor.**

Today a radiologist is both the referring physician’s doctor and also the patient’s doctor. Yet, the interaction between radiologists and patients isn’t a topic of discussion very high on the popularity scale among colleagues in medical imaging. Has the relationship between patients and radiologists gone off course recently, or has it been difficult since the early days of medical imaging?

During the era of x-ray fluoroscopy, there still was direct contact between patients and the radiologist; only after the introduction of computers, CT, and then MRI, did this contact weaken. In many countries, ultrasound is not in the realm of radiologists and is performed by technicians, so another opportunity for direct interaction vanished.

However, there is a big difference between radiologists in private practice and hospital-based radiologists. Patients being examined in private practice commonly appreciate the radiologist as a medical doctor, whereas radiologists in a hospital disappear in the cloud of white-gown employees.

In general, the relationship between radiologists and patients lacks empathy. Technology is not a magic bullet to solve all problems in medicine, including the patient-doctor relationship and the status of a radiologist.

There have been some studies on the topic during the last decades. A review of the literature can be found in an article by Bosmans et al. [5] The authors stated that patients are largely unaware of the nature and scope of a radiologist's practice, or at least of the meaning of the word "radiologist". They also often do not realize that radiologists are actually physicians; many believe that they are technicians or technologists. In hospitals, 62% mistook the technologist for a radiologist, while in private practice 84% correctly identified the radiologist as the person who obtains and interprets the images. Significantly more patients in private practice knew that the radiologist is actually a medical doctor, and even more that radiologists read the patient's images.

■ Some radiologists are upset because patients and their relatives don't recognize them as medical doctors; on the other hand, many radiologists never see or even greet their patients. The worst-case scenario for this is teleradiology where there is no contact with the patient, and often even a medical history of the patient is not provided.

If you don't ensure that you, a radiologist, are seen and recognized by the patients as a proper physician, you are also contributing to the fact that the specialty is not regarded as part of medicine. More so, a radiologist who sees and talks to a patient will have a diagnostic advantage when reading the images.

To add insult to injury, many colleagues working in clinical specialties do not take radiologists seriously, and they are still not considered "real physicians". Today's situation was recently summarized by a colleague as:

"The status of a radiologist is like being an extra in a stage adaptation of playing 'medicine' by the health care industry."

This statement goes hand in glove with an observation that also applies for radiologists by Giovanni Maio, a professor of medical ethics at the university of Freiburg in Germany:

"The treatment of the sick person increasingly follows the guidelines of industrial production ... The core qualification of a physician, however, lies in the skillful handling of complexity, in coping with uncertainty, in the professional handling of imponderables and, through these qualifications, ultimately in the careful exploration of what is best for the individual patient." [6]

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Rinckside, ISSN 2364-3889

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Citation: Rinck PA. Radiologists: To see and not to be seen. *Rinckside* 2019; 30,1. 1-2.

Getting ready for ECR ...

Peter A. Rinck



It's almost time again for ECR in Vienna and for the customary niceties and the intense chatter and babble, as we all dive into the social dynamics of the conference and face the constant barrage of questions:

"When did you arrive?" "Where do you stay?" "Which airline did you fly?" "How many participants attend the meeting this year?" "Will it snow again?" "Let's cross over to the industrial exhibition and pocket some souvenirs at the booths." "Great to see you. How's Amanda?"

Who the heck is Amanda?

"Let's have a drink, breakfast, lunch, dinner, a baby – at least we could try."

The informal social contact often appears to be more important than the learned papers and those poster sessions without posters. But still, there are some pompous, complacent scientific exchanges, misinterpreting the latest results of the barium enigma.

Talking shop, eating, drinking; you see people you never expected to have a private life. Fortunately, with your mouth full of Sachertorte, you cannot discuss imaging of the urinary tract. The topics at the next table are money, the crisis, holidays, incompetent sales representatives, incompetent CEOs, the crisis, the decline of the market, sales, hostile takeovers, the crisis, and sex.

And then we hear the next talks: Liver imaging for the advanced alcoholic. Cappuccino as a nonexpensive oral contrast agent. The influence of the Vienna Volksoper on the angiography of the lower extremities.

In the commercial exhibition, the booth of Lyserg & Sharp and Doom (LSD) offers an easy way to color coding of erstwhile black-and-white images: concentric visuals of colored patterns form behind the eyes in the mind of the customer, facilitating any diagnosis, with the stress on "any".

Telepathy International is the new star in teleradiology – wireless, monitor-free, cheap, and without any electronics, plain eclectic. Theoretical reasoning does it all. It generates an entire PACS in your hypnotically charged brain. The price is reasonable.

Speech Impediment, Inc., the new Ruritanian dictation management company offers their novel "William Henry Gates III Memorial" software with integrated speech recognition, workslow management, and automatic random erasure. "Crying rage is our goal."

This year's congress will touch on almost every imaginable topic in the radiological arena, drawing speakers from across the globe with the usual balance between youth and academic inexperience.

Hands-off courses

The new *hands-off courses* include the following:

■ **Topic 1:** Fighting the economic crisis in medical imaging. Does lobotomy help? Open forum and sterile resection.

■ **Topic 2:** Is there a crisis? Learn the French way of denial. Italian dinner included.

■ **Topic 3:** How to mix your own nontoxic contrast agents. Step by step, with PowerPoint presentation. Sponsored by Nestlé.

■ **Topic 4:** How to frame your MBA certificate and hang it on the wall front to back. Examples on video. Sponsored by Harvard Radiology Business Review.

■ **Topic 5:** Learning to live: Basic differences between hospital administrator and radiologist. Explanatory graphics and role playing. Bring your own Persian carpet.

■ **Topic 6:** PET on the Shmatterhorn. With bonus CME (approval pending). Sponsored by Union Bank of Switzerland and the Swiss taxpayer.

■ **Topic 7:** What happens to patients after the examination? Hide and seek through all changing cubicles and resuscitation. Real-life testimonials.

■ **Topic 8:** PACS for pygmies. How to reach the buttons. Requires knowledge of bungee and/or trampoline jumping.

■ **Topic 9:** Are you really a radiologist or only a BMW driver? An introduction to Freudian thinking. Help line and support groups. Sponsored by Dacia, the Logan manufacturer. Buy four tires and get a free car.

■ **Topic 10:** Digital mammography. Learning how to find things.

■ **Topic 11:** CT colonoscopy and bad breath. T1 and T2 relaxation exercises, meditation, and breathing techniques. Triple CME credits and double Austrian Airlines Miles and Less.

Note: Due to the complexity and level of difficulty of their contents, each course will accept a maximum of four to eight participants each. Couples preferred.

Have fun at the meeting.

Rinckside, ISSN 2364-3889

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Citation: Rinck PA. Getting ready for ECR Rinckside 2019; 30,2. 3-4. (Republication).

MR Imaging: Quo Vadis?

Peter A. Rinck



During the second part of the twentieth century, four new medical imaging modalities were established aside of conventional x-ray (Roentgen) imaging: ultrasound, computed tomography, radioisotope imaging and magnetic resonance imaging. These were great and exciting steps forward in science and medicine.

Paul C. Lauterbur, the father of MRI, died more than a decade ago. Interestingly, he didn't believe too much in high-tech medicine and refused at the end of his life to undergo dialysis when his kidneys were failing. Nobody and nothing would persuade him. He lived another two years and nine months – without machines and medical terror. Thirty years ago I might not have understood this decision, both as a human being and as a medical doctor; today I do.

Instrumentation

MR imaging became a clinical tool in the 1980s and has not much changed since the turn of the millennium; the technique remained the same, although the appearance of the machines might be different and hard- and software became more sophisticated.

Diagnostic imaging with magnetic resonance has developed into a stable technology and is an important part of medicine and the health consumer market. There is a wide range of machines, offered by numerous hardware manufacturers.

Today, there are approximately 50,000 whole-body MR machines worldwide. Most machines per country are found in the United States, followed by Japan, in the meantime also China, Germany, Brazil, Italy, and South Korea. To provide sufficient medical care for a population, 12 to 15 machines per one million inhabitants suffice. In countries with over-saturated markets there is a high risk of overuse and abuse of MR imaging.

Despite the commercial availability of 3.0 Tesla equipment for more than 15 years, the majority of routine imaging is done at 1.5 T; about two thirds of all machines in the United States and Europe operate

at this field strength. Gradient strength is already at its limit, imaging at higher fields is of unproven general advantage and patients suffer from the noise of 3T machines and unpleasant side effects at ultra-high fields [1]. There is also a lack of reliable, non-biased outcome studies on which field strengths and technologies are best suited for routine and everyday clinical imaging. The hardware industry and other circles block such studies.

Novel developments introduced by non-medical actors may even lead to actual reduction in patient well-being.

People from outside medical care (in this case, industry representatives and health administrators) have become more influential and finally taken over decision-making. The users, the radiologists, are often simply pushed aside. Medicine is being increasingly commercialized with limited respect for the human factor. Novel developments introduced by non-medical actors may even lead to actual reduction in patient well-being.

Cultural Differences

The cultures of these markets are different. Chinese MR sites, for instance, are less scientific or – better – pseudo-scientific players, but rather more patient and diagnostic focused. Of course, these countries are also consumer markets which reflects in their structure.

As mentioned before, in Europe and North America, one finds 15-18% 3 Tesla machines and about 66% 1.5 Tesla machines; in China the percentages are approximately 8% 3 Tesla, 45% 1.5 Tesla, and nearly 50% lower than 1.5 Tesla – a far healthier distribution for routine diagnostic necessities.

Changes within Societies

The human factor plays a major role in the changes occurring in radiology: A new generation of radiolo-

gists starts climbing the career ladder. Many of them grew up pampered in comfort and affluence, exposed to the digital revolution in a period when average quality of school and university education declined. They lack critical insight. Attached to playing computer games, digital imaging technologies are extremely attractive to them. On the other hand, lower working hours and higher salaries are also important to them.

During the last twenty years the generation gap has deepened to a chasm, and both younger medical doctors and older ones complain about of a mutual lack of comprehension of their respective worlds. The suitability of candidates for the existing, partly very demanding health system is decreasing. By many sociologists and psychologists they are seen as a possible threat to the existing stable society and workplace structures [2]. On a global scale, in particular for the operation of specialized MR equipment, radiologists will partly be replaced by medical doctors from other disciplines, e.g., by oncologists, neuroscientists and nuclear medicine specialists.

It is interesting to see that the sales representatives of some companies seem to have reacted to these changes, but not company management and developers – it's easier to deal with the existing present than with an unknown future. Companies target their potential younger customers with completely different marketing methods than twenty years ago.

Another important point is the change of age distribution in the population in Japan and numerous European countries. This different patient clientèle requires adaptation of MR machines and examinations.

Simplistic Academic Research

Research, fashions and hypes are a fundamental element of MR equipment and contrast agent sales not only in Europe and North America. The credo of "publish or perish" has left a terrible battlefield in the papers on MR imaging. Checking the contents of radiological journals of the last 30 years shows that few learned papers are relevant. Studies reveal that 90% and 95% were simply wrong, sense- and useless; still, they have influenced the use of magnetic resonance and medicine at large. This will not change in the near future, because climbing the entire career ladder in Europe and North America is based on this spiel – as well as major commercial interests, for instance, the annual congresses of the European Soci-

ety of Radiology and the MR societies [3, 4].

Fashions which came and went again during the last 35 years were, for instance, MR spectroscopy – the combination of high-resolution imaging and depiction of metabolism. MRS has more or less disappeared from the stage: Here today, gone tomorrow ...

Another idea in the earliest times of MRI, even before, was tissue characterization by in vivo relaxation time measurements. This was 40 years ago and the methods had gone out of date already in the mid-1980s: they didn't work in a clinical environment. More than 20 years later they were re-invented as "MR fingerprinting" and "biomarkers". Even dressed in new clothes they cannot be validated in independent trials and are mostly inadequate and deficient in precision and accuracy [5, 6]. Still companies jump on this bandwagon because they don't have anything novel to offer. Outdated ideas are repacked and sold with marketing gags as revolutionary developments. Here today, gone tomorrow.

Functional MR imaging (fMRI) was invented in the early 1990s, followed by MR tractography and the 1-billion-euro Connectome Project [7]. All are prone to disappoint. The most common software packages for (fMRI) analysis resulted in false-positive rates of up to 70%. These results question the validity of some 40,000 published fMRI studies and may have a large impact on the interpretation of neuro-imaging results [8]. Here today, gone tomorrow ...

Many people believe that numbers (data) are the truth. Many people do not understand how the numbers were acquired and what they stand for. Nature, biology and medicine are more complex and don't care much about numbers.

For decades the euphoria over new offspring techniques of MRI has been reliably followed by disillusionment. Exaggerations are and were widespread. There has been progress but much of the trust of the people who actually count on the developers and researchers was lost. They were taken on a constant roller coaster ride into nowhere. For some time, new developments in MR imaging have been merely apps and gadgets.

The latest hype, an exploding volcano, is "artificial intelligence". AI will come on the MR market; it's business value is enormous. But AI is mindless, lacks consciousness and curiosity. These are fundamental

flaws which can't be overcome, distinguishing it from real intelligence. The human mind must be critical; artificial intelligence won't be. The human mind is able to consider, reconsider and doubt. AI won't. But human laziness will rely on it anyway. Let's see what happens to it.

Still, it's not a disruptive technology for MRI, but just another still very immature app [9].

Disruptive Technologies

However, real disruptive technologies will hit MR imaging as well as contrast agent use and development, for instance ultrasound and in vitro tests. Soon we will have cheap smartphone-size ultrasound equipment that will revolutionize and shuffle the imaging market. Most likely, we will be moving towards earlier diagnosis and management, wherever possible, which implies ultrasound, optical or some other sort of high spatial resolution imaging technique, but not, for instance, ultra-high field MRI.

Manufacturers are first and foremost interested in money; this is their *raison d'être*, the purpose that justifies their existence – and, basically, there is nothing to criticize about it. The manufacturers are increasingly faced with the question whether new ideas have any clinical and commercial relevance. They still can try to invent some “relevance”. In general, MR research will move away from developing new pulse sequences or new coils; this will even hold for academic research, perhaps with the exception of superconducting materials.

MR Contrast Agents

What will be the clinical need for imaging agents when in vitro diagnostics will begin to provide useful information? If you know the patient has xxx from their in vitro analysis what is the role of imaging and what type of imaging will provide the clinical management information needed?

I have been involved in MR contrast agents since 1981, for nearly 40 years. The main question is if there is room for a new agent today or in the future – and if so, how and why – when the remaining Gd chelates are so universal in terms of their application. Gadolinium extra-cellular fluid agents are the only ones that have grown into a realistic market size. Thus, it will be extremely difficult to develop a new MR contrast agent that fulfills unsatisfied clinical

needs and has a large enough range of application to justify development.

The disaster of the nephrogenic systemic fibrosis (NSF) has left deep scars in the industry. Still, gadolinium agents are safe contrast agents when properly applied, far safer than, for instance, x-ray contrast agents. I believe it's unlikely that you can find something better than Gd that ticks all the boxes in terms of applications, higher safety profile and potential market size. Getting the market to embrace a new agent will be a slow process as radiologists are conservative and it will take years to grow the markets [10, 11].

As we have seen, for instance, with Novartis, the era of mass production in the pharmaceutical industry is claimed to be over: so-called “personalized medicine” is replacing “one-size-fits-all” pills. I doubt if this holds for contrast agents. It will be difficult to isolate unmet clinical needs, and the cost and approval processes are exorbitant. Today's contrast agents on the market were developed for field strengths below 2 Tesla; their relaxivity diminishes with increasing magnetic field strength. In the unlikely case that imaging will be performed at ultra-high fields of 7 Tesla or even higher, new classes of contrast agents must be developed for research applications, mostly for animal experiments. Again, costs will be prohibitive.

An interesting approach to new paradigms and elements is the production and distribution of already approved agents that were withdrawn from the market before the gadolinium phobia, such as Mn-DPDP for pancreas, liver, and cardiac applications and ferumoxtran for the enhancement of metastases. In these cases approval is relatively simple and distribution might be efficient even by small companies. Thus, new “old” players have entered and will enter the market. Gone yesterday, back here today?

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Rinckside, ISSN 2364-3889

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Citation: Rinck PA. MR Imaging: Quo Vadis? Rinckside 2019; 30,3, 5-8.

At the crossroads: MR contrast agents

Peter A. Rinck



For thirty years scientific leaders and young researchers in the development of magnetic resonance contrast agents have met at biennial conferences arranged by the European Magnetic Resonance Forum (EMRF) and The Round Table Foundation (TRTF).

From the beginning, the attendees comprised both university scientists and representatives from industry. Earlier, these meetings were very attractive for researchers working for the contrast agent manufacturers to present their basic research in a setting that fosters discussion, collaboration, and advancement in the field without being pressured by their sales and marketing departments. However, in the meantime commercial basic and applied research has been drastically cut back, some of the major companies have changed hands, and most companies focus mainly on marketing of generic compounds, some selling products developed by their competitors after the original agent's patent expiration.

■ The leitmotif of this year's two-day meeting in Mons, Belgium, was "Standing at the Crossroads: 40 Years of MR Contrast Agents" – what has happened in the field during the last 40 years after the first description of MR contrast agents by Paul C. Lauterbur in 1978 [1], what have we learned, what is the state-of-the-art, where will we go to? The conference was organized alternating review lectures of the developments, improvements, challenges, and failures of the last thirty years given by leading experts in the field and presentations of novel theoretical tools, new ideas, and new compounds by young scientists.

The opening lecture was entitled "MR imaging – Quo vadis?" It gave an account of the factors influencing the development of the technique, scientifically, commercially and socially. The talk was not about the development of techniques and great leaps forward in MR imaging coming up soon, but rather it described repercussions and forces from the outside – realities which during the last 40 years formed MR imaging – and will influence and guide the development in the future. This included its instrumentation and accessories, academic and industrial research, fashions and

hypes, global cultural differences, changes within societies and human factors, disruptive technologies, the worldwide market for MR instrumentation and contrast agents, and new paradigms. Excerpts have been published earlier in Rinckside [2].

Among the experts, there was agreement that the domain of medical imaging will be mostly at 1.5 Tesla in Europe, North America, and Japan, and 0.3 to 1.5 Tesla for instance in Russia and China; even in the future, clinical use of ultra-high field equipment at 3 Tesla will be limited and higher fields will be a domain for dedicated scientific research.

Gadolinium uptake in the brain

The likely lack of stability of linear Gd-compounds was already heatedly debated at the first conference of this series in 1988 [3, 4], long before the first occurrence of nephrogenic systemic fibrosis (NSF).

Increased signal intensity in plain T1-weighted MR images is observed in a number of brain structures of patients who had undergone several contrast-enhanced studies. These hyperintensities are believed to be induced by tiny amounts of gadolinium held back in the brain. At present, investigations are under way to try to understand how and why Gd is retained in brain and other tissues in the body. Studies focus on the contrast agents' *in vivo* stability (combination of equilibrium, kinetic and pharmacokinetic properties), the way how Gd-containing compounds cross biological barriers, the chemical form of the retained compounds (intact contrast agents, or soluble and insoluble Gd-containing compounds), and the relationship between Gd-compounds and local image hyperintensities.

These studies open new avenues beyond the potential toxicity of the used Gd-complexes since they allow to get advanced insights into thermodynamics and kinetics of metal containing preparations in living systems [5].

Possibly still unknown physiological-biochemical pathways allowing gadolinium to pass the blood-

brain-barrier are discussed by some researchers, but nobody at this conference presented any supporting evidence of such ideas.

My personal explanation of the uptake of gadolinium dates back to research done by our group in the 1980s, even before gadolinium agents entered the market. In a patient population of some 450 with definite, probable, and possible multiple sclerosis (MS) referred to us for MRI, some 40 suffering from definite MS were chosen randomly for relaxation time measurements of plaque-free grey and white matter. Overall white matter T2 was slightly higher in MS patients than in a non-MS population. These changes do not influence image contrast and are not visible in MR images [6].

However, it is known that in many different brain diseases localized or general breakdown of the blood-brain-barrier (BBB) can be observed – among them MS, Alzheimer's disease, epilepsy, amyotrophic lateral sclerosis (ALS), edema but also stroke and brain injuries as well as systemic diseases, such as liver failure. Work with animal models of disease and with cell culture BBB models has enabled the identification of some of the molecular mechanisms that cause changes to the BBB [7].

Thus, diminutive amounts of gadolinium may enter the brain in such patients and, after multiple applications of a Gd-based contrast agent, slowly accumulate and visibly change MR image contrast.

In the discussion of this topic it was also criticized that patents on contrast agents and accessories and the enforcement of poor quality patents by patent trolls, e.g. on contrast-enhanced MR angiography, have had a negative impact on the development of better and safer agents.

Signal and contrast enhancement

Another area of interest was the intrinsic insensitivity of MRI and possibly boosting procedures with un-specific or targeted molecules or techniques.

Overviews and new ideas covered the whole spectrum of prospects, from optimizing the relaxivity of existing or possible compounds, the use of CEST (Chemical Exchange Saturation Transfer) agents or hyperpolarized (HP) molecules providing the possibility of investigating *in vivo* metabolic processes.

Hyperpolarization requires specific and expensive additional equipment which makes it ill suited for routine clinical tasks. Hyperpolarized gases can be used for lung imaging, but the application of perfluorinated gases might be more practicable. As with CEST, additional hard- and software have to be installed.

New classes of contrast agents with relaxivities several hundred percent higher than today's agents in clinical use below 2 Tesla have been proposed; however, safety and stability of these complexes has not yet been examined in animals and humans. They might be necessary for ultra-high field research applications, mostly for animal experiments, where bigger contrast agent molecules will provide better relaxivity.

Yet, university researchers should not sit in their ivory towers and develop techniques and compounds that don't have any relevance for or chance to be used in a routine or even basic research medical environment as Robert N. Muller, one of the European leading scientists in the field, stressed in the closing remarks of the conference. From the onset of a research project, feedback with physicians should be sought so as not to end in blind alleyways.

Targeting

Targeted theragnostic compounds were proposed in an unpublished description by Paul C. Lauterbur already in 1977.

However, few have reached the clinical level, among them one novel project in France involving nanoparticles made of polysiloxane and gadolinium chelates. In a clinical phase Ib trial it has been shown that after intravenous administration they accumulate in tumors and act as a radiosensitizer to increase locally the effect of radiotherapy, for instance for the treatment of multiple brain metastases by whole brain irradiation. Their biodistribution and the accumulation in the tumor can be followed by MRI due to the presence of gadolinium.

It remains to be seen which of the hundreds of different projects will leave the labs of the research institutes and will be turned into routine patient applications. At present, we are using MR contrast agents introduced 25-30 years ago.

■ The respective abstracts of the talks mentioned can be found in the Book of Abstracts. It is available free of charge at the www.trtf.eu/events.html.

■ Last, but not least: The participants of the conference received an offprint from EMRF's MR textbook: "An Excursion into the History of Magnetic Resonance Imaging." It can be downloaded free of charge from www.magnetic-resonance.org.

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Rinckside, ISSN 2364-3889

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Citation: Rinck PA. At the crossroads: MR contrast agents. *Rinckside* 2019; 30,4. 9-11.

Artificial intelligence meets validity

Peter A. Rinck



Radiology has gone through turbulent years, even decades. It has changed permanently, from analog to digital, and from x-rays and radioisotope methods via ultrasound to magnetic resonance. The latest hyper-hype in radiology is artificial intelligence [1].

Today's healthcare system is no longer run by doctors, but by administrators, hospital managers, lawyers, and business economists applying corporate strategies. Many of them don't or don't want to understand the caring or human aspects of medicine but base their outcome merely on numbers and collected data. Most of these people seem to hazily consider AI to be anthropomorphic, but computers are and will be non-human entities.

"Great potential and promising results"

Internet opinion leaders, "experts" and "influencers" like to talk about artificial intelligence in general and in radiology in particular: "Great potential and promising results". If you check, many of them have financial interests in companies dealing with AI, even if they don't admit it publicly.

However, if you ask them about concrete applications, you get vague answers, such as that the introduction of AI has the potential to greatly enhance every component of the imaging value chain. It's all "beta", "will be" and you have to try it (you pay first, of course), to find out and incorporate it with your own results – which then will become the property of the distributing company. It's a commercial dream deal – little work, a lot of public relations and marketing, and a steady income.

Yet, in many cases the data quality of the input is bad and the necessary trustworthy infrastructure does not exist or requires a much greater technical effort than expected. In many instances the complexity of the problem to be solved is not taken into account by the promoters of the application nor by its users because

they don't understand the first thing about it.

Often complex software and hardware used are impossible to link – it's not only one program but many components that have to connect and grasp the incoming data to process them in the expected way. In newspeak, this is politely called "lack of maturity".

■ *Validation* is a neglected or simply ignored factor. How difficult it is to implement, for instance, contouring tools and applying them in AI studies is demonstrated in a recent paper by Zheng Chang:

"Before the AI contouring tool is fully adopted into clinical use as a part of standard practice, it needs validation in more independent multicenter studies with larger patient cohorts," he wrote. "Although the AI contouring tool shows promising results for NPC primary tumor delineation in this study, section-by-section verification of tumor contour by radiation oncologists should never be omitted [2]."

In the 1980s and 1990s I led an image processing group in the department I headed; a number of important innovations in the field of image processing, image visualization, data collection, and early applications of very specific AI were developed during this time and became basic and expert knowledge, including the knowledge of pitfalls and setbacks [3].

Validation is among them; it seems nearly impossible, because the parameters of most digital radiological examinations are not exactly reproducible [1]. However, extremely thorough validation must take place before AI algorithms are clinically feasible.

A Korean paper on AI highlighted that in the first half of 2018 "of 516 eligible published studies, only 6% (31 studies) performed external validation. None of the 31 studies adopted all three design features: diagnostic cohort design, the inclusion of multiple institutions, and prospective data collection for external validation ... Nearly all of the studies published in the study period that evaluated the performance of AI algorithms for diagnostic analysis of medical images were designed as proof-of-concept technical feasibility

ity studies and did not have the design features that are recommended for robust validation of the real-world clinical performance of AI algorithms [4]."

■ In June this year, Ranga Yogeshwar, a physicist from Luxembourg, turned German media science journalist and television presenter was interviewed for the newsletter of Deutsche Röntgengesellschaft. His comments were knowledgeable, competent, critical, and to the point. He also spoke out:

"The question [is] of how we validate data, also in science. Where do training data come from? Are they certified? How certain can we be that training data may not contain an a priori error? I still miss a differentiated discussion. It is sometimes frightening on what basis data are collected and trained, even in powerful AI systems.

"For me, it is a question of reflected progress, in which data is validated on the one hand and data flows and access rights are clearly regulated on the other [5]."

■ An intriguing contribution in one of the discussions of the recent conference "Standing at the Crossroads: 40 Years of MR Contrast Agents" [6] was the opinion of researchers in the exact sciences that radiologists will only be involved in patient studies with common techniques and contrast agents, but not in dedicated MR studies with techniques using novel diagnostic, therapeutic and theragnostic compounds. The reason given is the radiologists' lack of background in dedicated MR techniques and biochemical interactions of targeted compounds and tracers. Such examinations or interventions would become the domain of other disciplines, e.g., oncologists and neuroscientists, perhaps also specialists in nuclear medicine.

The scientists' comments were supported by a cardiologist who stressed that it is his feeling that radiology is experiencing a major change, most likely a decline. He described that he and his colleagues have undergone training and are now completely independent of any radiology input. He believed that there is a similar trend in neurology and orthopedics.

This complicates validation of possible AI data collection even more.

Another issue is the question whether radiologists really understand what is happening with and in their

equipment and the optimization of examinations. Basic T2- or T2*-weighted sequences, for instance, have been superseded with all sorts of concealed manipulations to improve speed – tricks that are hidden and users are largely unaware of. Similarly with CT, the impact of energy, contrast agent volume and timing means most radiologists are completely dependent on built-in protocols. Thus, average radiologists or other imaging professionals are excluded from making any changes of patient studies.

It is interesting how radiology is seen by some of the scientists developing the tools for radiology. This opinion will not find many friends in the radiological community, but the involvement of non-radiologists is already noticeable for some time. More so, simple applications of artificial intelligence will shift routine image assessment away from radiologists.

Human laziness will rely on AI. There is more to this laziness than commonly thought. The human brain delegates tasks to the background that it doesn't consider relevant. Relying on the "responsible" performance of hard- and software will allow vigilance to easily fade.

A good example is the shift of our cognitive systems from the task of supervising a fully autonomous device to a less relevant device, e.g. away from the performance of a radiological AI system. It was shown in a group of people that driving cars with manual transmission was associated with better attention and less failure than driving cars with automatic transmission [7]. To my knowledge, nobody has ever looked into such issues possibly also to be found with AI but it's important to be aware of it [8].

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Rinckside, ISSN 2364-3889

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Citation: Rinck PA. Artificial intelligence meets validity. Rinckside 2019; 30,5. 13-15.

The prime minister's wife builds a new hospital

Peter A. Rinck



The history of hospital planning and construction is an interesting subject of study. It reflects not only changes in medicine, new insights and discoveries, but also social, political and financial trends.

Until the 19th century, the traditional hospital was commonly little more than a place of custody of the severely sick, basically care homes, first and foremost for members of the military, built in the style of barrack-blocks – most often three-floor red brick-work buildings with hundreds, even thousands of beds.

The view that only the supply of fresh air could eliminate “hospital fever” led to a pavilion building style that originated in France and England.

Since the beginning of the 20th century, the introduction of operating rooms with a sterile environment, chemical laboratories, and special departments for x-ray diagnostics required a new functional building style with one single building complex, the general hospital style, collecting everything under one roof.

Among the first general hospitals created in this manner in Europe was Södersjukhuset in Stockholm. It opened in 1944 and was then one of the world's most modern hospitals.

It was designed by two of the leading hospital architects, Hjalmar Cederström and Hermann Imhäuser. They placed their emphasis on three perspectives: bodily, spiritual and economic. The design of the patient rooms was spacious and bright.

Good hospital design can make people get better more quickly.

Roger Ulrich, Professor of Architecture at Chalmers University of Technology in Sweden and at Texas A&M University, was one of the first to research how hospital buildings can affect patients. In 1984, he noted that patients looking out of their room into

nature recovered faster and required less painkillers: “Reducing stress, and distracting patients from their internal focus or their obsession on their own pain, reduces the pain [1].”

In other words, good hospital design can make people get better more quickly. Doctors and paramedical personnel are also thankful for good hospital design and administration.

When Florence Nightingale viewed with skepticism the dreadful hospitals of her times, she did not recommend shutting them down; she suggested that they were improved.

■ Stockholm's best known hospital abroad is the Karolinska, the teaching hospital of Karolinska Institute. The Nobel Assembly at the Karolinska Institute awards the Nobel Prize in Physiology or Medicine. Some 20 years ago some administrators and politicians decided that Karolinska Institute should get a new “world-renowned” centerpiece hospital. Hardly anybody else thought it was needed; it would have been more practical and far cheaper to update the existing hospital. Clearly, there was no solid determination of need.

The county council of Stockholm proposed a public-private partnership to finance, construct and run the new hospital – an approach that was developed for the profit-oriented health care in the United States, had not been tried in Sweden earlier but already failed in Great Britain [2]. The vision was of a specialized hospital with deeper ties between clinical care and research.

The minister of finance Anders Borg had the responsible county official Filippa Reinfeldt contacted to drop this idea. She said that this was a matter of political principle and refused. Borg then talked to her husband, prime minister Fredrik Reinfeldt, to have him change the deal.

Unfortunately, that happened to be the end of his intervention; the Reinfeldt couple had just decided to get a divorce.

Although Stockholm was offered an interest-free loan from the Bank of Sweden, the project was awarded to a consortium consisting of a big Swedish construction company and a British investment firm. There was no competition. The consortium needed to get the loans on the private market place. The entire deal was shrouded in secrecy. The agreement itself was designated as ‘confidential’ both before and after it was signed.

In an independent review of the entirety of the project the University of Stockholm clearly denounced this procedure: "... Several related matters were covered by secrecy. ... not only [were] certain actors excluded ... but [this] also affected the possibilities for accountability ... [3]."

The side effects of such mega-projects were well described in an article published in 2017 about mega-projects in Valencia, Spain: "The mechanisms used to implement mega-projects – including both exceptionality measures and privatisation of management through the creation of semi-public delivery bodies – result in a lack of transparency and democratic control, which in turn lead to more authoritative and privatised forms of decision-making. ... Mega-projects – through their focus on expertise and technocracy and a populist politics and discourse constructed around them – play a crucial role in the erosion of democracy ... [4]."

■ Built in the ungainly “modern” style of an insurance administration building of the 1960s and 1970s to the outside and not taking into account the necessary functionality of a general hospital in the inside, one has the feeling that the planners and architects in charge were on the apprentice level. Their lack of expertise is evident. They perfectly fulfilled the general prejudice of incompetent architects: first, the buildings are eyesores; second, they are built without consultation of people in the know; third and worst, they don’t accomplish the functions required.

Before the start of the construction, during the building period and after the project was finished neither the county council nor the companies involved chose to follow essential and professional recommendations. There was also no competitive procurement.

One revealing example is radiology. In dozens of committee meetings the radiologists suggested and worked out, for instance, a united radiology department with cooperation and localization close to

pathology. Then the consultants came and divided radiology into five to seven separate units depending on what is included. These units are practicing in about 15 different locations. No co-localization or cooperation with pathology existed, apparently the consultants nearly forgot to plan a department of pathology.

The old hospital had a lot of expensive and fairly new equipment. Little was reused and moved to the new hospital. It is said that the old equipment colors did not match the new examination rooms. New equipment for all of radiology was tendered for and only one company offer could be accepted. Philips won and was guaranteed to deliver 40% of all equipment. The rest Philips had to buy from Siemens, GE, Toshiba and others. This procurement system is, politically put, unconventional.

When faced with the new structure, the professor of radiology decided to step down. No new professor of radiology has been appointed. A large number of experienced and highly specialized radiologists left and are expected to be compensated for by more residents.

■ The building project culminated in disaster. The planners, architects and builders of this apocalyptic hospital failed the people for whom this hospital was built: patients and those who take care of them. It was a completely mismanaged and, for the taxpayer, an extremely costly political and financial experiment. The final expenses more than quadrupled to approximately 6 billion euros.

Not only in the diagnostic imaging units, but all over the building, there were no blinds on the windows. Thus, in some instances, the glass fronts had to be covered with paper by the employees.

In 2014, Fillipa Reinfeldt, now ex-wife of the now ex-prime minister was clearly fond of the idea that passers-by could look straight into the hospital: “People on the sidewalks will see the staff run with severely ill in the glass corridors above them. It’s pretty cool [5].” Gaping is not a socially appropriate behavior. Such a statement reveals a total lack of due diligence, dutifulness and sense of responsibility. Reinfeldt didn’t belong on the position she had.

■ With the opening of the new hospital a new health care management model was to be implemented: value-based care. The Boston Consulting Group was

in charge of this mega-project. The company promised that it would revolutionize the entire health care system and make Karolinska a global pioneer. The objective of value-based health care is to align physician and hospital profit and loss with cost, quality, and outcome measures – based on outcome studies [6]. Performance of examinations and treatment should be standardized. However, quantification of medicine is nearly impossible because medicine is not an exact science. In which unit do you measure “I am feeling well”?

This idea is based on a simplistic view of medicine and health. All people are the same, they suffer from one single disease when they need medical assistance. They will be diagnosed and treated in the same way. Multi-diseased, difficult-to-treat patients who do not give quick results will then not be high priority. They do not fit into the required setting of treatment pathways, into the assembly line of the medical factory.

After the misfit building this was the second disaster of the New Karolinska, another dysfunctional social utopia. The ideas of the Boston Consulting Group were doomed to fail. Any completely new, untried and untested approach should be implemented by people with knowledge and experience and grow organically over years.

The consequence of the introduction of the new system has been described in a more than 400-page book about the scandal. According to the authors Anna Gustafsson and Lisa Röstlund [7] the new system operates at very low speed; proven routines are gone.

Medical employees are leaving the already understaffed hospital. Members of the staff often do not have time to eat or go to the toilet. Qualified doctors and nurses say they are unable to do more, but the number of managers grew by 30 percent and the health care staff is increasingly devoting time to filling out forms. There is an atmosphere of suppressed fear and anger, but people don't speak up; they fear reprisals and to be bullied.

The two authors also reproach politicians and management that they do not abide by the law and responsibility necessary in health care. When moving into New Karolinska, 350 children had been waiting for surgery for more than 90 days. Almost a year later, 800 children were queuing up. Pancreatic can-

cer patients will be operated in Germany and Denmark within 14 days, in Sweden, the limit is raised to 36 days – a limit that Stockholm County could only manage in every third case in 2017. Several people with cancer died because Karolinska did not have time for them – and the hospital refuses to take help from elsewhere.

One central theme of “the hospital of the future” was that the routines were to be so effective that waiting rooms for patients and their families were not needed. However, as the patient flow tends to vary substantially, service capacity needs to be able to take care of the peaks, which leaves a lot of “air” in the system at other times. This high capacity was not acceptable; thus, the reality is that there are patients waiting but there are no waiting rooms. As the three main elevator shafts with 30 elevators have huge marble halls around them, these halls are gradually being transformed into primitive waiting areas.

The consulting company BCG also decided that no one of the hospital's medical staff needed a permanent office. Whoever needs an office for a couple of hours has to sign up in advance; the computer in the room will allow to access one's personal “cloud” account. Everything, including patient reports, was to be run through this cloud which did not function and had to be replaced.

More so, one's clothes are still to be left in the old hospital, since no wardrobes are available. Thus, every day begins and ends with a 15-minutes walk between the old and the new hospital. There is some unprotected shelf-space for “old-fashioned” books, but most doctors use that space for outdoor clothes. As one employee put it sarcastically: “This is of course ideal for the research work at this world-renowned university hospital.”

The new hospital buildings are failures of urban planning, without harmony, not inspired by local tradition, not places of meaning, and disconnected from human nature and concerns. They are also expensive to fix, and there is a lot to fix if you don't want to tear them down.

Other complains include “horrible” and “evil” colors all over the hospital such as strong orange, brown, even black walls, the color of mourning. The entire building has a sterile atmosphere without any soul. The obligatory pieces of art show frightening motives. They are not appropriate for a hospital.

■ New Karolinska is one of or even the most expensive hospital ever built in the world. It suffered from three consecutive disasters: The catastrophic building, the hoax of value-based medicine, and, finally, these failures unfortunately rubbing off on the reputation of the Karolinska Institute.

However, this project is an outstanding example to learn from.

■ **P.S.** The whole story reminds one of another project of utmost prestige, that of the flagship of the Swedish navy, the *Vasa*. During its maiden voyage on 10 August 1628 the ship sank after sailing about a mile.

The ship was built on the orders of the King of Sweden Gustav II Adolph at the navy yard in Stockholm under a contract with private entrepreneurs. Upon completion it was one of the most powerfully armed vessels in the world. However, *Vasa* was dangerously unstable and top-heavy with too much weight in the upper structure of the hull. Despite this lack of stability it was launched and capsized immediately.

An inquiry by the Swedish Privy Council to find those responsible for the disaster came to nothing, in the end no one was punished.

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Rinckside, ISSN 2364-3889

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Citation: Rinck PA. The prime minister's wife builds a new hospital. *Rinckside* 2019; 30,6. 17-20.

