Trial Description

Title

Cerebral hemodynamics after cerebral irradiation in pediatric patients with posterior fossa brain tumors

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

Our study compares the cerebral hemodynamics of children and young adults after irradiation of the brain due to posterior fossa brain tumors. Using ultrasound, we compare two mechanisms of cerebral hemodynamics: Cerebral autoregulation keeps cerebral blood flow at constant levels irrespective of varying systemic blood pressure values. Neurovascular coupling leads to increased blood supply of particularly active brain areas. Comparing the cerebral hemodynamics of children and young adults with and without brain irradiation, respectively, we want to improve follow-up care of patients with brain tumors necessitating radiotherapy.

Brief Summary in Scientific Language

Cerebral vasculopathy is a common late sequela after irradiation of the brain (Bitzer et al. 1995) which for instance has been demonstrated in patients with medulloblastoma (Grenier 1998, Maher 2000). Vasculopathy of cerebral vessels can lead to various clinical symptoms. Arterial stenosis comes along with an increased risk of ischemic stroke and can lead to neovascularisation/Moya-Moya disease (Omura 1997, Serdaroglu 2000). Moreover, there is an increased risk of other vascular malformations and bleedings (Liu 2009, Poussaint 1995).
Cerebral circulation is regulated by several mechanisms. Cerebral autoregulation keeps cerebral blood flow at constant levels irrespective of varying systemic blood pressure values. Slow oscillations of systemic and cerebral blood flow can be induced respiratorily by breathing slowly at 0.1 HZ. Physiologically the respiratory induced cerebral oscillations are time-shifted to the systemic oscillations in which the phase shift embodies functioning cerebral autoregulation (Kuo et al. 2003). Neurovascular coupling leads to increased blood supply of particularly active brain areas. For instance, visual stimulation leads to an increase of blood flow velocity in posterior brain areas. Both adaptive mechanisms can be evaluated by ultrasonic testing.
Ultrasonic testing of cerebral hemodynamics enables a functional and non-invasive evaluation of cerebral blood circulation beyond a morphological delineation of the vessels. Today, diagnosis of vasculopathy is predominantly diagnosed by the means of angiographic procedures (MR-angiography or conventional angiography). Comparing the cerebral hemodynamics of children and young adults with and without brain irradiation, respectively, we hope to improve diagnosis of vascular sequelae after irradiation. This should improve follow-up care of patiens with brain tumors necessitating radiotherapy and precocious

therapy of vascular complications.

Bitzer M, Topka H. Progressive cerebral occlusive disease after radiation therapy. Stroke. 1995 Jan;26(1):131-6.
Grenier Y, Tomita T, Marymont MH, Byrd S, Burrowes DM. Late postirradiation occlusive vasculopathy in childhood medulloblastoma. Report of two cases. J Neurosurg. 1998 Sep;89(3):460-4.
Grill J, Couanet D, Cappelli C, Habrand JL, Rodriguez D, Sainte-Rose C, Kalifa C. Radiation-induced cerebral vasculopathy in children with neurofibromatosis and optic pathway glioma. Ann Neurol. 1999 Mar;45(3):393-6.
Julious SA. Sample size of 12 per group rule of thumb for a pilot study. Pharm Stat 2005;4:287-291.
Kuo TB, Chern CM, Yang CC, Hsu HY, Wong WJ, Sheng WY, Hu HH. Mechanisms underlying phase lag between systemic arterial blood pressure and cerebral blood flow velocity. Cerebrovasc Dis 2003;16:402-409.
Liu AK, Bagrosky B, Fenton LZ, Gaspar LE, Handler MH, McNatt SA, Foreman NK. Vascular abnormalities in pediatric craniopharyngioma patients treated with radiation therapy. Pediatr Blood Cancer. 2009 Feb;52(2):227-30.
Maher CO, Raffel C. Early vasculopathy following radiation in a child with medulloblastoma. Pediatr Neurosurg. 2000 May;32(5):255-8.
Omura M, Aida N, Sekido K, Kakehi M, Matsubara S. Large intracranial vessel occlusive vasculopathy after radiation therapy in children: clinical features and usefulness of magnetic resonance imaging. Int J Radiat Oncol Biol Phys. 1997 May 1;38(2):241-9.
Poussaint TY, Siffert J, Barnes PD, Pomeroy SL, Goumnerova LC, Anthony DC, Sallan SE, Tarbell NJ. Hemorrhagic vasculopathy after treatment of central nervous system neoplasia in childhood: diagnosis and follow-up. AJNR Am J Neuroradiol. 1995 Apr;16(4):693-9.
Rosengarten B, Steen-Müller MK, Müller A, Traupe H, Voss RK, Kaps M. Contrast media effect on cerebral blood flow regulation after performance of cerebral or coronary angiography. Neurovasc Dis 2003;16(1);42-6.;155(1):37-43.
Serdaroğlu A, Simşek F, Gücüyener K, Oğuz A, Karadeniz C, Balibey M. Moyamoya syndrome after radiation therapy for optic pathway glioma: case report. J Child Neurol. 2000 Nov;15(11):765-7.

Do you plan to share individual participant data with other researchers?

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Description IPD sharing plan

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Organizational Data

- DRKS-ID: **DRKS00005702**
- Date of Registration in DRKS: **2014/02/12**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
-

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Ethics Approval/Approval of the Ethics Committee: **Approved**
(leading) Ethics Committee Nr.: **531/13 , Ethik-Kommission der Albert-Ludwigs-Universität Freiburg**

Secondary IDs

- Universal Trial Number (UTN): **U1111-1152-8993**

Health condition or Problem studied

- ICD10: **C71 - Malignant neoplasm of brain**
- ICD10: **I67.9 - Cerebrovascular disease, unspecified**
- Free text: **Y84.2 Radiological procedure and radiotherapy**

Interventions/Observational Groups

- Arm 1: **Cerebral autoregulation (phase and gain) and neurovascular coupling (resting flow velocity, overshoot flow velocity, steady-state flow velocity) of children and young adults with history of radiotherapy due to a posterior fossa brain tumor will be assessed by a single-time dopplersonographic exmination. Clinical data will be assessed by means of a questionnaire.**
- Arm 2: **Cerebral autoregulation (phase and gain) and neurovascular coupling (resting flow velocity, overshoot flow velocity, steady-state flow velocity) of healthy age-matched children and young adults will be assessed by a single-time dopplersonographic exmination. Clinical data will be assessed by means of a questionnaire.**

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Other**
- Allocation: **Non-randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Other**

Study Type: **Non-interventional**

Study Type Non-Interventional: **Other**

Allocation: **Non-randomized controlled trial**

Blinding: **[---]***

Who is blinded: **[---]***

Control: **Other**

- Purpose: **Basic research/physiological study**
- Assignment: **Parallel**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

Single-time dopplersonographic ultrasound examination of cerebral autoregulation (phase and gain) as well as neurovascular coupling (resting flow velocity, overshoot flow velocity, steady-state flow velocity) at study inclusion.

Secondary Outcome

At study inclusion, cinical data regarding cerebral vasculopathy, cerbrovascular events and cardiovascular risk factors will be assessed by a questionnaire. Clinical data will be correlated with the parameters of cerebral hemodynamics.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **ZKJ, Freiburg im Breisgau**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2014/04/01**
- Target Sample Size: **24**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **6 Years**
- Maximum Age: **35 Years**

Additional Inclusion Criteria

1.Children and young adults (age 6-35 years) a) with a history of cerebral radiotherapy during childhood due to a posterior fossa brain tumor (patients) b) age-matched healthy children and young adults (control). 2. patients: in remission, time interval to last chemotherapy and radiotherapy at least 12 months. 3. Written informed consent to the study by the patient/proband or accordingly the person having the care and custody of the child.

Exclusion criteria

1. No ultrasound window for transtemporal ultrasound. 2. controls: Disease of central nervous system, history of chemotherapy of radiotherapy

Addresses

- **Primary Sponsor**

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Sources of Monetary or Material Support

- **Institutional budget, no external funding (budget of sponsor/PI)**

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Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*