How to keep your integrity while performing sponsored trials

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Imaging studies are increasingly used to assess endpoints in clinical trials. Validation of new results relies heavily on the quality and quantity of clinical and imaging research. It is therefore not surprising that radiology plays a rapidly growing role in the development of adequate research protocols, the conduct and monitoring imaging studies, and qualitative and quantitative data analysis. Most large-scale clinical trials are sponsored by “contract research organizations”, including scientific organizations and societies, government agencies, academic centers, imaging laboratories, professional organizations, and industry.

The purpose of this presentation is to discuss some of the ethical dilemmas that confront radiologists and other imaging professionals during the conduct of clinical trials. We shall review how we can maintain our integrity and independence, and, at the same time, contribute towards improving research, protecting patients, assuring standards of good clinical practice, and enhancing the competitiveness of large-scale medical trials.

Maintaining imaging standards in clinical trials involves several key issues, including:

- **Image Acquisition**: Radiologists should be aware of quality control concepts, even at the early stage of trial design. They should assume responsibility for recommending and validating the equipment to be used. Ideally, they should conduct initial studies on phantoms or volunteers, when feasible, and perform a so-called “dummy run”, to validate the technical platform.

- **Image Interpretation**: Imaging professionals should be involved in decision-making regarding local vs. central read design, sources and solutions to read variability, etc.

- **Data Management**: Issues such as display, storage, transmission of images, and anonymity of patient data must be addressed prior to the start of the trial.

Special care should be given towards the protection of all individuals involved in clinical trials, and several basic ethical principles must be respected:

- **Do no harm**. This simple ethical principle is and should be the first and foremost concern.

- **Maximize benefits and minimize harms**. This implies careful scrutiny of imaging protocols. Potential risks and complications must be taken into account, and alternative imaging techniques should be investigated. The benefits of research should be distributed fairly.

- **Respect for Persons**. The opinions of participants in clinical trials, whether volunteers or patients must be respected, and they should be given an individual choice to participate or not. Special care and protection should be given to individuals not fully capable of self-determination (e.g. children or patients with mental incapacities).

In applying those ethical principles, radiologists, technologists and other imaging
professionals should give special consideration to the following requirements:

- **Informed consent.** In order to provide fully informed consent, the potential subject (patient or volunteer) must first be given full information about the research project. Second, that information must be presented in a way that is easy to understand, taking into account the subject's intellectual capacities. If these capacities are limited, as in children or mentally disabled people, the consent of responsible third parties must be sought. Third, consent must be truly voluntary, and free from coercion and undue influence.

- **Assessment of risks and benefits.** The dangers involved in any clinical trial must not exceed its potential benefits. The researcher and imaging professional must consider not only the risks to a particular research subject, but also the risks to the subject's family and to society at large. Issues such as RF deposition, nerve stimulation, radiation dose, adverse effects of contrast agents, etc. should be kept in mind.

- **Selection of subjects.** There must be fair procedures for the selection of research subjects. Investigators must not select certain patients merely because they like them. Conversely, investigators must not seek out undesirable people, such as prisoners, for especially risky experiments.

Adherence to these regulations has significantly improved protection for research subjects. Clinical trials are conducted far more ethically and are far safer now than they were only a few decades ago. However, this does not imply that every ethical problem has been solved. On the contrary, the elimination of gross abuses tends to highlight more subtle ethical problems. In many, if not most, industry-sponsored trials, the researchers with the greatest influence over the set-up and management of the trial are often those individuals that have the closest financial ties to the pharmaceutical and other industries that benefit from positive clinical trials' results. This is a disturbing and alarming fact. However, it is not surprising, since the trend has been for stronger ties between research and corporate interests so this comes as yet one more indication that trials results may be tainted.

The best way for radiologists and other imagers to maintain their intellectual integrity and independence from the industrial partner, is to be financially independent from the parent company and the trial's results. This goal can be achieved by negotiating a separate contract for the conduct of the imaging studies, and for data analysis if this should be required. At Antwerp University Hospital (Belgium), we use a standardised “price list” for imaging studies, on a “fee for service” basis, without involvement in the other clinical aspects of the study. This strategy does not completely rule out industry influence, but it reduces the attachment between the imaging department and the industry.

In summary, the set-up and conduct of clinical and imaging trials should be based on robust evidence. The accumulating evidence must be brought to the attention of local, national and international authorities, and all other partners involved in the processing or approving of clinical trials. The views of all the stakeholders involved in the process of designing and performing the study should be taken into account, and this includes radiologists and/or other imaging professionals. ISMRM, as a scientific organization, is in an excellent position to assess the impact of medical trials involving magnetic resonance imaging (or, in a broader sense, medical imaging as a whole). It would therefore be useful to set up an ISMRM standing committee for clinical trials to document, and if possible, quantify the continuing impact of clinical trials on our practice, particularly with regard to research involving imaging. In this way, ISMRM could significantly contribute towards maintaining the integrity of the imaging community with regard to industry sponsored studies.