## **Curriculum Vitae**

## **Professor Thomas Brunner**

## **Contact Information:**

Thomas Brunner, MD University Hospitals of Freiburg Department of Radiation Oncology Robert-Koch-Str. 3 D-79106 Freiburg im Breisgau Germany

Citizenship: Germany

## **EDUCATION**

1988 - 91	Medical Faculty, University of Erlangen
1991 - 92	Integrated ERASMUS studies at Rennes/France (Higher
	Education section of the European Community action)
1992 - 94	Medical Faculty, University of Erlangen
1994 - 95	Practical training year (final study year):
	-Hôpital Cantonal Universitaire Geneva/Switzerland
	(Internal Medicine; April through July 1994)
	-University Hospitals of Erlangen (Anesthesiology;
	August through November 1994)
	-Municipal Hospitals of Nuremberg (Surgery; 12/1994
	through 3/1995)
10/1995	M.D. thesis, University of Erlangen, Germany
11/2005	Habilitation at the University of Erlangen (Privatdozent) (research qualification for academic appointments)

# **Postgraduate Training and Fellowship Appointments:**

7/1995-12/1996	Internship, University Hospitals, Erlangen
1/1997-6/2001	Residency, Department of Radiation Oncology, University Hospitals, Erlangen
7/2001-6/2003	Postdoctoral Fellowship, University of Pennsylvania, Philadelphia
4/2004-9/2004	Radiation Diagnostics Fellowship. Institute of Diagnostic Radiology, University of Erlangen

## **Specialty Certification:**

15/9/2004 'Facharztzeugnis' (Certificate of Completion of Specialist Training

in Radiation Oncology, Chamber of Physicians, Munich, Germany)

Licensure:

12/1996 Full registration with General Medical Council,

Chamber of Physicians, Munich (Full medical license in Germany)

### **HOSPITAL APPOINTMENTS**

1/2000-12/2000 Advisor, Radiation Treatment Planning Unit, University Hospitals,

Erlangen

1/2000-6/2000 Advisor, Brachytherapy Unit, University Hospitals, Erlangen

7/2003-9/2004 Instructor, Outpatient Unit, University Hospitals, Erlangen

7/2003-12/2006 Authorized representative for DRG-management of the

Department

10/2004-12/2006 Consultant, Outpatient Unit, University Hospitals, Erlangen

01/2007 - 06/2012 Senior Research Fellow and Honorary Consultant at Oxford

University, Radiation Oncology and Biology

From 07/2012 Managerial Consultant at Albert-Ludwigs-University Freiburg,

Department of Radiation Oncology

#### **AWARDS AND HONOURS**

01/2000 Award of the 'Arbeitsgemeinschaft Gastroenterologische Onkologie'

(AGO; Working Group Gastroenterological Oncology).

Poster presentations: Preoperative chemoradiation in locally

advanced pancreatic carcinoma: a phase II study. And: Phase I trial of strictly time-scheduled gemcitabine and cisplatin with concurrent radiotherapy in patients with locally advanced pancreatic cancer.

2002-2003 DFG postdoctoral fellowship grant (German Research Foundation)

Studied under Dr. Eric Bernhard at the University of Pennsylvania,

Philadelphia.

2005 Hanns-Langendorff Award for Radiation Biology at DEGRO

(German Society for Radio-Oncology) conference, Karlsruhe. Poster presentation: *Molecular verification of stereotactic* 

radiotherapy in rats using pS1981ATM immunofluorescence as a

basis for orthotopic tumor models.

01.02.2009 "Professor of Translational Clinical Oncology"

(University of Oxford, Recognition of Distinction)

Cancer Research UK Award "Future Leaders in Oncology". Awarded at 7<sup>th</sup> NCRI Cancer Conference, Liverpool

## **RESEARCH ACTIVITIES**

7/2001-6/2003

06.11.2011

Pancreatic cancer cell radiation survival and prenyltransferase inhibition: the role of K-Ras. The role of downstream signalling of Ras (MAPK and PI3K cascades) in pancreatic carcinoma for radiation resistance. PI: Eric J. Bernhard, PhD

Radiobiology of mouse pancreatic ductal cells: functional properties of the Ki-RASG12V oncogene. Pl's: Anil K. Rustgi, MD and Eric J. Bernhard, PhD

9/2004 -12/2006

Molecular verification of stereotactic radiotherapy in rats using pS1981ATM immunofluorescence as a basis for orthotopic tumor models. Co-l's: Prof Gerald Niedobietek, MD (Pathology), Dr L Distel (Radiation Biology)

Stromal markers in specimen from patients with pancreatic carcinoma prior to chemoradiation. Co-l's: Priv.Doz. Arno Dimmler, MD (Pathology) and Priv.Doz. Franz Roedel, PhD (Radiation Biology)

<u>Pilot Study using an inhibitor of akt with chemoradiation for patients</u> <u>with pancreatic cancer</u>. Co-I: Susanne Herold, MD (Radiation Oncology)

<u>Principal Investigator of ARC-Phase I-Study</u> (Radiation Oncology) EudraCT-Number: 2006-001766-17 nelfinavir with chemoradiation for patients with pancreatic cancer

1/2007 -current

Tumour stroma interactions and its consequences on tumour biology and radiation sensitivity. Co-l's: Dr Ruth Muschel, MD/PhD (Gray Institute for Radiation Oncology and Biology)

Cancer Stem Cells in Radiobiology. Co-l's: Sir Walter Bodmer, FRCPath, FRS, Weatherall Institute of Molecular Medicine

### **Research Supervisory Activities**

7/03 – 12/06 Coordinator of the prospectively randomized multi-centre study

protocol "Primary resection versus neoadjuvant chemoradiation followed by resection for locally resectable or potentially resectable pancreatic carcinoma without distant metastasis. A multi-centre prospectively randomised phase II-study of the Interdisciplinary Working Group Gastrointestinal Tumours (AIO, ARO, and CAO).

7/03 – 12/06 Mentor for research in upper GI malignancies

- Immunhistochemical analysis of the tumoral and stromal factors in patients treated with chemoradiation for pancreatic carcinoma (Roy Schendel, M.D. thesis student)
- Prognostic factors in neoadjuvant and difinitve chemoradiation of patients with pancreatic carcinoma
- Adenocarcinoma of the esophagogastric junction: Elective lymphatic target volume definition based on the pattern of metastatic lymph node dissemination.
- A prospective phase II study of external beam chemoradiation plus endoluminal boost in the treatment of patients with esophageal cancer

1/07 – present

Research Group Leader: 'Tumour stroma interactions' and 'Cancer Stem Cells in Radiobiology';

#### **TEACHING ACTIVITIES**

Lecturer at the Medical Faculty of the Friedrich-Alexander University of Erlangen

University of Oxford MSc Course in Radiobiology Module Leader: Principles of Clinical Radiation Biology (from September 2009 - present)

#### MEMBERSHIP OF PROFESSIONAL AND SCIENTIFIC SOCIETIES

European Society of Therapeutic Radiology (ESTRO)
American Association of Cancer Research (AACR)
American Society of Therapeutic Radiology (ASTRO)
German Society of Therapeutic Radiology (DEGRO)

### **EDITORIAL BOARD MEMBERSHIP**

Clinical Oncology Strahlentherapie und Onkologie

## **INVITED MAJOR LECTURES**

International Symposium: Kinetics and mechanism of repopulation during radiotherapy: Biological basis, clinical significance, interventions. Dresden, 23. September 2002

K-Ras activation in pancreatic cancer: Implications for radiotherapy. Research Seminar of the Dept. of Radiation Oncology at the University of Pennsylvania, Philadelphia. March 27, 2003

Successful growth and characterization of mouse pancreatic ductal cells: functional properties of the *Ki-RASG12V* oncogene. AACR 95<sup>th</sup> Annual Meeting Orlando, FL, March 27-31. 2004

Pancreatic carcinoma: (Neo)adjuvant Chemo(radio)therapy. GI-Oncology 2005 – 1. Interdisciplinary Update. 09/07/2005 Kurhaus Wiesbaden.

Pancreatic carcinoma: Adjuvant therapy in 2006. GI-Oncology 2006 – 2. Interdisciplinary Update. 08/07/2005 Kurhaus Wiesbaden.

Chemoradiation only as a curative concept: Do we still need surgery? Excellence in Gastroenterology "Esophageal carcinoma" Wiesbaden, 09/12/2006

Refresher Course Gastric Carcinoma and Pancreatic Carcinoma. Joint Annual Meeting of the German and Austrian Societies of Therapeutic Radiation Oncology (DEGRO/ÖGRO) Vienna, 02/05/2008

Combining signal transduction targeting agents with radiotherapy. Inaugural Symposium of the Gray Institute for Radiation Oncology and Biology, University of Oxford 02/09/2008

Actual controversy: Does radiation enhance metastasis? 18th Symposium for Experimental Radiotherapy and Clinical Radiobiology, Dresden, 26. – 28. February 2009

Radioresistance of cancer stem cells. Special Session: Cancer stem cells and radiation resistance. Joint ECCO 15 - 34th ESMO Multidisciplinary Congress, Berlin, Monday 21 September 2009

Visualization of tumor biology: Hypoxia. The Oxford Experience: Imaging the effects of signal transduction inhibitors in the context of radiotherapy. 3<sup>rd</sup> Langendorff Symposium Imaging in Radiation Oncology, Freiburg, 23. October 2009

Ultrasound imaging of preclinical tumours focussing on the microenvironment (vascularity and stroma). The British Medical Ultrasound Society. Pre-clinical ultrasound study day. Chandos House, London, November 20<sup>th</sup> 2009

Radiosensitivity of stem-like cells from cancer cell lines. The British Insititute of Radiology: Radiation and the Genome: From Risks to Opportunities for Therapeutic Exploitation, London, Tuesday 1 December 2009

Symposium Gastrointestinal Tumors: Pancreatic cancer – gemcitabine only is not enough! 16. Jahrestagung der Deutschen Gesellschaft für Radioonkologie, Magdeburg, 3. – 6. Juni 2010

Symposium New strategies in the management of upper GI malignancies: Pancreatic adenocarcinoma: Light at the end of the tunnel? ESTRO 29 Barcelona, Spain, September 14, 2010.

Functional imaging in Radiotherapy. The British Institute of Radiology: So You Think You Know IGRT? Radiotherapy Imaging: Goals, Challenges and the Diagnostic Basics. London, 17-18 November 2010

Signal Transduction - Biological Rationale of Using Inhibitors with Radiation and Clinical Update. The British Institute of Radiology: Advances in Radiobiology, London, 8 December 2010

Teaching Lecture: Combining Molecular Targeted Agents and Radiotherapy. European Cancer Conference 16, Stockholm, 23-27 September 2011

The combination of novel agents with radiotherapy. Department of Oncology Clinical Academic Meeting, 18 January 2012

Multimodal approaches in pancreatic cancer today and tomorrow from the perspective of radiation oncology. Seminary of the Department of Radiation Oncology, University of Freiburg, Germany, 3 February 2012

## **PUBLICATIONS**

#### **Peer-Reviewed Articles**

- Grabenbauer GG, Steininger H, Meyer M, Fietkau R, **Brunner T**, Heinkelmann P, Hornung J, Iro H, Spitzer W, Kirchner T, Sauer R, Distel L. Nodal CT density and total tumor volume as prognostic factors after radiation therapy of stage III/IV head and neck cancer. Radiother Oncol. 1998;47:175-83.
- Baum U, Lell M, Nömayr A, Wolf H, **Brunner T**, Greess H, Bautz W. Multiplanar spiral CT in the diagnosis of pancreatic tumors. Radiologe. 1999;39:958-64.
- **Brunner TB**, Grabenbauer GG, Baum U, Hohenberger W, Sauer R. Adjuvant and neoadjuvant radiochemotherapy in ductal pancreatic carcinoma. Strahlenther Onkol. 2000:176:265-73.
- **Brunner TB**, Grabenbauer GG, Kastl S, Herrmann O, Baum U, Fietkau R, Klein P, Bautz W, Schneider T, Hohenberger W, Sauer R. Preoperative chemoradiation in locally advanced pancreatic varcinoma: a phase II study. Onkologie. 2000;23:436-442.
- Kastl S, **Brunner T**, Herrmann O, Riepl M, Fietkau R, Grabenbauer G, Sauer R, Hohenberger W, Klein P. Neoadjuvant radio-chemotherapy in advanced primarily non-resectable carcinomas of the pancreas. Eur J Surg Oncol. 2000;26:578-82.
- Grabenbauer GG, Rödel C, **Brunner T**, Schulze-Mosgau S, Strnad V, Muller RG, Iro H, Sauer R. Interstitial brachytherapy with Ir-192 low-dose-rate in the treatment of

- primary and recurrent cancer of the oral cavity and oropharynx. Review of 318 patients treated between 1985 and 1997. Strahlenther Onkol. 2001;177:338-44.
- **Brunner TB**, Grabenbauer GG, Klein P, Baum U, Papadopoulos T, Bautz W, Hohenberger W, Sauer R. Phase I trial of strictly time-scheduled gemcitabine and cisplatin with concurrent radiotherapy in patients with locally advanced pancreatic cancer. Int J Radiat Oncol Biol Phys. 2003;55:144-53.
- Grabenbauer GG, Rödel C, Ernst-Stecken A, **Brunner T**, Hornung J, Kittel K, Steinhart H, Iro H, Sauer R, Schultze-Mosgau S. Neck dissection following radiochemotherapy of advanced head and neck cancer--for selected cases only? Radiother Oncol. 2003;66:57-63.
- Fuchs S, Rödel C, **Brunner T**, Iro H, Niedobitek G, Sauer R, Grabenbauer GG. Patterns of failure following radiation with and without chemotherapy in patients with nasopharyngeal carcinoma. Onkologie. 2003;26:12-8.
- **Brunner TB**, Gupta AK, Shi Y, Hahn SM, Muschel RJ, McKenna WG, Bernhard EJ. Farnesyltransferase inhibitors as radiation sensitizers. Int J Radiat Biol. 2003;79:569-76.
- **Brunner TB**, Hahn SM, Gupta AK, Muschel RJ, McKenna WG, Bernhard EJ. Farnesyltransferase inhibitors: an overview of the results of preclinical and clinical investigations. Cancer Res. 2003;63:5656-68.
- Schreiber FS, Deramaudt TB, **Brunner TB**, Boretti MI, Gooch KJ, Stoffers DA, Bernhard EJ, Rustgi AK. Successful growth and characterization of mouse pancreatic ductal cells: functional properties of the *Ki-RASG12V*oncogene. Gastroenterology 2004;127:250-60.
- Martin NE, **Brunner TB**, Kiel KD, DeLaney TF, Regine WF, Mohiuddin M, Rosato EF, Haller DG, Stevenson JP, Smith D, Pramanik B, Tepper J, Tanaka WK, Morrison B, Deutsch P, Gupta AK, Muschel RJ, McKenna WG, Bernhard EJ, Hahn SM. A phase I trial of the dual farnesyltransferase and geranylgeranyltransferase inhibitor L-778,123 and radiotherapy for locally advanced pancreatic cancer. Clin Cancer Res 2004:10:5447-54.
- **Brunner TB**, Hahn SW, McKenna GW, Bernhard EJ. Radiation Sensitization by Inhibition of Activated Ras. Strahlenther Onkol 2004;180:731-40.
- **Brunner TB**, Schwab D, Meyer T, Sauer, R. Chemoradiation may prolong survival of patients with non-bulky unresectable extrahepatic biliary carcinoma a retrospective analysis. Strahlenther Onkol 2004;180:751-7.
- **Brunner TB**, Merkel S, Grabenbauer GG, Meyer T, Baum U, Papadopoulos T, Sauer R, Hohenberger W. Definition of elective lymphatic target volume in ductal carcinoma of the pancreatic head based on histopathologic analysis. Int. J. Radiation Oncology Biol. Phys. 2005;62(4): 1021-1029.
- **Brunner TB**, Cengel KA, Hahn SM, Wu J, Fraker DL, McKenna WG, Bernhard EJ. Pancreatic cancer dell radiation survival and prenyltransferase inhibition: the role of K-Ras. Cancer Res. 2005; 65: 8433-41.
- **Brunner TB**, Ernst-Stecken A, Jeske I, Grabenbauer GG, Sauer R, Distel L. Molecular verification of stereotactic radiotherapy in rats using ATMpS1981 immunofluorescence. Radiother Oncol. 2006 Apr;79(1):109-14.
- **Brunner TB**, Tinkl D, Grabenbauer GG, Meyer T, Brueckl WM, Sauer R. Maintenance chemotherapy after chemoradiation improves survival of patients with locally advanced pancreatic carcinoma: a retrospective analysis of prospectively recruited patients. Strahlenther Onkol. 2006 Apr;182(4):210-25.
- **Brunner TB**, Baum U, Grabenbauer, Sauer, and Lambrecht U (2006)

  Large topographic variability of upper abdominal lymphatics and the consequences for radiation treatment planning. Radiother Oncol, 81(2):190-5.

Brueckl WM, Herbst L, Lechler A, Fuchs F, Schoeberl A, Zirlik S, Klein P, **Brunner TB**, Papadopoulos T, Hohenberger W, Hahn EG, Wiest GH. Predictive and prognostic factors in small cell lung carcinoma (SCLC)—analysis from routine clinical practice. Anticancer Res. 2006;26:4825-32.

Brunner TB, Grabenbauer GG, Meyer, Golcher H, Sauer R, and Hohenberger W. Primary resection versus neoadjuvant chemoradiation followed by resection for locally resectable or potentially resectable pancreatic carcinoma without distant metastasis. A multi-centre prospectively randomised phase II-study of the Interdisciplinary Working Group Gastrointestinal Tumours (AIO, ARO, and CAO). BMC Cancer, 7:41.

Cengel KA, Voong KR, Chandrasekaran S, Maggiorella L, **Brunner TB**, Stanbridge E, Kao GD, McKenna WG, and Bernhard EJ.

Oncogenic K-Ras signals through epidermal growth factor receptor and wild-type H-Ras to promote radiation survival in pancreatic and colorectal carcinoma cells. Neoplasia 2007;9(4):341-8.

Cordes N, Frick S, **Brunner TB**, Pilarsky C, Grutzmann R, Sipos B, Kloppel G, McKenna WG, and Bernhard EJ.

Human pancreatic tumor cells are sensitized to ionizing radiation by knockdown of caveolin-1. Neoplasia. 2007 Apr;9(4):341-8.

**Brunner TB,** Rupp A, Melzner W, Grabenbauer GG, Sauer R. Esophageal cancer: A prospective phase II study of concomitant boost external beam chemoradiation with a top up endoluminal boost. Strahlenther Onkol 2008;184:15-22.

Meier I, Merkel S, Papadopoulos T, Sauer R, Hohenberger W, **Brunner TB**. Adenocarcinoma of the esophagogastric (AEG) junction: the pattern of metastatic lymph node dissemination as a rationale for elective lymphatic target volume definition. Int. J. Radiation Oncology Biol. Phys 2008;70(5):1408-17

Semrau R, Hansemann K, Adam M, Andratschke N, **Brunner T**, Heinzelmann F, Hildebrandt G, Vordermark D, Zips D.

Quality of Training in Radiation Oncology in Germany – Results of a 2006 Survey. Strahlenther Onkol 2008;184(5):239-44

Golcher H, **Brunner T**, Grabenbauer GG, Merkel S, Papadopoulos T., Hohenberger W, Meyer T. A single centre's experience with pancreatic cancer. Development of a new treatment strategy using preoperative chemoradiation for pancreatic carcinoma deemed to be resectable by CT-scan. Eur J Surg Oncol 2008 34(7):746-64

**Brunner TB**, Geiger M, Grabenbauer GG, Lang-Welzenbach M, Mantoni TS, Cavallaro A, Sauer R, Hohenberger R, McKenna WG.

A phase I-trial of the HIV protease inhibitor nelfinavir and chemoradiation for locally advanced pancreatic cancer. J Clin Oncol 2008:26(16):2699-706

Mantoni TS, Schendel RR, Rödel F, Niedobitek G, Al-Assar O, Masamune A, **Brunner TB**. Stromal SPARC expression and patient survival after chemoradiation for non-resectable pancreatic adenocarcinoma. Cancer Biol Ther. 2008 Nov 24;7(11):1806-15

Klautke G, **Brunner TB**. Radiotherapy in Pancreatic Cancer. Strahlenther Onkol. 2008 Nov;184(11):557-564

Tinkl D, Grabenbauer GG, Golcher H, Meyer T, Papadopoulos T, Hohenberger W, Sauer R, **Brunner TB**. Downstaging of pancreatic carcinoma after neoadjuvant chemoradiation. Strahlenther Onkol. 2009 Sep;185(9):557-66.

Al-Assar O, Muschel RJ, Mantoni TJ, McKenna WG, **Brunner TB**. Radiation response of cancer stem-like cells from established human cell lines after sorting for surface markers. Int. J. Radiation Oncology Biol. Phys. 2009 Nov 15; 75(4): 1216-25.

Eckel, F., **Brunner, T.**, Jelic, S. Biliary cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010;21 Suppl 5:v65-9

Maughan TS, Illidge TM, Hoskin P, McKenna WG, Brunner TB, Stratford IJ, Harrington KJ, Plummer R, Billingham LJ, Nutting C, Burnet NG, Mackay RI, Oliver A, Young C, Chan CS: Radiotherapy research priorities for the UK, Clinical oncology 2010, 22:707-709

**Brunner TB**, Scott-Brown, M. The role of radiotherapy in multimodal treatment of pancreatic carcinoma. Radiat Oncol 2010:5(1):64

**Brunner TB**, Eccles CL. Radiotherapy and chemotherapy as therapeutic strategies in extrahepatic biliary duct carcinoma. Strahlenther Onkol 2010:186(12):672-80

Mantoni TS, Lunardi S, Al-Assar O, Masamune A, **Brunner TB**. Pancreatic stellate cells radioprotect pancreatic cancer cells through  $\beta$ 1-integrin signaling. Cancer Res. 2011 May 15;71(10):3453-8. Epub 2011 May 10.

Al-Assar O, Mantoni T, Lunardi S, Kingham G, Helleday T, **Brunner TB**. Breast cancer stem-like cells show dominant homologous recombination due to a larger S-G2 fraction. Cancer Biol Ther. 2011 Jun 15;11(12):1028-35.

Harrington KJ, Billingham LJ, **Brunner TB**, Burnet NG, Chan CS, Hoskin P, Mackay RI, Maughan TS, Macdougall J, McKenna WG, Nutting CM, Oliver A, Plummer R, Stratford IJ, Illidge T. Guidelines for preclinical and early phase clinical assessment of novel radiosensitisers. Br J Cancer. 2011 Aug 23;105(5):628-39

**Brunner TB**, Sauer R, Fietkau R. Gemcitabine/cisplatin versus 5-fluorouracil/mitomycin C chemoradiotherapy in locally advanced pancreatic cancer: a retrospective analysis of 93 patients. Radiat Oncol. 2011 Jul 27;6:88.

**Brunner T**, McKenna G. Combining molecular targeted therapeutics (MTT) and radiotherapy: MTT and MTD. Eur J Cancer. 2011 Sep;47 Suppl 3:S373-4

Miles KA, Lee TY, Goh V, Klotz E, Cuenod C, Bisdas S, Groves AM, Hayball MP, Alonzi R, **Brunner T**. Current status and guidelines for the assessment of tumour vascular support with dynamic contrast-enhanced computed tomography. Eur Radiol. 2012 Feb 26.

**Brunner TB**, Kunz-Schughart LA, Grosse-Gehling P, Baumann M. Cancer stem cells as a predictive factor in radiotherapy. Semin Radiat Oncol. 2012 Apr;22(2):151-74