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From ECR 2006: Drive for perfection has potential downside

Peter A. Rinck

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Everything functions like clockwork. You enter Vienna's Austria Center, collect your badge, receive a radio (why a radio?), pick up your conference bag complete with program and book of abstracts, drop off your coat in the basement (free of charge), and off you go to lectures, courses, and meetings.

Participants at the European Congress of Radiology are pampered. They get free water in small bottles and apples to crunch. There are hardly any queues. The congress infrastructure runs smoothly. The professional organizers and radiologists responsible for staging the show display enthusiasm and initiative.

Everybody appears to like the annual ECR in Vienna. The number of attendees reached 16,000 this year, and more than 200 commercial exhibitors showed their products. Meanwhile, the ECR organization itself has become a major player in the medical congress market, arranging a host of different meetings and teaching courses for different radiological societies throughout Europe every year.

So why are some participants upset? Previously, most feedback about ECR and its organizers had been positive. Suddenly, there is criticism, and when you talk to people, you hear complaints. In medical terms, the pains are more moderate and diffuse than acute and terrifying. Something is wrong, but nobody can pinpoint exactly what that is.

Three days into the conference in March, I suddenly realized the cause of the discontent. ECR 2006 marked the end of an epoch. A congress has turned into an event. Professional event management has taken over and is organizing a flawless show. We have creative meeting solutions and new formats to liven up the scientific backbone of the meeting.

Why do people attend ECR? To mingle with foreign colleagues is one answer, though I doubt this is the main reason. The principal reasons are to keep up with cutting-edge science, refresh one's knowledge, get an overview of technical developments and the medical marketplace, and then yes, to meet people. Despite late-winter blizzards that have coincided with the past two conferences, Vienna itself is an attractive city for enjoying leisure time during out-of-congress hours.

Has the composition of the target group changed during the past decade? Are participants less interested in continuing education and scientific progress, and keener to be entertained and fed superficial information? Do they want to attend a trade fair and pay for it?

The line separating science (or in this case medical radiology), commerce, and entertainment, between seriousness and show, has become blurred. Walking into the Austria Center, you hardly recognize that ECR is a medical imaging congress. It looks like infotainment for people somehow connected to medical imaging. Not only this, individuality has been lost. Intermediaries arrange the congress on behalf of radiologists attracted by a circus sideshow. Watering down ECR to an infotainment show will, perhaps, appeal to the majority that follows the trend toward presentation over objective contents.

You are standing there, admiring the success, and watching the train depart in the wrong direction. Or are you on the wrong train? Is ECR catering to a younger generation of radiologists who tackle science, medicine, patient care, learning, teaching, and continuing education with a different approach from the generation before? Does the younger generation of radiologists want infotainment? I am curious to get some reactions or feedback. Are the organizers trying to tune in to the under-35 MP3 generation? Or are there other reasons?

ECR appears to be moving off focus, albeit slowly. Of course, a major conference of this size, with a target audience that ranges from private-practice radiologists to scientists, is not meant to be a purely scientific or educational endeavor. Rather, it is a combination of these two components, with social elements and a sales fair as well.

I do not intend to criticize without providing possible solutions. I am just describing the situation. Turning back the wheel never works. The question is not whether something is right or wrong, but what the consequences will be. Perhaps this does not matter. Yet I predict that genuine scientific presentations and discussions will move to smaller "elite" conferences in the future.

Infrastructure Innovations

The organizers of ECR say that it is the world's most innovative congress. It is the first congress to offer a digital preview system that enables speakers to prepare their presentations, upload them in advance into a centralized computer system, and test their functionality. It offers the possibility of copying them onto CD-ROM and having them included in eECR, the electronic congress. So all presentations are available on a central server, which also means that everything is copied, want it or not.

Every year trots out a new feature like this one. Last year, registration badges contained a chip that, for the first time, made it possible to tag and trail participants. Big Brother is watching where you are and when. Not all attendees appreciated this kind of surveillance. Some even stopped using the internal messaging system, believing it could be bugged.

EPOS, the electronic poster system, is another example of well-meant but overabundant perfectionism. It has democratized the poster sessions, and presentations are now basically standardized. EPOS has leveled poster presentations.

Watching congress attendees staring at the EPOS screens, you realize that there is hardly any contact between neighboring screens. There is no academic exchange. Participants sitting in front of their monitors have mostly retreated within themselves, creating an air of autism.

Paper posters promoted conversations and exchange. This social and scientific contact is lacking with EPOS. EPOS is useful for animations and novel presentations, but it cannot recreate the environment of ad hoc discussion that could happen when several people met, often incidentally, in front of one poster. The individualism of paper posters might be off-putting to some people. But at least they allowed congress delegates to walk through exhibitions, assess single posters at a glance, and grasp their essence within seconds. EPOS does not allow this.

One does not need EPOS at a conference. Everything could be watched from home over the Web. ECR already offers such presentations. You don't have to attend the conference, just pay a small fee, and your learned paper will show up in the EPOS system.

Multimedia

ECR introduced radio and television coverage this year. All participants receive a miniature radio. Most people must have thought that it was a nice gift to take back home for their children. I did not see anybody listening to the radio during the meeting. Why should they? They went to Vienna to talk or to listen to people. The same holds for the television program which, to add insult to absolute dispensability, was periodically interrupted by CNBC news. Participants do not attend ECR to watch television. Radio and television coverage does not fit the social dynamics of a conference of this kind.

I personally missed the welcome additional information from ECR Today, the daily newspaper that ECR Radio and TV have replaced. I used to take my copies of the newspaper back to my hotel, and back home, to read about those sessions I had not attended.

The most striking feature of ECR for me this year was the expansion of company-sponsored satellite meetings. While they were usually limited to lunch sessions, they also now run in parallel to proffered papers, competing with scientific sessions. There has never been a clear-cut distinction between the presentation of "clean" scientific results and "sponsored" results. There has been a gentlemen's agreement, though. The buck stops here. Sponsorship of scientific events can be advantageous and ethical, as long as both sides agree to this unwritten law.

Satellite symposia are considered to be sales shows, even if attendees receive CME points. Be careful. These points might not be recognized in all countries. There is no free lunch.

Succinct Expressions

The annual review of advertising slogans and mottoes at ECR used to be an entertaining game. But even this has been replaced by marketing fast food. ECR itself claims "We make congresses – and it

shows." Shows with a capital "S"?

Some slogans are empty talk, some aggressive or offensive, some are rude, some likeable. They have no influence on sales. At least they do not increase them.

One company promotes itself with the message "Proven Outcome," and adds that it is "Setting the trend again." For *trend*, see the earlier discussion. In medicine, a proven outcome requires outcomes research, that is, the study and eventual improvement of the end results of healthcare. This would be counterproductive for sales. Most likely, they mean "Proven Income" [1].

We also have "Let's make things better." They aren't so bad, are they? "Inspire the next." The next what? "Life from inside." From inside what? "Imagination at work" will be turned into "Imagine it works."

One of the worst mottoes is the oft-quoted "Making medicine work." This implies that medicine does not work without that particular company. Doctors are morons. There are even worse slogans, not to be discussed here. Why this lack of subtlety and lack of cultural and historical understanding?

I prefer the catchphrase, "Sense and simplicity."

I should add that these comments do not imply any endorsement or sanction of certain manufacturers. They are just subjective reflections.

Reference

1. Proven Outcome at South Carolina Heart Center. We see a way to generate an additional $720,000 in annual revenue via increased cath lab capacity (www.medical.siemens.com/...). [The page has disappeared: "We recently updated our website and the page you are trying to access is no longer available."].

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MR contrast agents reach 25-year landmark

Peter A. Rinck

One sunny day in late spring 1982, I stood on the public observatory deck at the top of the Empire State Building in New York City with a visitor from Berlin in Germany. I recall being on crutches, my foot and ankle encased in a plaster cast, having stumbled awkwardly while walking on a Long Island beach.

My visitor, Hanns-Joachim Weinmann, had traveled to New York to study a new chemical compound on our experimental MR machine. It came in a small vial directly from Berlin and was called Gd-DTPA. Gd stood for gadolinium, an element hardly any radiologist had ever heard of at that time. Today, gadolinium agents are well established, as if they had been with us forever.

The idea of using lanthanide compounds as contrast agents originated at State University of New York at Stony Brook, where I used to work. We knew that certain elements could shorten MRI relaxation times, so could they perhaps highlight certain tissues [1]? Researchers in Berlin quickly understood the theory of influencing relaxation times and the possible impact of MRI on radiology, despite the lack of any MRI system in Germany. Their high-risk gamble paid off [2].

In the end, we never tested the contents of the vial. The head of our university laboratory deemed that commercial cooperation was not desirable. As it subsequently turned out, the scientists at Schering had produced a compound with marginal acute toxicity and excellent contrast-enhancing properties. Schering's MR contrast agent Magnevist was launched in 1988. Guerbet followed some months later with Dotarem, Nycomed a little later with Omniscan, and then Squibb with ProHance.

Bracco's R&D department had something far better than all of the others: MultiHance, a compound with better relaxivity and higher contrast, enhancing both in the central nervous system and liver. But it took them far too long to bring this product to their customers. It came quite late to a market dominated by other products.

MR contrast agents are among the safest compounds in medical imaging, safer than x-ray contrast media.

They have some common side effects [3]; severe side effects of at least one compound became publicly known only twenty years after their introduction [4]. But what really makes these agents unsafe is illconsidered and careless use.

Indications for the original nonspecific gadolinium agents and reimbursement rules vary from country to country. Head and brain MR examinations are usually performed unenhanced and again after contrast injection so as not to miss any small metastases or leptomeningeal pathologies. Lesion characterization often requires a dynamic contrast series. This is particularly true when examining the liver and pancreas, though it is also the case for unclear soft-tissue masses. Most MR angiograms are performed following bolus injection as well.

Procedures and indications continue to be a subject for debate. Contrast-enhanced studies may show pathologies better than plain images or assist in diagnosis. Few will be truly decisive. But they facilitate treatment and mental comfort for patients and radiologists alike. The only clear and undisputed indication is breast MRI. Without a contrast agent, this examination is useless. With contrast, it is the best mammography technique we have.

"Contrast-enhanced studies facilitate treatment and mental comfort for patients and radiologists alike."

Development Dilemmas

R&D associated with contrast agents suffers from the rapid, unpredictable development of imaging hardware and software. Eight to 12 years from idea to rollout is a long time. R&D has to be done conscientiously and thoroughly. Companies complain about the bureaucracy imposed by regulatory agencies, and

their objections are partly justified, partly not. Many pencil pushers at many desks have to be fed – including those sitting in the companies themselves.

When all preclinical and clinical studies are finished and the paperwork is complete, the new compound can be submitted for approval in a European Union member state. If approved, as hoped, it may be mutually recognized by all other EU member states. Similar procedures are required for the U.S., Japan, and the rest of the world.

The contrast business can also involve infighting between companies. By this, I mean a patent war. Schering, for example, held a leading patent position for MR contrast. [Meanwhile, Schering does not exist any more; the company has been swallowed by another one.]

Contrast agents are drugs. They should be used only when necessary for the benefit of patients. Yet patent attorneys handle them as commodities. Some sales personnel have, unfortunately, done the same. A number of companies, their sales staff, and greedy radiologists have paid for this dearly. They were sentenced in court for buying and selling contrast agents like coffee or pork bellies, to the detriment of their patients. This has harmed their reputation and, by extension, the reputation of these agents.

Meanwhile we have seen many compounds come and go. Failures may be due to a bad product, incorrect marketing, absence of any market at all, an overconfident CEO, or developments in MR hardware and software that render the agent obsolete. The latter has an unpredictable impact on contrast development. New agents need several years from the first step of development to marketability. But if manufacturers suddenly adopt new technology that offers significant advantages over rival modalities and needs no contrast, the market for the new agent could collapse overnight.

Look Back, Move Forward?

The names of the original unspecific gadolinium agents may change and they may become available as generic drugs, but they will be with us for some time. Their concentration was determined empirically in the mid-1980s. Both tissue contrast and the relaxivity of contrast agents change independently of one another with field strength. These compounds were sufficiently good for low, midstrength and high-field MRI, though in hindsight, double concentration would have been appropriate. Adjusting the dose or concentration, or using a new class of agents with optimized relaxivity, would help improve contrast enhancement at these field strengths and hence aid diagnosis [5].

Concentration is also sufficient at ultrahigh-field strengths such as 3T, though standard contrast agents might not enhance properly at even higher field strengths. Particulate agents could work better for ultrahigh-field MRI.

The manufacturers' hardware branches want to sell ultrahigh-field machines because that is where the money is, both in sales and maintenance. Yet no synergy exists with the wishes of their brothers and sisters who are promoting contrast media. This is another nightmare for manufacturers, particularly those who have bought into contrast agent companies – and lost.

Some companies with a long-standing involvement in contrast agents seem to have learned from their mistakes of the past 20 years. The results are fairly cruel. Cuts have been made in research labs, and some big players have closed down their R&D facilities or disappeared from the scene altogether. Years ago, company executives were knowledgeable about their products, the pros and cons of agents, the diagnostic wishes of the medical community. Scientists, medical staff, management, and marketing personnel would all cooperate. Some companies today have a lack of trained researchers and – worse for customers and patients – few knowledgeable representatives. It is painful for customers to talk to clueless company managers who are untouched by medical reality.

"Greedy radiologists were sentenced in court for buying and selling contrast agents like coffee or pork bellies."

Every other year since 1988, the European Magnetic Resonance Forum (EMRF) arranges a conference on contrast agent research, mostly focusing on MRI and molecular imaging. The 14th meeting in this series took place in Valencia, Spain, in February 2013.

A fresh breeze was blowing from some of the university-based research groups; however, hardly any radiologist is involved. It seemed that we had returned to

the times when contrast R&D was performed by a few academic groups, though without a link to economic reality and commercial concerns. Italy and Belgium excel in this area, with France, Germany, and the Netherlands following on. Research is aplenty in the U.S. as well.

We should return to the good old role of the radiologist; that is, trying to understand enough in many areas and combining this knowledge to deliver something useful. Regrettably, there is a problem. As a professor at one of the major Nordic university hospitals pointed out, young radiologists using contrast agents in their clinical routine have no background knowledge about how these agents function. They just ask technologists/radiographers to inject the agent according to agreed protocols and then read the images later.

So what does the future hold? Conventional demand for contrast agent R&D is focusing on "personalized" diagnosis. Fashionable "molecular imaging" is targeted at small patient groups, individual diagnosis, and, hopefully, treatment. Everybody, myself included, is fascinated by the possibilities molecular agents promise. Even some of the traditional hardware manufacturers are trying to move into molecular imaging on their own. The results of their involvement remain to be seen. Personalized contrast agents are economically and commercially difficult.

They are not unfeasible, but there is no shareholder value. Today's megacompanies want and need blockbuster drugs.

Imaging is not only anatomy. The interaction between chemistry, physiology, metabolic processes, pathological changes on a cellular level, and the application of an enhancing imaging agent offers numerous diagnostic possibilities. Contrast agents can provide a plethora of additional, different information. New ideas should focus on medical, not technically feasible development. This can be achieved at a reasonable price, though perhaps only by small, dedicated companies.

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