

# Department of Radiation Oncology

## Chair of Radiotherapy

### Address

Universitätsstraße 27  
91054 Erlangen  
Phone: +49 9131 8533405  
Fax: +49 9131 8539335  
www.strahlenklinik.uk-erlangen.de

### Director

Prof. Dr. med. Rainer Fietkau

### Contact

Prof. Dr. med. Rainer Fietkau  
Phone: +49 9131 8533405  
Fax: +49 9131 8539335  
sekretariat.strahlenklinik@uk-erlangen.de

### Research focus

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

### Structure of the Department

Professorships: 2

Personnel: 140

- Doctors (of Medicine): 24
- Scientists: 29 (thereof funded externally: 11)
- Graduate students: 50

### 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. U.S. Gaipl, PD Dr. M. Haderlein, PD Dr. M. Hecht, Dr. G. Lahmer, Prof. Dr. O. Ott, PD Dr. S. Semrau, Prof. Dr. V. Strnad

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/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 SSSN 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 (IMMO-LDRT-01)

Observational trials:

1. Efficacy and Safety of Fractionated Stereotactic Radiation Therapy versus Single Fraction Stereotactic Radiosurgery for Large Brain Metastases (FSRT-Trial)

The Department of Radiation Oncology is participating in numerous externally led phase-I-III trials around the globe.

### Clinical trials office

PI: Dr. S. Rutzner, Dr. A. Kallies, PD Dr. M. Hecht

The clinical-trial office is responsible for centrally coordinating all clinical trials, including:

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

We analyse the individually different radiation sensitivity of normal tissue is the most important factor for the dose-limiting occurrence of therapy-related side effects. With different institutions the radiosensitivity in rare diseases is studied. Today the importance of tumor infiltrating lymphocytes for the efficacy of radiotherapy is still largely unknown. In a joint project with the Institute of Pathology, the importance of CD4, CD8, B cells, macrophages and the influence of regulatory T cells is studied in patients with head and neck tumors, gastric carcinomas and rectal carcinomas as well as glioblastomas. The non-professional phagocytosis of tumor and normal tissue cells and its mechanism will be studied as well as its prognostic significance in tumor diseases. In addition the interaction of ionizing radiation and kinase inhibitors in tumor and normal tissue cells will be studied.

### Physical aspects of radiation oncology

PI: Prof. Dr. C. Bert

1. Verification of interstitial brachytherapy by an electromagnetic tracking system, EMT-based CT estimation. Funding: Elekta
2. MR-based treatment planning – optimization of sequence parameters, establishing MR-scans in the patient specific immobilization device (mask), quality assurance
3. Development of a digital twin for the medical devices network of radiation oncology. Funding: StMWi, Bayern
4. Optimization of the medical physics quality assurance methods for 4DCT, total skin irradiation, surface guided radiation therapy, risk management

### Interdisciplinary workgroup Radiomics and Artificial Intelligence

PI: Dr. F. Putz, Prof. Dr. C. Bert, PD Dr.-Ing. B. Frey

The main emphasis of the Working group Radiomics and Artificial Intelligence in Radiooncology is to gain novel insights into the spatiotemporal dissemination of malignant tumors and to enable spatial predictions by large-scale analyses of imaging studies in order to improve and individualize radiotherapy target volume design and prescription dose distribution. The group uses radiomics and deep learning-based methods to enable imaging-based predictions and integration of imaging with non-imaging biomarkers to guide optimal treatment selection in radiotherapy. Moreover, the working group evaluates novel image informatics methods, like deep learning-based auto-segmentation, in their potential to improve and evolve current Radiooncologic treatment concepts.

### Translational Radiobiology

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 clinical hyperthermia) 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, DI-REKHT, 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. Creation of advanced cancer treatment planning to boost the effect of radiotherapy by combining with hyperthermia, heating the tumor, Hyperboost  
Funding: European

Commission, ITN-ETN

6. Fine-tuners of the adaptive immune response,  
FAIR GRK 2599, Funding: DFG



*Physicists of our Department together with colleagues from HNO discuss together the treatment regime of patients and common clinical investigative trials. The translational and interdisciplinary examination of the therapy plays a major role in the scientific actions of the Department.*

### Translational Immunoncology

PI: PD Dr. M. Hecht

The research group investigates immunomodulatory effects of radiotherapy in combination with immune checkpoint inhibitors. Both local and systemic immunological effects of radiotherapy are investigated, which may improve the therapeutic response to immune checkpoint inhibitors. In addition, prognostic and predictive markers will be identified to enable patient selection for future clinical radio-immunological trial designs. Another focus of the group is on direct radiosensitizing effects of targeted tumor therapeutics that can enhance the efficacy of radiation treatment and the underlying mechanisms in DNA damage repair.

### Teaching

Radiation Clinic organizes the cross-sectional course 11, Imaging Techniques, Radiation Treatment and Radiation Protection. In the practical course, the new online course Conrad was introduced. In cross-sectional course 6, the Radiation Clinic organizes the interdisciplinary lecture series. As part of this course, students work on an online module, which was partly developed by employees of the Radiation Clinic for the Virtual University of Bavaria. Here, patient examples are used to demonstrate the interdisciplinary approach in oncology. A radiation protection course with practical training for PJ students under recognition of the Bavarian Medical Association is held twice a year. An accompanying teaching concept is offered for PJ students. The lecture series "Prevention, Diagnosis, Therapy and Aftercare of Malignant Diseases" is offered for students of the Medical Process Management program. 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 our department. Laboratory rotations are offered for students of GK 2599 (compare own report). In addition, the department offers interdisciplinary courses for students of physics, medical technology, molecular medicine, medicine, and natural sciences.

### Selected publications

Sun R, Sundahl N, Hecht M, ..., Deutsch E. Radiomics to predict outcomes and abscopal response of patients with cancer treated with immunotherapy combined with radiotherapy using a validated signature of CD8 cells. *J Immunother Cancer*. 2020 Nov;8(2):e001429.

Goerig NL, Frey B, Korn K, ..., Gaipl US\*, Fietkau R\* (\*equal contribution). Early Mortality of Brain Cancer Patients and its Connection to Cytomegalovirus Reactivation During Radiochemotherapy. *Clin Cancer Res*. 2020 Jul 1;26(13):3259-3270

Fietkau R, Hecht M, Hofner B, ..., Balermipas P; PacCis-Study Group. Randomized phase-III-trial of concurrent chemoradiation for locally advanced head and neck cancer comparing dose reduced radiotherapy with paclitaxel/cisplatin to standard radiotherapy with fluorouracil/cisplatin: The PacCis-trial. *Radiother Oncol*. 2020 Mar;144:209-217. doi: 10.1016/j.radonc.2020.01.016.

Schnellhardt S, Erber R, Büttner-Herold M, ..., Distel L. Accelerated Partial Breast Irradiation: Macrophage Polarisation Shift Classification Identifies High-Risk Tumours in Early Hormone Receptor-Positive Breast Cancer. *Cancers (Basel)*. 2020 Feb 14;12(2):446. doi: 10.3390/cancers12020446. PMID: 32075091; PMCID: PMC7072550.

### International cooperations

Dr. K. Luminczky, 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,

Prof. Dr. Eric Deutsch, Department Radiotherapy, Gustave Roussy Cancer Campus, Villejuif Cedex: France,

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