White Paper: Clinical Studies in Radiology

White Paper: Klinische Studien in der Radiologie

Introduction

Clinical trials represent a major part of clinically oriented research. At the same time they are an absolute necessity for the introduction of new methods for the diagnosis and (image-guided) treatment of our patients. Radiology plays an important role in preclinical and clinical trials. Imaging methods are often decisive for the evaluation of new drugs or innovative treatment measures. Their results are used as endpoints for clinical trials. Both the correct selection of the examination modality, acquisition technique, and examination interval and the quality of the image evaluation have a significant effect on the trial results. As a professional scientific association, the German Radiological Society therefore supports professionalization of clinical trial results. This includes: Image data including evaluation, technical implementation and standardizing data analysis including the necessary materials and personnel resources.

Basic principles

Experimental research approaches are to be differentiated from clinical research. The German Council of Science and Humanities defines clinical research as follows: Clinical research “includes all research of the etiology, development, and course of diseases and the scientific study of their detection and treatment” (German Council of Science and Humanities: Recommendations for Clinical Research at Universities, 1986 ISBN 978-3-923 203-14-7). Based on this definition, a differentiation is made between “knowledge-oriented research with a focus on gaining knowledge of biological systems, disease-oriented research using model systems including animal experiments, and patient-oriented research performed directly on and with patients or subjects” as different but inseparable aspects of clinical research in the memorandum of the German Research Foundation regarding clinical research from the year 2000. Patient-oriented research includes “primarily clinical trials in all phases.” (URL: http://www.dfg.de/download/pdf/dfg_im_profil/reden_stellungnahmen/download/denkschrift_klin_forschung.pdf, last access 11/6/2013). The categorization of clinical trials into phases is based on the corresponding FDA classification for drug trials in which pharmacokinetic and pharmacodynamic examinations are initially performed in small patient populations in phase I and phase II, the treatment concept is examined in phase III, and significant evidence of efficacy must be provided in phase IV to justify market introduction (this is similar for the introduction of medicinal products). Radiological examinations as part of clinical trials provide raw data for the trials. This includes:

- Image data including evaluation,
Results of a quantification in absolute numbers (e.g., bone density values in osteoporosis or lung density measurements in patients with pulmonary emphysema or fibrosis)

Determination of a diagnosis on the basis of radiological examinations,

Determination of the presence of an inclusion criterion for the clinical trial via radiological methods (e.g., exceeding of a threshold value in the quantification of coronary calcification via cardiac CT).

Based on the above-cited definition of clinical research by the German Council of Science and Humanities and the German Research Foundation, radiological examinations as part of a clinical trial are not “contract work” but rather provide essential raw data for the clinical trial and are equal to other examinations, follow-ups, and treatment measures. Due to the structural and personnel requirements for collecting this data, the laws and guidelines regarding data collection and evaluation, and the time expenditure, as described in detail in the following sections, clinical trials require significant resources. This fact must be duly taken into account by the involvement of radiology, including third-party funding.

Third-party funding is a decisive factor not only in the performance-oriented allocation of funds but also in the academic positioning of radiology. Important aspects of radiology are the increasing qualifications of participating radiologists due to clinical investigator training courses, knowledge regarding the amendment of the German Medical Devices Act and the German Medicinal Products Act as well as the constant implementation of technical and methodical improvements in examination methods, the implementation and interpretation thereof, and specialized knowledge of standardized evaluation techniques, for example in accordance with RECIST (Response Evaluation Criteria in Solid Tumors) and comparable standards including the WHO recommendations.

Centers for clinical trials – some of which are the product of the competence centers for clinical trials which have been funded by the Federal Ministry of Education and Research since 1998 – support multidisciplinary clinical research approaches at several locations. These structures are based on the recommendations of the German Council of Science and Humanities and simplify collaboration between disciplines with incorporation of the competences of each area of specialization. The position of the German Council of Science and Humanities regarding the importance of interdisciplinary collaboration among the different disciplines for creating “profile centers” and for conducting clinical research is significant here. The German Council of Science and Humanities defines profile centers as “organizational networks” that bundle expertise across departments. They are intended to “supplement the basic structures of the departments and clinics” and to provide a “concentration of research and teaching or research and patient care” (general recommendations regarding university medicine of the German Council of Science and Humanities; URL: www.wissenschaftsrat.de/download/archiv/allgemein_uni_med.pdf, last access 11/6/2013). The German Council of Science and Humanities also states the following in the same document: “Profile centers can ideally improve the integration of patients in research, clinical trials, and courses.” They should have maximum flexibility so that they can be set up both for short-term projects and for the long-term study of complex topics. Therefore, the German Council of Science and Humanities recommends that individual persons should be able to be members of multiple profile centers without this being complicated by formal rules. Thematic bundling in profile centers should facilitate translation between the different clinical research areas.

High-quality trials require professional planning, preparation, and implementation as explained in the detail in the following. Centers for clinical trials and profile centers can support and facilitate this by providing suitable basic conditions and simplifying interdisciplinary dialog.

Radiology tasks and responsibilities

Responsibilities can be categorized as: a) trial planning tasks, b) trial implementation tasks, and c) data evaluation tasks (central or local).

a) Trial planning:
All uses of ionizing radiation in people for the purpose of medical research require approval in Germany. This is regulated by the X-Ray Ordinance. Examination methods not involving the use of ionizing radiation, such as ultrasound and MRI, are excluded.

The X-Ray Ordinance differentiates between medical practice and medical research. The use of radiation in medical practice (§ 23 X-Ray Ordinance) requires determination of the justifying indication by a qualified physician who also assumes legal responsibility.

The use of radiation in medical research is regulated in § 28a – § 28g and mandatory regulatory approval by the Federal Agency for Radiation Protection replaces the determination of the justifying indication by a qualified physician. Regardless of regulatory approval, the physicians overseeing the use of radiation in a research project remain medically and legally responsible.

Particularly in clinical trials using imaging methods for determining inclusion criteria or endpoints, it can be difficult to differentiate between applications in medical practice and medical research. According to § 2 No. 8 of the X-Ray Ordinance, the use of radiation in medical research is defined as use for the advancement of medicine, dentistry, or medical science and not primarily for the examination or treatment of individual patients. The decisive requirement for classification as medical practice is that all subjects would receive the type and scope of radiation even if not participating in the trial. Answering this key question requires a high level of radiological expertise. Therefore, the German Radiological Society established an independent panel of experts under the scientific direction of Prof. Dr. med. Christian Stroszczyński for advising trial directors and sponsors. For more information, refer to http://www.drg.de/de-DE/52/studienkoordination.

If the primary objective of a clinical trial is classified as medical research, approval must be obtained from the Federal Agency for Radiation Protection. The amendment of the X-Ray Ordinance in 2011 introduced a simplified approval procedure for so-called “accompanying diagnostics”. In the case of research regarding testing of the safety or efficacy of a treatment in patients, the use of radiation can be recognized as accompanying diagnostics if the following points
are satisfied (see list in § 28b Paragraph 1 of the X-Ray Ordinance):

- The use of X-ray radiation is not the object of the research.
- The manner in which X-ray radiation is used is in accordance with the medical practice standard.
- The manner and frequency of the use of X-ray radiation correspond to the research objective.
- Only competent persons who have the disease being studied in the research project and who are over the age of 18 are included. The use prohibitions and restrictions for example in pregnant women according to § 28 d of the X-Ray Ordinance must also be observed.
- Approval of an ethics commission registered with the Federal Agency for Radiation Protection in accordance with § 28 g of the X-Ray Ordinance has been obtained.

Therefore, a radiologist wishing to participate in a clinical trial must first familiarize himself with the trial protocol. Approval must then be obtained from the ethics commission and it must be clarified whether radiation will be used for the purpose of medical practice or medical research. This decision can only be made by a qualified physician. In cases of doubt, review by the independent panel of experts of the German Radiological Society should be performed. In multicenter studies, the radiologist is responsible for performing these tasks at the site of the director of the clinical trial.

Another important task of the radiologist during trial planning is to adjust the measurement parameters defined in the trial protocol to the available equipment. For CT examinations this is usually a manageable process while serious problems that can only be resolved with significant effort and radiological expertise often arise in the case of MRI examinations. For example, the sequence parameter information is incomplete, or the parameters do not correspond to the clinical standard but to the lowest common denominator of various devices, or the parameters were defined for a certain system or the systems of one manufacturer and cannot simply be transferred to the scanners of other manufacturers. Time- and personnel-intensive phantom measurements that must be taken into consideration in trial cost estimates are typically needed to overcome these problems.

b) Trial implementation

Since the management of imaging examinations and interventions performed as part of clinical trials differs in almost every stage of processing from application, evaluation, and result documentation to the billing of corresponding services performed as part of the provision of medical care, the establishment of a radiological trial center for the coordination of complex tasks is useful. Such centers should be staffed with specially trained personnel who can provide support for the implementation of radiological tasks in all process steps of a clinical trial and act as an interface between clinical trial centers, referring physicians, routine radiological service providers (medical technical radiology assistants, physicians), hospital administrators, and sponsors. Professional standardization of the interdisciplinary and multivariable procedure should be targeted. Availability of the following must be ensured: Facilities (office, archive room) and appropriate IT equipment allowing networking with the software of the center or coordination center for clinical trials usually present at universities,

- Use of preexisting electronic checklists and formulas, and
- Automatic electronic sending of pseudonymized image datasets to the sponsor.

Moreover, the ability to electronically identify trial services within the radiology information system (RIS) and the availability of software programs for semiautomatic image evaluation are desirable.

Depending on the workload, a radiological trial center should have one or more radiologists and one or more study nurses. According to the 2nd law amending pharmaceutical and other regulations dated 10/19/2012 (16th amendment of the German Medicinal Products Act, Federal Law Gazette I pg. 2192), it is possible for a physician to act as a Germany-wide director of a clinical trial, as an investigator, as the investigator’s representative, or as a medical member of a typically interdisciplinary clinical trial team. In general, radiologists can participate in clinical trials as an investigator or investigator’s representative after successfully completing at least a 16-hour course meeting the requirements according to the announcement of the German Medical Association entitled “Curricular continuing education: basic course for investigators/representatives and members of a clinical trial team in clinical trials according to the Medicinal Products Act and for investigators according to the Medical Devices Act” (Dtsch Arztebl 2013; 110(23 – 24): A-1212 / B-1056 / C-1048). In addition, a Germany-wide clinical trial director overseeing the individual centers of a multicenter trial must have at least 2 years of experience in the conducting of clinical trials according to the stipulations of § 40 Paragraph 5 of the German Medicinal Products Act. This could affect radiology, for example in the rare case of a contrast agent trial. A certain margin of discretion is allowed with respect to the requirements regarding the clinical trial experience of an investigator, the investigator’s representative, and the medical members of a clinical trial team. Therefore, the requirements for complex oncological CT and MRI evaluations (RECIST, etc.) are typically higher than for comparatively simpler diagnostic issues.

Study nurses should have at least 3 months of professional experience or have completed a 2-week practical course at a hospital conducting clinical trials. In addition, study nurses should ideally have successfully completed a 120-hour study nurse course based on the curriculum of the network of the coordination centers for clinical trials and in compliance with the valid regulations (GCP, ICH GCP, Declaration of Helsinki 1996/2008, German Medicinal Products Act, German Medical Devices Act, anticorruption laws, EU directives 2001/20/EC and 2005/28/EC, etc.).

Study nurses support the principal investigator during the conducting of clinical trials. They serve as a central contact person for all participants in a clinical trial and support the coordination of tasks and processes within the radiological trial center. The tasks of the radiological trial center include: Prior to the start of the trial phase (start-up after trial planning as described under point 3a has been successfully completed):
During the trial phase:
- Schedule examinations in accordance with the inclusion and exclusion criteria and the intervals specified by the trial protocol and possibly by the Federal Agency for Radiation Protection.
- Provide patient counseling and obtain informed consent.
- Review/evaluate inclusion, exclusion, and termination criteria.
- Evaluate adverse events, adverse drug reactions, and reports to the sponsor.
- Make decisions regarding unblinding and evaluate possible consequences during/after unblinding.
- Make decisions regarding diagnostic and therapeutic measures including treatment changes.
- Provide medical care for a trial participant during and after trial participation in the case of adverse events.
- As necessary, provide individual information for the radiological workstations regarding the specifics of the examination technique (upper exposure limit according to Federal Agency for Radiation Protection, display of templates, etc.). This requires special knowledge and qualifications also for the use of non-ionizing radiation.
- As necessary, provide individual information for the principal radiological investigator regarding the type of evaluation (RECIST 1.0 or 1.1, etc.).
- As necessary, pseudonymize electronic image data and electronically send pseudonymized image data to a central evaluation site, and
- Recording of services and billing with the clinical trial center and/or the sponsor via the administration according to the compensation regulations explained under point 4.

After conclusion of the trial phase:
- Complete the final queries of the Federal Agency for Radiation Protection regarding radiation exposure during a clinical trial with approval from the Federal Agency for Radiation Protection.

The following tasks are primarily assigned to the radiological member of a clinical trial team:
Prior to the start of the trial phase (start-up):
- Participate in local interdisciplinary trial initiation by the sponsor, participate in trial-specific (online) training, etc.

During the trial phase:
- Individually review the justifying indication for examinations involving X-ray radiation (approval as accompanying research by the Federal Agency for Radiation Protection vs. indication based on medical care).
- Provide individual assurance of use of the appropriate examination technique according to the trial protocol and possibly in accordance with the approval from the Federal Agency for Radiation Protection (examination volume?, exposure dose?).
- Counsel subjects (patients) with regard to the potential risks of the examination/intervention in accordance with §28c of the X-Ray Ordinance in addition to the clarification by the principal clinical investigator as specified by the trial protocol; written informed consent from the subject is required.
- Scientific evaluation of the examination and result documentation (e.g. according to RECIST 1.0 or 1.1, see point 3c). This should be performed in coordination with parallel reporting to the clinical referring physician after the provision of medical care (diagnostic report) and does not necessarily have to be performed by the principal investigator but can also be performed by other radiologists. Discrepancies between the scientific evaluation and the data in the diagnostic report due to interobserver variability must be avoided.
- Make decisions regarding additional diagnostic and therapeutic measures possibly resulting from a finding, in coordination with the investigator or with the responsible member of the clinical trial team.
- Inform the investigator or at least a medical member of the clinical trial team and in the rare case of a proprietary radiological trial also inform the sponsor of examination or intervention complications and other adverse events and adverse drug reactions observed during an examination.
- Radiology can support the deblinding decision (disclosure of the identity of a blinded investigational product or an investigational method) in the case of a suspected unexpected and severe adverse reaction (SUSAR) by providing diagnostic information. However, the actual decision is typically made by the principal investigator.

After conclusion of the trial phase:
- Provide responsible reporting of the examination and exposure parameters to the Federal Agency for Radiation Protection in trials approved as part of accompanying research (§28b Paragraph 2 of the X-Ray Ordinance) or proprietary radiological research by the Federal Agency for Radiation Protection (§28b Paragraph 1 of the X-Ray Ordinance). Communicate with the Federal Agency for Radiation Protection as required.

Through the course of the trial:
- Provide responsible support of the quality assurance measures implemented by the German Radiological Society during trial planning, implementation, and evaluation (refer to point 5).
- Consult with the Federal Agency for Radiation Protection as necessary.
- In the case of a trial of a medicinal product in accordance with the Medicinal Products Act or the clinical trial of a drug (e.g. innovative X-ray contrast agent): interact with the Federal Institute for Drugs and Medical Devices as necessary.

c) Trial evaluation:
A differentiation must be made in the clinical trial evaluati—
Evaluation by the individual centers must be performed for many issues on the basis of structured procedures developed specifically for trial evaluations, such as RECIST 1.1, the WHO recommendations, the guidelines of the responsible committees, or the recommendations of professional organizations. Such evaluations differ significantly from purely diagnostic reporting with respect to scope and are associated with a comparatively higher time expenditure that must be included in calculation of costs. The evaluation or authorization of an evaluation prepared by a resident physician can only be performed by a radiologist with experience in this regard. The precise, objective, and reproducible assessment of radiological follow-ups requires comprehensive knowledge of the response criteria defined for the particular trial. Different criteria are currently used, such as WHO (diagnostic criteria of the World Health Organization), RECIST (Response Evaluation Criteria in Solid Tumors), m-RECIST (modified RECIST, for hepatocellular carcinoma), ir-RECIST (immune-related response criteria for evaluating immunotherapy in solid tumors), depending on the particular tumor entity and the particular treatment protocol. In addition, the criteria are sometimes subject to corrections with modification of the rules to be applied. Exact knowledge of the criteria is essential both for the inclusion of patients and the categorization of the treatment course. Moreover, the evaluation of the image data is typically performed by different radiologists at different points in time resulting in numerous possible sources of error. Particularly in multicenter trials, adequate, cross-institute training of participating radiologists must therefore be ensured to guarantee a high, objective and reproducible quality standard for the evaluation. Moreover, to ensure the greatest possible standardization of findings, special software modules should be used for follow-up according to RECIST. These are commercially available and are billed either as a total product or on an individual basis (“pay per use”). To ensure consistently high quality, this should be performed either by a few individual persons or a slightly larger, clearly defined group depending on the scope of the trial. Cross-institute coordination and training of the participating radiologists is also extremely important here to ensure a consistently high quality standard. The scope of the trial also determines the extent to which these persons perform other tasks or only evaluate examinations. Non-medical personnel can be included in data processing and presentation and data management during trial evaluation. Costs should be calculated on the basis of the estimation of the time requirement per patient and the subsequent summation of the number of patients included in the trial plus calculation of a possibly necessary overall evaluation.

Guidance with respect to trial evaluation and coordination of the evaluation by different centers can only be provided by a radiologist who has experience in this regard and whose research is ideally focused on this topic. Costs for subsequent time expenditure are often more difficult to estimate in advance but must also be duly taken into consideration with inclusion of all individual aspects to be expected.

For the evaluation of examinations performed at other centers or the preparation of a secondary evaluation of an examination as a core lab for the trial, an infrastructure allowing trial evaluation must first be created. This includes the necessary hardware (computer or server) including the necessary software as well as the development of logistics facilitating the provision of data for the evaluation. This can include the use of non-medical personnel for assistance in the evaluation in the form of data management and data presentation. The actual evaluation can then be performed analogously to the evaluation at the trial center or as described above. For core labs it must be taken into consideration that interim evaluations are typically performed at previously defined intervals and the overall evaluation is performed after conclusion of the trial. This can only be performed by radiologists with scientific experience in the corresponding subject area and with the support of statisticians as needed.

Compensation

The determination of the appropriate compensation for radiologists for participation in clinical trials and their inclusion in trial planning and contract formulation in a timely manner are currently not absolutely ensured. To fundamentally and permanently improve such limitations, the following aspects should be consistently taken into consideration in the future by radiological institutes participating in clinical trials. A consistent approach to ensuring sufficient compensation based on the services rendered in a clinical trial can improve the following frequently reported criticisms:

- homogenization and uniform implementation of the applications required by the Federal Agency for Radiation Protection and radiation hygienic trial conditions for conducting clinical trials. From a radiological standpoint, this means an improvement of ethical trial aspects.
- reduction of a financing downward spiral as a result of statements regarding purportedly significantly cheaper service providers at other participating trial centers under the cost-covering amounts.

A standardized radiological procedure in this area would relieve the pressure on individual trial centers because they are currently often told that the start of a clinical trial is delayed because of their procedures although they were only required to adhere to ethical and radiation hygienic standards at the time of inclusion in the trial. Relieving the pressure on individual radiological centers by implementing standardized procedures also strengthens the position of radiology for participation in clinical trials in general.

As a rule, a full cost approach that includes the most important aspects of radiological services, personnel, and material costs should be targeted for the calculation of the compensation for radiological services. Institutes must continue to be allowed to differentiate between industry-sponsored trials and university-based investigator initiated trials (IIT). With respect to compliance, services and consideration in clinical trials must be appropriate. For example, a lump sum payment or permanent loaning of devices as consideration is an unacceptable form of compensation. Four central basic principles must be observed when concluding contracts between medical facilities:

- the principle of separability,
- the transparency or approval principle.
the equivalence principle
the documentation principle.

According to the principle of separability, the compensation must not influence the physicians with regard to purchasing, prescribing, or treatment decisions. The transparency/approval principle is intended to ensure the disclosure of relationships between physicians and the industry to employers or medical associations. The equivalence principle requires an appropriate balance between service and consideration. The suspicion of an unacceptable contractual relationship can be avoided or eliminated by the documentation principle. The corresponding legal requirements in this regard are contained in the FSA Code of Conduct on the Collaboration with Healthcare Professionals, in university regulations at university facilities, and in professional codes of conduct for physicians.

In the case of industry-sponsored trials, usual market prices should be used as a rule. The usual market prices defined in the medical fee schedule should be used for outpatients and those defined by the tariff scheme of the German Hospital Federation for inpatients, including an incremental factor depending on the scope of the rendered trial services. This has the advantage that radiology does not have to engage in misguided discussions to define estimated prices to be kept low from an industry standpoint. The core services must be defined together with the relevant partners in order to specify the compensation for IIT. A differentiation must be made as to whether radiology is to be viewed as a scientific partner in an IIT or only radiological trial services are to be rendered as in industry-sponsored trials. In the latter case, compensation in accordance with the structure for industry-sponsored trials would be defined.

According to the German Radiological Society, compensation of trial services in industry-sponsored trials is also necessary when the examinations to be performed are defined as “standard of care”. In addition, it must be noted at this point that the “standard of care” cannot be defined by the sponsor. On the one hand sponsors are not impartial in this matter and on the other hand radiologists are ethically obliged to make this decision independently of the trial on a purely medical basis. Despite the opinion of other parties, examinations to be performed as “standard of care” require a number of radiological trial services to be compensated by the sponsor. While in the case of purely medically indicated radiological examinations outside of clinical trials only devices, disposables, and personnel for data acquisition and reporting need to be taken into consideration, additional costs which are not to be indirectly carried by (university) hospitals or health insurance companies are incurred in trial patients for participating centers. These trial-based services include the following tasks already described in detail as well as personnel and material costs:

- review of trial contracts by the trial coordinator of the trial center together with the medical specialist/chief physician and the study nurse,
- review of and assistance for the submission of applications to the Federal Agency for Radiation Protection and applications to the expert panel of the German Radiological Society,
- trial initiation by the responsible medical specialist/chief physician and study nurse,
- storing of trial-based examination protocols on devices and trial-compliant training of medical technical radiology assistants and resident physicians,
- provision of software structures for ethical and trial-compatible additional documentation of e.g. RECIST 1.1, WHO results,
- data anonymization, documentation, and shipment by study nurse,
- review of Federal Agency for Radiation Protection final reports,
- additional trial-based reporting of examinations above the “standard of care”, e.g. volumetric measurements by resident physician and chief physician.

Quality assurance

Quality assurance in clinical trials in radiology should be performed within the relevant radiology clinic as well as externally via central data acquisition at the German Radiological Society:

A prerequisite for internal quality assurance is internal trial coordination. As described above, this coordination should ideally be performed by an employee employed explicitly for this purpose, e.g. a scientific assistant with previous clinical trial experience or a study nurse. Alternatively, internal trial coordination can also be performed by an employee who is made available for this task at regular intervals. However, experience at large radiological centers has shown that regular availability of trial coordinators is necessary due to the tasks to be performed as part of different trials and inquiries from clinical referring physicians and the industry. The costs for such coordination within radiology are described on the basis of the calculation of costs specified under “4. Compensation”.

Internal trial coordination functions as a central point of contact for all aspects of clinical trials in radiology. In addition to functioning as a point of contact for all questions regarding radiological services in clinical trials, internal radiology trial coordination is also responsible for quality assurance. This includes:

- patient scheduling,
- monitoring of compliance with the trial protocol,
- documentation of trial services,
- archiving of trial data,
- provision of anonymized data to the client,
- support of trial audits.

These tasks are performed in close coordination with radiologists responsible for the trial or the director of radiology. In addition to internal quality assurance, superordinate recording of the central data of clinical trials with the participation of radiology is necessary. This central recording is performed by the German Radiological Society in Berlin. The following data are centrally stored for every trial:

- trial number (ClinicalTrials-ID, EudraCT-number, trial protocol number if applicable),
- title of the trial,
- list of participating centers,
- contact person for every participating center with contact data (radiology trial coordinator or responsible radiologist),
- the name of the trial sponsor with contact data.

The goal of this external quality assurance is increased transparency and simplification of the processes of trial planning, implementation, and evaluation via better coordination of the individual trial centers. As a result, a direct contact person is available for questions for every trial center and every trial.

Affiliations

1 Institut für Diagnostische und Interventionelle Radiologie, Universitätsklinikum Düsseldorf, Düsseldorf
2 Klinik für Radiologie und Nuklearmedizin, Universitätsklinikum S-H Campus Lübeck, Lübeck
3 Klinik und Poliklinik für Diagnostische und Interventionelle Radiologie, Universitätsmedizin Mainz, Mainz
4 Klinische Studienkoordination, Deutsche Röntgengesellschaft e. V., Berlin
5 Institut für Klinische Radiologie, Universitätsklinikum Münster, Münster
6 Diagnostische und Interventionelle Radiologie, Universitätsklinikum Giessen und Marburg GmbH, Giessen
7 Institut und Poliklinik für Radiologische Diagnostik, Uniklinik Köln, Köln
8 Radiologie, Deutsches Krebsforschungszentrum, Heidelberg
9 Institut für Klinische Radiologie und Nuklearmedizin, Universitätsmedizin Mannheim, Mannheim
10 Kanzlei Rechtsanwälte Dr. Wigge, Kleinke, Frehse, Münster
11 Klinik und Poliklinik für Diagnostische und Interventionelle Radiologie, Universitätsklinikum Hamburg-Eppendorf, Hamburg
12 Klinik für Diagnostische und Interventionelle Radiologie, Universitätsklinikum Ulm, Ulm
13 Institut für Diagnostische und Interventionelle Radiologie, Universitätsklinikum Würzburg, Würzburg
14 Klinik für Diagnostische und Interventionelle Radiologie, Universitätsklinikum des Saarlandes, Homburg
15 Diagnostische und Interventionelle Radiologie, Tübingen
16 Institut für Diagnostische und Interventionelle Radiologie und Neuroradiologie, Universitätsklinikum Essen, Essen
17 Institut für Radiologie, Charité Universitätsmedizin Berlin, Berlin
18 Institut für Diagnostische und Interventionelle Radiologie, Universitätsklinikum Rostock, Rostock
19 Institut für Diagnostische Radiologie und Neuroradiologie, Klinikum der Ernst-Moritz-Arndt-Universität, Greifswald
20 Institut für Neuroradiologie, Universitätsklinikum Campus Kiel, Kiel
21 Klinik und Poliklinik für Diagnostische und Interventionelle Radiologie, Universitätsklinikum Leipzig, Leipzig
22 Zentrum für Radiologie, Universitätsklinikum Jena
23 Diagnostische und Interventionelle Radiologie, Universitätsklinikum Heidelberg, Heidelberg
24 Klinik für Diagnostische und Interventionelle Radiologie, Universitätsklinikum Aachen, Aachen
25 Klinik für Radiologie, Universitätsklinikum Freiburg, Freiburg
26 Institut und Poliklinik für Radiologische Diagnostik, Universitätsklinikum Carl-Gustav-Carus, Dresden
27 Institut für Diagnostische und Interventionelle Radiologie, Universitätsmedizin Göttingen / Georg-August-Universität, Göttingen
28 Klinik für Diagnostische und Interventionelle Radiologie, Universitätsklinikum Gießen und Marburg GmbH, Marburg
29 Institut für Klinische Radiologie, Universität München-Großhadern, München
30 Klinik für Radiologie und Nuklearmedizin, Universitätsklinikum Magdeburg, Magdeburg
31 Institut für diagnostische und interventionelle Radiologie, Universitätsklinikum der Freien Universität Berlin, Berlin
32 Radiologische Klinik, Universitätsklinikum, Bonn
33 Klinik für Diagnostische Radiologie, Universitätskliniken, Halle
34 Institut für Röntgendiagnostik, Universitätsklinikum Regensburg, Regensburg
35 Radiologisches Institut, Universitätsklinikum Erlangen, Erlangen
36 Institut für Diagnostische und Interventionelle Radiologie, Universitätsklinikum Jena, Jena
37 Institut für Diagnostische und Interventionelle Radiologie, Universitätsklinikum der Johann-Wolfgang-Goethe-Universität, Frankfurt a. M.
38 Institut für Diagnostische und Interventionelle Radiologie, Medizinische Hochschule Hannover, Hannover
39 Institut für Diagnostische und Interventionelle Radiologie, Klinikum Ingolstadt, Ingolstadt
40 Siemens AG, Vice-President Innovation, Erlangen
41 Praxis für radiologische Diagnostik, DiaCura, Coburg
42 Deutsche Röntgengesellschaft e. V., Berlin