Abend M, Rothkamm K, Romm H, Badie C, Balagurnathan Y, Barnard S, Bernard N, Boulay-Greene H, Brengues M, De Amicis A, De Sanctis S. Greither R, Herodin F, Jones A, Knie T, Kabacik S, Kulka U, Lista F, Martigne P, Missel A, Moquet J, Oestreicher U, Peinnequin A, Poyot T, Roessler U, Scherthan H, Terbrueggen B, Thierens H, Valente M, Vral A, Zenhausern F, Meineke V, Little MP, Beinke C
NATO Exercise 2011: Intra- and inter-assay comparison of established and emerging biodosimetry assays – preliminary results.
In: NATO Science and Technology Organization Report 10/2012; STO-MP-HFM-223:20, 1-8. DOI:ISBN 978-92-837-0179-8

Compare the suitability of the well established dicentric chromosome assay [DCA] and cytokinesis-block micronucleus assay [CBMN] and the emerging g−H2AX foci and gene expression assays for biodosimetry and radiation injury assessment.

Lithium-heparinized whole blood from one healthy donor was X-irradiated. Ten blind (and calibration) samples were irradiated with single doses between 0.1-6.4 Gy and send to participants to run their assays. Provided dose estimates were analyzed using a linear model, logistic regression analysis and report time was documented.

The minimum reporting times for dose estimates were 2.4 days for DCA and 4 days for CBMN but only 0.3 days for foci and gene expression assays. However, inter-laboratory variance of dose estimates was smallest for DCA (about 2.3-5.6 times relative to all other assays) and increased in an assay-dependent manner as DCA < CBMN < gene expression < gH2AX foci. Comparable performance and concordance was found for automatic and manual scoring procedures using DCA and CBMN assays. Binary categories of dose estimates could be discriminated with equal efficiency for all assays, but at doses > 1.5 Gy a 10% decrease in efficiency was observed for the foci and the gene expression assays.

Dose estimates based on g−H2AX foci and gene expression assays are reported 8-13 times earlier compared to the DCA and CBMN assays, but estimates are 2.3-5.6 times more precise when running the DCA. This advantage in precision becomes negligible when discriminating dose estimates merged in binary categories of clinical relevance. Automatic and manual scoring procedures using DCA and CBMN assays were of comparable quality. All assays show an upper limit of applicability below 6.4 Gy. Scoring 50 instead of 20 cells did not lead to increased precision of dose estimates using the DCA or the foci assay.

Allinson S, Asmuß M, Baldermann C, Bentzen J, Buller D, Gerber N, Green AC, Greinert R, Kimlin M, Kunrath J, Matthes R, Pölzl-Viol C, Rehfuess E, Rossmann C, Schüz N, Sinclair C, Deventer E, Webb A, Weiss W, Ziegelberger G
Validity and use of the UV index: report from the UVI working group, Schloss Hohenkammer, Germany, 5-7 December 2011
Health physics 2012 Sep;103(3):301-6

The adequacy of the UV Index (UVI), a simple measure of ambient solar ultraviolet (UV) radiation, has been questioned on the basis of recent scientific data on the importance of vitamin D for human health, the mutagenic capacity of radiation in the UVA wavelength, and limitations in the behavioral impact of the UVI as a public awareness tool. A working group convened by ICNIRP and WHO met to assess whether modifications of the UVI were warranted and to discuss ways of improving its effectiveness as a guide to healthy sun-protective behavior. A UV Index greater

than 3 was confirmed as indicating ambient UV levels at which harmful sun exposure and sunburns could occur and hence as the threshold for promoting preventive messages. There is currently insufficient evidence about the quantitative relationship of sun exposure, vitamin D, and human health to include vitamin D considerations in sun protection recommendations. The role of UVA in sunlight-induced dermal immunosuppression and DNA damage was acknowledged, but the contribution of UVA to skin carcinogenesis could not be quantified precisely. As ambient UVA and UVB levels mostly vary in parallel in real life situations, any minor modification of the UVI weighting function with respect to UVA-induced skin cancer would not be expected to have a significant impact on the UV Index. Though it has been shown that the UV Index can raise awareness of the risk of UV radiation to some extent, the UVI does not appear to change attitudes to sun protection or behavior in the way it is presently used. Changes in the UVI itself were not warranted based on these findings, but rather research testing health behavior models, including the roles of self-efficacy and self-affirmation in relation to intention to use sun protection among different susceptible groups, should be carried out to develop more successful strategies toward improving sun protection behavior.

Brix G

Risk assessment, justification, and optimization of PET/CT and PET/MRI procedures.

Der Nuklearmediziner (2012) 35: 227-237

Clinical studies demonstrate a gain in diagnostic accuracy by employing combined PET/CT instead of separate CT and PET imaging. However, whole-body PET/CT examinations result in a comparatively high radiation exposure to patients as compared to other imaging techniques and thus require a proper justification and optimization to avoid repeated examinations or unnecessary high radiation exposures. *The advent* of the hybrid *PET/*MRI technology in clinical practice may not only lead to a further progress in diagnostic imaging but can also substantially reduce exposure of patients to ionizing radiation. But there are also health risks associated with the use of MRI that have to be considered carefully. This review provides for radiologists and nuclear physicians the essential biophysical and biological basics for the assessment of risks associated with PET/CT and PET/MRI procedures. Moreover, considerations and strategies regarding the justification and the optimization of these imaging procedures, respectively, will be presented with the objective of balancing the diagnostic needs and potential health risks.

Brix G, Griebel J, Delorme S

Dynamic contrast-enhanced CT: Tracerkinetic and radiation hygienic basics

Radiologe (2012) 52: 277-298

Technical innovations in multislice computed tomography (CT) allow for larger volume coverage in ever shorter scan times. This progress has stimulated the clinical application of dynamic contrast-enhanced (DCE) CT techniques, which offer the possibility to noninvasively characterize tissue microcirculation in terms of well-defined physiological quantities. This educational review imparts to radiologists the essential physiological terms and definitions as well as the basic tracerkinetic concepts required for the analysis of DCE-CT data. In particular, four different approaches are presented and exemplified by the analysis of representative DCE data:

the steepest-gradient method, model-free algebraic deconvolution in combination with the indicator-dilution theory, two-compartment modelling, and the so-called adiabatic approximation to the homogeneity model. Even though DCE-CT offers substantial methodological and practical advantages as compared to DCE-MRI, there are also two serious and interconnected shortcomings: the low contrast enhancement in relation to the noise level and the high exposure of patients to ionizing radiation. These limiting aspects are considered in detail from a radiation hygienic point of view, emphasizing the basic principles of justification and optimization.

Brix G, Salehi Ravesh M, Zwick S, Griebel J, Delorme S
On impulse response functions computed from dynamic contrast-enhanced image data by algebraic deconvolution and compartmental modeling
Phys Med (2012) 28: 119-128

Concentration-time courses measured by dynamic contrast-enhanced (DCE) imaging can be described by a convolution of the arterial input with an impulse response function, $Q_T(t)$, characterizing tissue microcirculation. Data analysis is based on two different approaches: computation of $Q_T(t)$ by algebraic deconvolution (AD) and subsequent evaluation according to the indicator dilution theory (IDT) and parameterization of $Q_T(t)$ by analytical expressions derived by compartmental modeling. Pitfalls of both strategies will be addressed in this study. Tissue data acquired by DCE-CT in patients with head-and-neck cancer and simulated by a reference model (MMID4) were analyzed by a two-compartment model (TCM), a permeability-limited two-compartment model (PL-TCM) and AD. Additionally, MMID4 was used to compute the 'true' response function that corresponds to the simulated tumor data. TCM and AD yielded accurate fits, whereas PL-TCM performed worse. Nevertheless, the corresponding response functions diverge markedly. The response curves obtained by TCM decrease exponentially in the early perfusion phase and overestimate the tissue perfusion, $Q_T(0)$. AD also resulted in response curves starting with a negative slope and not – as the 'true' response function in accordance with the IDT – with a horizontal plateau. They are thus not valid responses in the sense of the IDT that can be used unconditionally for parameter estimation. Response functions differing considerably in shape can result in virtually identical tissue curves. This *non-uniqueness* makes a strong argument not to use algebraic but rather analytical deconvolution to reduce the class of solutions to representatives that are in accordance with a-priori knowledge. To avoid misinterpretations and systematic errors, users must be aware of the pitfalls inherent to the different concepts.

Giussani A, Janzen T, Uusijärvi-Lizana H, Tavola F, Zankl M, Sydoff M, Bjartell A, Leide-Svegborn S, Söderberg M, Mattsson S, Hoeschen C, Cantone MC
A compartmental model for biokinetics and dosimetry of 18F-choline in prostate cancer patients
J Nucl Med (2012) 53: 985-993

PET with ^{18}F-choline (^{18}F-FCH) is used in the diagnosis of prostate cancer and its recurrences. In this work, biodistribution data from a recent study conducted at Skåne University Hospital Malmö were used for the development of a biokinetic and dosimetric model. The biodistribution of ^{18}F-FCH was followed for 10 patients using PET up to 4 h after administration. Activity concentrations in blood and urine samples were also determined. A compartmental model structure was developed, and values

of the model parameters were obtained for each single patient and for a reference patient using a population kinetic approach. The model structure consists of a central exchange compartment (blood), 2 compartments each for the liver and kidneys, 1 for spleen, 1 for urinary bladder, and 1 generic compartment accounting for the remaining material. The model can successfully describe the individual patients' data. The parameters showing the greatest inter-individual variations are the blood volume (the clearance process is rapid, and early blood data are not available for several patients) and the transfer out from liver (the physical half-life of ^{18}F is too short to follow this long-term process with the necessary accuracy). Radiation doses to the organs were determined using computational (voxel) phantoms for the determination of the S factors. The organs receiving the highest doses are the kidneys (reference patient, 0.079 mGy/MBq; individual values, 0.033–0.105 mGy/MBq) and the liver (reference patient, 0.062 mGy/MBq; individual values, 0.036–0.082 mGy/MBq). The dose to the urinary bladder wall of the reference patient varies between 0.017 and 0.030 mGy/MBq, depending on the assumptions on bladder voiding.

Giussani A, Risica S

Validation of the ICRP model for caesium intake by lactating mothers with Italian data after the Chernobyl fallout.

J Environ Radioact (2012) 39: 122-127

In the aftermath of the Chernobyl nuclear power plant accident, a research group of the Italian National Institute of Health (Istituto Superiore di Sanità) carried out two research programmes on maternal milk. One concerned the transfer of caesium radionuclides from the diet to breast milk. In the other, the activity concentrations of ^{137}Cs were also determined in urine and placenta. The first study estimated the mothers' average ^{137}Cs dietary intake, in the second study the intake was evaluated individually for each subject. In 2004, the International Commission on Radiological Protection published modified systemic biokinetic models which also account for transfer to breast milk. The model for caesium radionuclides was implemented and tested by the authors with the experimental data described above. A good agreement was obtained between measured data and model simulations of ^{137}Cs activity concentration in human milk. The model, however, tends to systematically overestimate ^{137}Cs activity concentration in urine, in which case the agreement is to be considered satisfactory in terms of order of magnitude.

Greve B, Bölling T, Amler S, Rössler U, Gomolka M, Mayer C, Popanda O, Dreffke K, Rickinger A, Fritz E, Eckardt-Schupp F, Sauerland C, Braselmann H, Sauter W, Illig T, Riesenbeck D, Könemann S, Willich N, Mörtl S, Eich HT, Schmezer P

Evaluation of different biomarkers to predict individual radiosensitivity in an inter-laboratory comparison-lessons for future studies

PLoS One. 2012;7(10):e47185. Epub 2012 Oct 23

Radiotherapy is a powerful cure for several types of solid tumours, but its application is often limited because of severe side effects in individual patients. With the aim to find biomarkers capable of predicting normal tissue side reactions we analysed the radiation responses of cells from individual head and neck tumour and breast cancer patients of different clinical radiosensitivity in a multicentric study. Multiple parameters of cellular radiosensitivity were analysed in coded samples of peripheral blood lymphocytes (PBLs) and derived lymphoblastoid cell lines (LCLs) from 15 clinical

radio-hypersensitive tumour patients and compared to age- and sex-matched non-radiosensitive patient controls and 15 lymphoblastoid cell lines from age- and sex-matched healthy controls of the KORA study. Experimental parameters included ionizing radiation (IR)-induced cell death (AnnexinV), induction and repair of DNA strand breaks (Comet assay), induction of yH2AX foci (as a result of DNA double strand breaks), and whole genome expression analyses. Considerable inter-individual differences in IR-induced DNA strand breaks and their repair and/or cell death could be detected in primary and immortalised cells with the applied assays. The group of clinically radiosensitive patients was not unequivocally distinguishable from normal responding patients nor were individual overreacting patients in the test system unambiguously identified by two different laboratories. Thus, the in vitro test systems investigated here seem not to be appropriate for a general prediction of clinical reactions during or after radiotherapy due to the experimental variability compared to the small effect of radiation sensitivity. Genome-wide expression analysis however revealed a set of 67 marker genes which were differentially induced 6 h after in vitro-irradiation in lymphocytes from radio-hypersensitive and non-radiosensitive patients. These results warrant future validation in larger cohorts in order to determine parameters potentially predictive for clinical radiosensitivity.

Habeck M, Epsch R, Minkov V, Langer M, Griebel J, Brix G

Neuerungen im Genehmigungsverfahren "Medizinische Forschung" gemäß Röntgen- und Strahlenschutzverordnung

RöFo: Fortschritte auf dem Gebiet der Röntgenstrahlen und der bildgebenden Verfahren 184 (2012), Nr. 6, 513-519

This publication outlines the “medical research” licensing procedure as specified in the amendment of the German Radiation Protection Ordinance of November 1, 2011. The general licensing requirements for the use of radiation have not been changed by the amendment. Three so-called use restrictions (i. e., dose limits of 10 mSv and 20 mSv, age limit of 50 years) have been modified. They will only apply to healthy volunteers in the future. In addition, there are considerable simplifications with respect to applications and licensing procedures of the Federal Office for Radiation Protection (Bundesamt für Strahlenschutz, BfS) regarding the use of radiation in the newly introduced “accompanying diagnostics” (“Begleitdiagnostik”) case group. The newly established, independent panel of experts at the German Radiological Society (Deutsche Röntgengesellschaft, DRG) may provide essential support to principal investigators, qualified physicians and sponsors for differentiating between “medical research” and “health care”, the latter not being subject to licensing. An expert statement will be issued by the DRG within four weeks of an inquiry. This consulting service is subject to confidentiality, and is free of charge for inquirers and without any commitment.

Heidenreich W F; Tomasek L, Grosche, B, Leuraud K, Laurier D

Lung cancer mortality in the European uranium miners cohorts analyzed with a biologically based model taking into account radon measurement error

Radiation and environmental biophysics 51 (2012), 263-275

The biologically based two-stage clonal expansion (TSCE) model is used to analyze lung cancer mortality of European miners from the Czech Republic, France, and Germany. All three cohorts indicate a highly significant action of exposure to radon

and its progeny on promotion. The action on initiation is not significant in the French cohort. An action on transformation was tested but not found significant. In a pooled analysis, the results based on the French and German datasets do not differ significantly in any of the used parameters. For the Czech dataset, only lag time and two parameters that determine the clonal expansion without exposure and with low exposure rates (promotion) are consistent with the other studies. For low exposure rates, the resulting relative risks are quite similar. Exposure estimates for each calendar year are used. A model for random errors in each of these yearly exposures is presented. Depending on the used technique of exposure estimate, Berkson and classical errors are used. The consequences for the model parameters are calculated and found to be mostly of minor importance, except that the large difference in the exposure-induced initiation between the studies is decreased substantially.

Kulka U, Ainsbury L, Atkinson M, Barquinero JF, Barrios L, Beinke C, Bognar G, Cucu A, Darroudi F, Fattibene P, Gil O, Gregoire E, Hadjidekova V, Haghdoost S, Herranz R, Jaworska A, Lindholm C, Mkacher R, Mörtl S, Montoro A, Moquet J, Moreno M, Obazghi A, Oestreicher U, Palitti F, Pantelias G, Popescu I, Prieto JM, Romm H, Rothkamm K, Sabatier L, Sommer S, Terzoudi G, Testa A, Thierens H, Trompier F, Turai I, Vandersickel V, Vaz P, Voisin P, Vral A, Ugletveit F, Woda C, Wojcik A

RENEB - Realizing the European network of BioDosimetry

Radiation protection dosimetry (2012) 151 (4): 621-625

In Europe, a network for biological dosimetry has been created to strengthen the emergency preparedness and response capabilities in case of a large-scale nuclear accident or radiological emergency. Through the RENEB (Realizing the European NEtwork of Biodosimetry) project, 23 experienced laboratories from 16 European countries will establish a sustainable network for rapid, comprehensive and standardized biodosimetry provision that would be urgently required in an emergency situation on European ground. The foundation of the network is formed by five main pillars, 1) the ad-hoc operational basis, 2) a basis of future developments, 3) an effective quality management system, 4) arrangements to guarantee the long-term sustainability and 5) awareness of the existence of RENEB. RENEB will thus provide a mechanism for quick, efficient and reliable support within the European radiation emergency management. The scientific basis of RENEB will concurrently result in contributions to increased safety in the field of radiation protection.

Laurier D, Guseva Canu I, Baatout S, Bertho JM, Blanchardon E, Bouffler S, Cardis E, Gomolka M, Hall J, Kesminiene A, Kreuzer M, Rage E

DoReMi workshop on multidisciplinary approaches to evaluating cancer risks associated with low-dose internal contamination

Radioprotection 2012; 47:119-148

A workshop dedicated to cancer risks associated with low-dose internal contamination was organized in March 2011, in Paris, in the framework of the DoReMi (Low Dose Research towards Multidisciplinary Integration) European Network of Excellence. The aim was to identify the best epidemiological studies that provide an opportunity to develop a multidisciplinary approach to improve the evaluation of the cancer risk associated with internal contamination. This workshop provided an opportunity for in-depth discussions between researchers working in different fields including (but

not limited) epidemiology, dosimetry, biology and toxicology. Discussions confirmed the importance of research on the health effects of internal contamination. Several existing epidemiological studies provide a real possibility to improve the quantification of cancer risk associated with internal emitters. Areas for future multidisciplinary collaboration were identified, that should allow feasibility studies to be carried out in the near future. The goal of this paper is to present an overview of the presentations and discussions that took place during this workshop.

Little MP, Azizova TV, Bazyka D, Bouffler SD, Cardis E, Chekin S, Chumak VV, Cucinotta FA, de Vathaire F, Hall P, Harrison JD, Hildebrandt G, Ivanov V, Kashcheev VV, Klymenko SV, Kreuzer M, Laurent O, Ozasa K, Schneider T, Tapio S, Taylor AM, Tzoulaki I, Vandoolaeghe WL, Wakeford R, Zablotska LB, Zhang W, Lipshultz S

Systematic review and meta-analysis of circulatory disease from exposure to low-level ionizing radiation and estimates of potential population mortality risks

Environmental health perspectives 2012 Nov;120(11):1503-11.

Although high doses of ionizing radiation have long been linked to circulatory disease, evidence for an association at lower exposures remains controversial. However, recent analyses suggest excess relative risks at occupational exposure levels. We performed a systematic review and meta-analysis to summarize information on circulatory disease risks associated with moderate- and low-level whole-body ionizing radiation exposures. We conducted PubMed/ISI Thomson searches of peer-reviewed papers published since 1990 using the terms "radiation" AND "heart" AND "disease," OR "radiation" AND "stroke," OR "radiation" AND "circulatory" AND "disease." Radiation exposures had to be whole-body, with a cumulative mean dose of < 0.5 Sv, or at a low dose rate (< 10 mSv/day). We estimated population risks of circulatory disease from low-level radiation exposure using excess relative risk estimates from this meta-analysis and current mortality rates for nine major developed countries. Estimated excess population risks for all circulatory diseases combined ranged from 2.5%/Sv [95 % confidence interval (CI): 0.8, 4.2] for France to 8.5 %/Sv (95% CI: 4.0, 13.0) for Russia. Our review supports an association between circulatory disease mortality and low and moderate doses of ionizing radiation. Our analysis was limited by heterogeneity among studies (particularly for noncardiac end points), the possibility of uncontrolled confounding in some occupational groups by lifestyle factors, and higher dose groups (> 0.5 Sv) generally driving the observed trends. If confirmed, our findings suggest that overall radiation-related mortality is about twice that currently estimated based on estimates for cancer end points alone (which range from 4.2 % to 5.6 %/Sv for these populations).

Marsh JW, Blanchardon E, Gregoratto D, Hofmann W, Karcher K, Noßke D, Tomasek L

Dosimetric calculations for uranium miners for epidemiological studies

Radiation protection dosimetry 2012; 149(4):371-383

Epidemiological studies on uranium miners are being carried out to quantify the risk of cancer based on organ dose calculations. Mathematical models have been applied to calculate the annual absorbed doses to regions of the lung, red bone marrow, liver, kidney and stomach for each individual miner arising from exposure to radon

gas, radon progeny and long-lived radionuclides (LLR) present in the uranium ore dust and to external gamma radiation. The methodology and dosimetric models used to calculate these organ doses are described and the resulting doses for unit exposure to each source (radon gas, radon progeny and LLR) are presented. The results of dosimetric calculations for a typical German miner are also given. For this miner, the absorbed dose to the central regions of the lung is dominated by the dose arising from exposure to radon progeny, whereas the absorbed dose to the red bone marrow is dominated by the external gamma dose. The uncertainties in the absorbed dose to regions of the lung arising from unit exposure to radon progeny are also discussed. These dose estimates are being used in epidemiological studies of cancer in uranium miners.

Merk R

Numerical modeling of the radionuclide water pathway with HYDRUS and comparison with the IAEA model of SR 44

Journal of environmental radioactivity (2012) 105: 60-69

This study depicts a theoretical experiment in which the radionuclide transport through the porous material of a landfill consisting of concrete rubble (e.g., from the decommissioning of nuclear power plants) and the subsequent migration through the vadose zone and aquifer to a model well is calculated by means of the software HYDRUS-1D (Simunek et al., 2008). The radionuclides originally contained within the rubble become dissolved due to leaching caused by infiltrated rainwater. The resulting wellwater contamination (in Bq/L) is calculated numerically as a function of time and location and compared with the outcome of a simplified analytic model for the groundwater pathway published by the IAEA (2005). Identical model parameters are considered. The main objective of the present work is to evaluate the predictive capacity of the more simple IAEA model using HYDRUS-1D as a reference. For most of the radionuclides considered (e.g., ^{129}I, and ^{239}Pu), results from applying the IAEA model were found to be comparable to results from the more elaborate HYDRUS modeling, provided the underlying parameter values are comparable. However, the IAEA model appears to underestimate the effects resulting from, for example, high nuclide mobility, short half-life, or short-term variations in the water infiltration. The present results indicate that the IAEA model is suited for screening calculations and general recommendation purposes. However, the analysis of a specific site should be accompanied by detailed HYDRUS computer simulations. In all models considered, the calculation outcome largely depends on the choice of the sorption parameter Kd.

Pernot E, Hall J, Baatout S, Benotmane MA, Blanchardon E, Bouffler S, El Saghire H, Gomolka M, Guertler A, Harms-Ringdahl M, Jeggo P, Kreuzer M, Laurier D, Lindholm C, Mkacher R, Quintes R, Rothkamm K, Sabatier L, Tapio S, De Vathaire F, Cardis E

Ionizing radiation biomarkers for potential use in epidemiological studies

Mutation research 2012; 751(2):258-86

Ionizing radiation is a known human carcinogen that can induce a variety of biological effects depending on the physical nature, duration, doses and dose-rates of exposure. However, the magnitude of health risks at low doses and dose-rates (below 100 mSv and/or 0.1 mSv min^{-1}) remains controversial due to a lack of direct human

evidence. It is anticipated that significant insights will emerge from the integration of epidemiological and biological research, made possible by molecular epidemiology studies incorporating biomarkers and bioassays. A number of these have been used to investigate exposure, effects and susceptibility to ionizing radiation, albeit often at higher doses and dose rates, with each reflecting time-limited cellular or physiological alterations. This review summarises the multidisciplinary work undertaken in the framework of the European project DoReMi (Low Dose Research towards Multidisciplinary Integration) to identify the most suitable biomarkers for use in population studies. In addition to logistical and ethical considerations for conducting large-scale epidemiological studies, we discuss the relevance of their use for assessing the effects of low dose ionizing radiation exposure at the cellular and physiological level. We also propose a temporal classification of biomarkers that may be relevant for molecular epidemiology studies which need to take into account the time elapsed since exposure. Finally, the integration of biology with epidemiology requires careful planning and enhanced discussions between the epidemiology, biology and dosimetry communities in order to determine the most important questions to be addressed in light of pragmatic considerations including the appropriate population to be investigated (occupationally, environmentally or medically exposed), and study design. The consideration of the logistics of biological sample collection, processing and storing and the choice of biomarker or bioassay, as well as awareness of potential confounding factors, are also essential.

Paunesku T, Wanzer M, Kirilova E, Muksinova K, Revina V, Lyubchansky E, Grosche B, Birschwilks M, Vogt S, Finney L, Woloschak G

X-ray fluorescence microscopy for investigation of archival tissue

Health physics 103 (2012), Nr. 2, 181-186

Several recent efforts in the radiation biology community worldwide have amassed records and archival tissues from animals exposed to different radionuclides and external beam irradiation. In most cases, these samples come from lifelong studies on large animal populations conducted in national laboratories and equivalent institutions throughout Europe, North America, and Japan. While many of these tissues were used for histopathological analyses, much more information may still be obtained from these samples. A new technique suitable for imaging of these tissues is x-ray fluorescence microscopy (XFM). Following development of third generation synchrotrons, XFM has emerged as an ideal technique for the study of metal content, speciation, and localization in cells, tissues, and organs. Here the authors review some of the recent XFM literature pertinent to tissue sample studies and present examples of XFM data obtained from tissue sections of beagle dog samples, which show that the quality of archival tissues allows XFM investigation.

Rosenberger A, Rössler U, Hornhardt S, Sauter W, Bickeböller H, Wichmann HE, Gomolka M

Heritability of radiation response in lung cancer families

Genes 2012, 3 (248-269)

Radiation sensitivity is assumed to be a cancer susceptibility factor due to impaired DNA damage signalling and repair. Relevant genetic factors may also determine the observed familial aggregation of early onset lung cancer. We investigated the heritability of radiation sensitivity in families of 177 Caucasian cases of early onset lung

cancer. In total 798 individuals were characterized for their radiation-induced DNA damage response. DNA damage analysis was performed by alkaline comet assay before and after in vitro irradiation of isolated lymphocytes. The cells were exposed to a dose of 4 Gy and allowed to repair induced DNA-damage up to 60 minutes. The primary outcome parameter Olive Tail Moment was the basis for heritability estimates. Heritability was highest for basal damage (without irradiation) 70% (95%-CI: 51%–88%) and initial damage (directly after irradiation) 65% (95%-CI: 47%–83%) and decreased to 20%–48% for the residual damage after different repair times. Hence our study supports the hypothesis that genomic instability represented by the basal DNA damage as well as radiation induced and repaired damage is highly heritable. Genes influencing genome instability and DNA repair are therefore of major interest for the etiology of lung cancer in the young. The comet assay represents a proper tool to investigate heritability of the radiation sensitive phenotype. Our results are in good agreement with other mutagen sensitivity assays.

Saey PRJ, Ringbom A, Bowyer TW, Zähringer M, Auer M, Faanhof A, Labuschagne C, Al-Rashidi MS, Tippawan U, Verboomen B

Worldwide measurements of radioxenon background near isotope production facilities, a nuclear power plant and at remote sites: the ‘‘EU/JA-II’’ Project.

Journal of radioanalytical nuclear chemistry (2012),
DOI 10.1007/s10967-012-2025-2

The Comprehensive Nuclear-Test-Ban Treaty (CTBT) specifies that radioxenon measurements should be performed at 40 or more stations worldwide within the International Monitoring System (IMS). Measuring radioxenon is one of the principle techniques to detect underground nuclear explosions. Specifically, presence and ratios of different radioxenon isotopes allows determining whether a detection event under consideration originated from a nuclear explosion or a civilian source. However, radioxenon monitoring on a global scale is a novel technology and the global civil background must be characterized sufficiently. This paper lays out a study, based on several unique measurement campaigns, of the worldwide concentrations and sources of verification relevant xenon isotopes. It complements the experience already gathered with radioxenon measurements within the CTBT IMS programme and focuses on locations in Belgium, Germany, Kuwait, Thailand and South Africa where very little information was available on ambient xenon levels or interesting sites offered opportunities to learn more about emissions from known sources. The findings corroborate the hypothesis that a few major radioxenon sources contribute in great part to the global radioxenon background. Additionally, the existence of independent sources of ^{131m}Xe (the daughter of ^{131}I) has been demonstrated, which has some potential to bias the isotopic signature of signals from nuclear explosions.

Schmid E, Wagner F, Canella H, Romm H, Schmid T

RBE of thermal neutrons for induction of chromosome aberrations in human lymphocytes

Radiation and environmental biophysics 52 (2012), Nr. 1, 113-121

The induction of chromosome aberrations in human lymphocytes irradiated in vitro with slow neutrons was examined to assess the maximum low-dose RBE (RBEM) relative to ^{60}Co γ-rays. For the blood irradiations, cold neutron beam available at the prompt gamma activation analysis facility at the Munich research reactor FRM II was

used. The given flux of cold neutrons can be converted into a thermally equivalent one. Since blood was taken from the same donor whose blood had been used for previous irradiation experiments using widely varying neutron energies, the greatest possible accuracy was available for such an estimation of the RBEM avoiding the inter-individual variations or differences in methodology usually associated with inter-laboratory comparisons. The magnitude of the coefficient a of the linear dose–response relationship (a = 0.400 ± 0.018 Gy-1) and the derived RBEM of 36.4 ± 13.3 obtained for the production of dicentrics by thermal neutrons confirm our earlier observations of a strong decrease in a and RBEM with decreasing neutron energy lower than 0.385 MeV (RBEM = 94.4 ± 38.9). The magnitude of the presently estimated RBEM of thermal neutrons is—with some restrictions—not significantly different to previously reported RBEM values of two laboratories.

Schöllnberger H, Kaiser JC, Jacob P, Walsh L

Dose-response from multi-model inference for the non-cancer disease mortality of atomic bomb survivors

Radiat environ biophys 2012; 51:165-78

The non-cancer mortality data for cerebrovascular disease (CVD) and cardiovascular diseases from Report 13 on the atomic bomb survivors published by the Radiation Effects Research Foundation were analysed to investigate the dose-response for the influence of radiation on these detrimental health effects. Various parametric and categorical models (such as linear-no-threshold (LNT) and a number of threshold and step models) were analysed with a statistical selection protocol that rated the model description of the data. Instead of applying the usual approach of identifying one preferred model for each data set, a set of plausible models was applied, and a sub-set of non-nested models was identified that all fitted the data about equally well. Subsequently, this sub-set of non-nested models was used to perform multi-model inference (MMI), an innovative method of mathematically combining different models to allow risk estimates to be based on several plausible dose-response models rather than just relying on a single model of choice. This procedure thereby produces more reliable risk estimates based on a more comprehensive appraisal of model uncertainties. For CVD, MMI yielded a weak dose-response (with a risk estimate of about one-third of the LNT model) below a step at 0.6 Gy and a stronger dose-response at higher doses. The calculated risk estimates are consistent with zero risk below this threshold-dose. For mortalities related to cardiovascular diseases, an LNT-type dose-response was found with risk estimates consistent with zero risk below 2.2 Gy based on 90% confidence intervals. The MMI approach described here resolves a dilemma in practical radiation protection when one is forced to select between models with profoundly different dose-responses for risk estimates.

Schöppner M, Kalinowski M, Plastino W, Budano A, De Vincenzi M, Ringbom A, Ruggieri F, Schlosser C

Impact of monthly radioxenon source time-resolution on atmospheric concentration predictions.

Pure and applied geophysics (2012), DOI 10.1007/s00024-012-0499-z.

The general characterisation of the global radioxenon background is of interest for the verification of the Comprehensive Nuclear-Test-Ban Treaty. Since the major background sources are only a few isotope production facilities, their source term has

an emphasized influence on the worldwide monitoring process of radioxenon. In this work, two different datasets of source terms are applied through atmospheric transport modelling, to estimate the concentration at two radioxenon detection stations in Germany and Sweden. One dataset relies on estimated average annual emissions; the other includes monthly resolved measurements from an isotope production facility in Fleurus, Belgium. The quality of the estimations is then validated by comparing them to the radioxenon concentrations that have been sampled at two monitoring stations over the course of 1 year.

Sogl M, Taeger D, Pallapies D, Brüning T, Dufey F, Schnelzer M, Straif K, Walsh L, Kreuzer M

Quantitative relationship between silica exposure and lung cancer mortality in German uranium miners, 1946-2003

Br J Cancer 2012; 107(7):1188-94

Background: In 1996 and 2009, the International Agency for Research on Cancer classified silica as carcinogenic to humans. The exposure–response relationship between silica and lung cancer risk, however, is still debated. Data from the German uranium miner cohort study were used to further investigate this relationship.

Methods: The cohort includes 58 677 workers with individual information on occupational exposure to crystalline silica in mgm^{-3}-years and the potential confounders radon and arsenic based on a detailed job-exposure matrix. In the follow-up period 1946–2003, 2995 miners died from lung cancer. Internal Poisson regression with stratification by age and calendar year was used to estimate the excess relative risk (ERR) per dust-year. Several models including linear, linear quadratic and spline functions were applied. Detailed adjustment for cumulative radon and arsenic exposure was performed.

Results: A piecewise linear spline function with a knot at 10 mgm^{-3}-years provided the best model fit. After full adjustment for radon and arsenic no increase in risk <10 mgm^{-3}-years was observed. Fixing the parameter estimate of the ERR in this range at 0 provided the best model fit with an ERR of 0.061 (95% confidence interval: 0.039, 0.083) >10 mgm^{-3}-years.

Conclusion: The study confirms a positive exposure–response relationship between silica and lung cancer, particularly for high exposures.

Steinhauser G, Lechermann M, Axelsson A, Böck H, Ringbom A, Saey P R J, Schlosser C, Villa M

Research reactors as sources of atmospheric radioxenon

Journal of radioanalytical and nuclear chemistry (2012),
DOI 10.1007/s10967-012-1949-x

Radioxenon emissions of the TRIGA Mark II research reactor in Vienna were investigated with respect to a possible impact on the verification of the Comprehensive Nuclear Test-Ban-Treaty. Using the Swedish Automatic Unit for Noble Gas Acquisition (SAUNA II), five radioxenon isotopes ^{125}Xe, ^{131m}Xe, ^{133m}Xe, ^{133}Xe and ^{135}Xe were detected, of which ^{125}Xe is solely produced by neutron capture in stable atmospheric ^{124}Xe and hence acts as an indicator for neutron activation processes. The other nuclides are produced in both fission and neutron capture reactions. The detected activity concentrations ranged from 0.0010 to 190 Bq/m^3. The source of the radioxe-

non is not yet fully clarified, but it could be micro-cracks in the fuel cladding, fission of ^{235}U contaminations on the outside of the fuel elements or neutron activation of atmospheric Xe. Neutron deficient ^{125}Xe with its highly complex decay scheme was seen for the first time in a SAUNA system. In many experiments the activity ratios of the radioxenon nuclides carry the signature of nuclear explosions, if ^{131m}Xe is omitted. Only if ^{131m}Xe is included into the calculations of the isotopic activity ratios, the majority of the measurements revealed a ''civil'' signature (typical for a NPP). A significant contribution of the TRIGA Vienna to the global or European radioxenon inventory can be excluded. Due to the very low activities, the emissions are far below any concern for human health.

Walsh L, Dufey F, Tschense A, Schnelzer M, Sogl M, Kreuzer M

Prostate cancer mortality risk in relation to working underground in the Wismut cohort study of German uranium miners, 1970-2003.

BMJ OPEN 2012; 2(3), pii: e001002.
doi: 10.1136/bmjopen-2012-001002

Objective: A recent study and comprehensive literature review has indicated that mining could be protective against prostate cancer. This indication has been explored further here by analysing prostate cancer mortality in the German 'Wismut' uranium miner cohort, which has detailed information on the number of days worked underground.

Design: An historical cohort study of 58 987 male mine workers with retrospective follow-up before 1999 and prospective follow-up since 1999.

Setting and participants: Uranium mine workers employed during the period 1970 - 1990 in the regions of Saxony and Thuringia, Germany, contributing 1.42 million person-years of follow-up ending in 2003.

Outcome measure: Simple standardised mortality ratio (SMR) analyses were applied to assess differences between the national and cohort prostate cancer mortality rates and complemented by refined analyses done entirely within the cohort. The internal comparisons applied Poisson regression excess relative prostate cancer mortality risk model with background stratification by age and calendar year and a whole range of possible explanatory covariables that included days worked underground and years worked at high physical activity with γ-radiation treated as a confounder.

Results: The analysis is based on miner data for 263 prostate cancer deaths. The overall SMR was 0.85 (95% CI 0.75 to 0.95). A linear excess relative risk model with the number of years worked at high physical activity and the number of days worked underground as explanatory covariables provided a statistically significant fit when compared with the background model (p=0.039). Results (with 95% CIs) for the excess relative risk per day worked underground indicated a statistically significant (p=0.0096) small protective effect of -5.59 (-9.81 to-1.36) $\times 10^{-5.}$

Conclusion: Evidence is provided from the German Wismut cohort in support of a protective effect from working underground on prostate cancer mortality risk.