

Department of Radiation Oncology

Chair of Radiotherapy

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Research focus

- Clinical trials
- Clinical trials office
- Radiation biology
- Physical aspects of radiation oncology
- Radiation immunobiology

Structure of the Department

Professorships: 2

Personnel: 151

- Doctors (of Medicine): 21
- Scientists: 31 (thereof funded externally: 6)
- Graduate students: 65

Clinical focus areas

- Percutaneous radiotherapy
- Treatment planning
- Image guided radiotherapy (IGRT)
- 3D conformal radiotherapy
- Intensity modulated radiotherapy (IMRT)
- Intensity modulated arc therapy (VMAT)
- Stereotactic body radiation therapy (SBRT)
- Whole-skin- and whole-body-irradiation
- Brachytherapy
- Intensity modulated brachytherapy (IMBT)
- Image guided brachytherapy (IGBT)
- Deep regional hyperthermia with MR-Thermometry
- Local hyperthermia for the treatment of superficial tumors
- Radio-chemo-therapy
- Radio-immuno-therapy
- Low dose radiation therapy (LDRT)

Research

Clinical, biological, immunological as well as physical aspects of radiation oncology are scientifically analyzed. Clinical aspects of radiation oncology are predominantly examined within phase I, II, and III trials. This takes place on the ward, in the outpatient department, the therapeutics department (including brachytherapy)

as well as the treatment planning department and hyperthermia unit. Coordination of the clinical trials is carried out by the in-house clinical trials office. Translational and basic radio(immune)-biological research is carried out by two groups, the classical radiation biology group and the radiation immune biology group. The "Medical Radiation Physics" group has the main scientific focus in respiratory and general organ motion during radiation therapy. In addition, the group is responsible for all medical physics duties of clinical radiation therapy (including control of brachytherapy implants).

Clinical trials

PI: Prof. Dr. R. Fietkau, Prof. Dr. V. Strnad, Prof. Dr. O. Ott, PD Dr. S. Semrau, Prof. Dr. U. Gaipl, Dr. M. Haderlein, Dr. G. Lahmer, Dr. M. Hecht, Dr. N. Goerig

Phase-III multicenter trials:

1. First-line treatment of locally advanced HNSCC with double checkpoint blockade and radiotherapy dependent on intratumoral CD8+ T cell infiltration (CheckRad-CD8) - IIT
Funding: AstraZeneca GmbH

2. Preoperative radiochemotherapy and adjuvant chemotherapy with 5-fluorouracil versus preoperative radio-chemotherapy and adjuvant chemotherapy with 5-fluorouracil combined with oxaliplatin in patients with locally advanced UICC stage II and III rectal cancer (CAO/ ARO/AIO-04)
Funding: German Cancer Aid

3. Comparison of partial breast interstitial brachytherapy with external whole breast beam radiotherapy in patients with low risk invasive and in situ breast carcinomas (APBI-III)
Funding: German Cancer Aid

4. Salvage Brachytherapy and Hyperthermia for Recurrent H&N-tumors (HyBT-H&N)

5. Pancreatic carcinoma: chemoradiation compared with chemotherapy alone after induction chemotherapy (CONKO-007)
Funding: German Cancer Aid

6. Effects of deep regional hyperthermia in patients with anal carcinoma treated by standard radiochemotherapy (HYCAN)

7. Cetuximab in combination with platinum-based chemotherapy or radiotherapy in patients with recurrent and/or metastatic SSCHN in clinical routine (SOCCER)
Funding: Merck Serono GmbH

Phase-II trials:

1. Randomized phase II study of immune stimulation with Pembrolizumab and radiotherapy in second line therapy of metastatic head and neck squamous cell carcinoma (IMPORTANCE), IIT
Funding: MSD

2. PDR/HDR interstitial brachytherapy alone in patients with pT1/pT2 pN0 breast carcinomas after breast conserving surgery (APBI-IV)

3. 3D conformal, external partial breast irradiation in patients with pT1/2 pN0 breast carcinomas after breast conserving surgery (APBI-V)

4. Neoadjuvant chemoradiation with 5-FU (or capecitabine) and oxaliplatin combined with deep regional hyperthermia in locally advanced or recurrent rectal cancer (HyRec)

5. Enhancement of neurocognitive functions by hippocampal sparing radiotherapy (HIPPOSPARE 01)

6. Efficacy of dose intensified radiotherapy of spinal metastases by hypofractionated radiation and IGRT hfsRT mediated boost (SPIN-MET)

7. Salvage brachytherapy and interstitial hyperthermia for locally recurrent prostate carcinoma following radiation therapy (Prostata-BT-HT)

8. De-intensification of postoperative radiotherapy in selected patients with head and neck cancer (DIREKHT)

9. Investigation of the timely-coordinated therapy of patients with metastatic cancer by radiotherapy together with immune checkpoint inhibition (ST-ICI)

10. Analysis of CMV infections in patients with brain tumors or brain metastases during and after radio(Chemo)therapy (GLIO-CMV-01)

11. Immunophenotyping from blood of patients with malignant gliomas (IMMO-GLIO-01)

12. Immunophenotyping from blood of patients suffering from chronic degenerating joint diseases and receiving LDRT (IMMOLDRT-01)

The Department of Radiation Oncology is participating in numerous externally led phase-III trials. In addition the Department is conducting many phase-I and phase-II trials.

Clinical trials office

PI: Dr. D. Lubgan, M. Lang-Welzenbach, S. Rutzner

Coordination of the clinical trials is carried out in our in-house clinical-trials office. Our tasks cover all activities that are directly related to:

1. Planning, organizing, leading, and controlling of clinical trials (IIT and as participating center)
2. Organization of meetings and international training courses
3. Scientific research

Radiation biology

PI: Prof. Dr. L. Distel

Individual differences in the sensitivity of normal tissues to radiation are the most important determinant for the occurrence of dose limiting side effects of radiotherapy. In a project run jointly with the University of Würzburg (Prof. Dr. T. Djuzenova), the usefulness of a bed-side test in determining the gamma-H2AX phosphorylation status is compared to the established assay based on the analysis of chromosomal aberrations in pe-

ripheral blood lymphocytes. Patients with rectal and breast tumors serve as study population.

Funding: German Cancer Aid

The role played by tumor infiltrating lymphocytes in determining the efficacy of a course of radiotherapy is still largely unknown. In a project run jointly with the Institute of Pathology, the role of CD4, CD8, B cells, macrophages, and the influence of regulatory T cells is studied in patients with head and neck tumors, gastric cancer, and carcinoma of the rectum.

Physical aspects of radiation oncology

PI: Prof. Dr. C. Bert

1. Geometrical and dosimetric verification for interstitial brachytherapy by an electromagnetic tracking system.

Funding: Elekta

2. Automated analysis of clinical data from record and verify (R+V) and treatment planning systems.

3. Four dimensional radiation dose calculation of motion compensated radiotherapy

4. New techniques in hyperthermia quality assurance

Radiation immunobiology

PI: Prof. Dr. U. Gaipl, PD Dr.-Ing. B. Frey

Connections between local and systemic, immune-mediated effects of ionizing radiation alone and in combination with immunotherapy (vaccination, immune checkpoint blockade) and the underlying immune mechanisms are examined. A further research aim is the analysis of osteoimmunological effects of low dose radiation (X-Ray and radon radiation). Moreover, detailed immunomonitoring of radiation-exposed patients is performed in the framework of clinical trials (IMPORTANCE, CheckRadCD8, IMMO-LDRT, IMMO-GLIO, CONKO, GLIO-CMV, DIREKHT, ST-ICI, RAD-ON02) and respective biomaterial is stored in the in-house biobank.

The following third-party supported projects are currently handled:

1. Modulation of inflammation and genetic risks of dense ionizing radiation

Funding: BMBF, GREWISalpha network

2. Impact and mechanisms of PD-L1, PD-L2 and EGF-R expression on glioma cells following radiochemotherapy and its consequences for combination with vaccination and PD-1 inhibition

Funding: DFG

3. Multi-scale-analyses of deep regional hyperthermia as a novel and additive tumor treatment – Microthermia

Funding: Bavarian Research Foundation

4. RAD-ON02 trial: Determination of immunologic and pain relieving effects of radon spa therapy in patients with musculoskeletal disorders

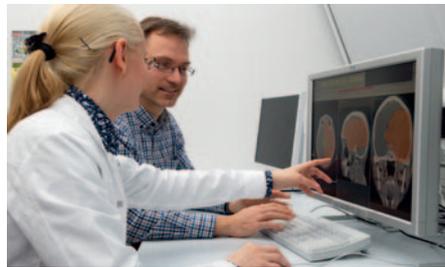
Funding: Bavarian State Ministry of Health and Care

5. Validation *in vivo* of immune biological indicators of radiation exposure to use for emergency situations, the determination of health effects and molecular epidemiology, VIBRATO

Funding: EU, Open Project for the European Radiation Research Area (OPERRA)

6. Role of dendritic cells and T cells in the local and systemic anti-tumor immune response induced by fractionated radiotherapy in combination with immunotherapy

Funding: DFG, GK 1660



Radiation therapy planning at the Department of Radiation Oncology: A medical physics expert is discussing the treatment plan together with a physician

The translational and interdisciplinary examination of the therapy plays a major role in the scientific actions of the Department. (Image: UK Erlangen/M. Kohler)

Teaching

Apart from the traditional radiotherapy teaching sessions embedded in the course covering the related fields of medical imaging, radiotherapy treatment and radiation protection, the Department organizes an interdisciplinary lecture series in collaboration with the Comprehensive Cancer Center (CCC). In the context of this course, students complete an online-module. This module was in part prepared by employees of the Department of Radiation Oncology in collaboration with the Bavarian Virtual University. Students learn by these clinical case studies the interdisciplinary approach in oncology. A course in radiation protection including practical teaching sessions for students that is recognized by the Bavarian State Chamber of Physicians is held semi-annually. For students doing practical clinical work in their pre-registration year, a complementary teaching program is offered. New teaching course "prevention, diagnostics, therapy, and after-care of cancer" was offered to the students of the degree program Medical Process Management. The practical and theoretical training of Bachelor and Master students takes place within the basic training "Infections Immunology" and the specialization module "Immunobiology". In addition the Department offers interdisciplinary courses for students of physics, medical technology, molecular medicine, medicine, and natural sciences.

Students have the opportunity to work on the Bachelor's or Master's theses and graduates are supervised during their PhD and MD projects, all embedded in the research focus of the Department. Laboratory rotations are offered for fast-track students of GK 1660 (compare own report).

Selected publications

Frey B, Rückert M, Deloch L, Rühle PF, Derer A, Fietkau R, Gaipl US. Immunomodulation by ionizing radiation-impact for design of radio-immunotherapies and for treatment of inflammatory diseases. *Immunol Rev.* 2017 Nov;280(1): 231-248

Frey B, Rückert M, Weber J, Mayr X, Derer A, Lotter M, Bert C, Rödel F, Fietkau R, Gaipl US. Hypofractionated Irradiation Has Immune Stimulatory Potential and Induces a Timely Restricted Infiltration of Immune Cells in Colon Cancer Tumors. *Front Immunol.* 2017 Mar 8;8:231

Polgár C et al. Late side-effects and cosmetic results of accelerated partial breast irradiation with interstitial brachytherapy versus whole-breast irradiation after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: 5-year results of a randomised, controlled, phase 3 trial. *Lancet Oncol.* 2017 Feb;18(2):259-268

Fietkau R. Which fractionation of radiotherapy is best for limited-stage small-cell lung cancer? *Lancet Oncol.* 2017 Aug;18(8):994-995

Deloch L, Derer A, Hueber AJ, Herrmann M, Schett GA, Wölfelschneider J, Hahn J, Rühle PF, Stillkrieg W, Fuchs J, Fietkau R, Frey B, Gaipl US. Low-Dose Radiotherapy Ameliorates Advanced Arthritis in hTNF- α tg Mice by Particularly Positively Impacting on Bone Metabolism. *Front Immunol.* 2018 Sep 18;9:1834

Kallis K, Kreppner S, Lotter M, Fietkau R, Strnad V, Bert C. Introduction of a hybrid treatment delivery system used for quality assurance in multi-catheter interstitial brachytherapy. *Phys Med Biol.* 2018 May 2;63(9):095008

International cooperations

Dr. K. Luminczyk, Prof. G. Safrany, Frédéric Joliot-Curie National Research Institute for Radiobiology and Radiohygiene (NRIRR), Budapest: Hungary

Prof. Dr. C. Polgár, Center of Radiotherapy, National Institute of Oncology, Budapest: Hungary

Dr. S. Candéias, CEA Laboratoire de Chimie et Biologie des Métaux Biosciences and Biotechnology Institute of Grenoble, Grenoble: France

Dr. C. Badie, Public Health England, Centre for Radiation, Chemical & Environmental Hazards Didcot: UK