Fall 2022

NEUROtransmitter

Communicating our message.

Feature Article: 20th International Symposium on Pediatric Neuro-Oncology

The Childhood Brain Tumor Foundation was pleased to be a Silver Sponsor of the 20th International Symposium on Pediatric Neuro-Oncology, a comprehensive conference. This article provides an overview of some highlights from the symposium. It was an outstanding hybrid conference, and attendees found it very informative.

Welcome Address, Monday, June 13, 2022: CHAIRS: Prof. Dr. med. Stefan Rutkowski, University Hospital Hamburg-Eppendorf (UKE); and Prof. Dr. Stefan M. Pfister, Hopps Children's Cancer Center, Heidelberg and Heidelberg University Hospital, and Peter Schenscher, Hamburg, Germany.

Chair: Helen Paisley, Liverpool, UK; Wim Tissing Utrecht, The Netherlands

Keynote, Monday, June 13: Quality of Life (QoL), Neuropsychology and Rehabilitation, Session Chairs: Mathilde Chevignard and Ulrike Leiss

Improving Cognitive Outcomes for Children Treated for Cancer, Moving Beyond the Cure; Heather Conklin, Ph.D., St. Jude's, Memphis, Tennessee

Deficits prevalent in children diagnosed with a brain tumor and its treatments are associated with reduced QoL. One of the goals is to improve cognitive outcomes by characterizing cognitive problems associated with treatment, improving specifications, and valid interventions. Survival rates have been improving but the QoL can be

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Grants 2023: CBTF will re-open our grants application process for 2023 in the winter of 2022. A limited number of number of applications will be funded.

We are delighted to announce the return of the Casino Party event after two years of cancelations. Interested in attending or donating toward the auction, e-mail the foundation: ***cbtf@childhoodbraintumor.org***

Please Join Us: Saturday, December 3, 2022 at the Rockville Civic Center, Glenview Mansion, 603 Edmonston Drive, Rockville, MD We look forward to seeing everyone!

CBTF Raises Funds for Research

*Funds raised benefit pediatric brain tumor research and other **CBTF** programs*

The Childhood Brain Tumor Foundation

Our mission is to support and fund basic science or clinical research for childhood brain tumors. We are dedicated to heightening public awareness of this devastating disease. and improving the quality of life for those that it affects by funding vital research initiatives.

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Series One, Online: Video sessions with the experts are posted on our website.

Lunch with a Purpose at Eggspectation, Ellicott City

On May 17th, 2022, an awesome event was held by a group of dedicated ladies that come together to raise funds for charity. Lunch with a Purpose. The organizers were excited that the event sold out and had a waiting list. Debbie Nesbitt and the group held a fantastic auction raffle that was a huge success.

Michael Schoenfeld and Jeanne Young were guest speakers to share information about pediatric brain tumors. Michael shared his story and Jeanne spoke about the CBTF mission, thanking the attendees for their support.

Please support CBTF: Your monetary support is always meaningful to CBTF and we hope we can count on your continued support.

CBTF has posted a series of videos on many relevant topics.

Childhood Brain Tumor Foundation
Visit our GIVE ONLINE donation button:

The Childhood Brain Tumor Foundation is dedicated to funding research for all pediatric brain tumor types.

Visit our secure website:
www.childhoodbraintumor.org

Go to our Support page and click on the Give2Charity button.

CBTF Sponsorships:

We will provide a **Silver sponsorship** for the 21st International Symposium on Pediatric Neuro-Oncology (**ISPNO**) for the **2024 conference.**

2023 Society for Neuro-Oncology (**SNO**), International, Sub-Saharan Africa or other location will be provided a sponsorship shortly.

If you are interested in learning more about the Childhood Brain Tumor Foundation, Inc.,
E-MAIL: cbtf@childhoodbraintumor.org or jeanneyoung@childhoodbraintumor.org (**E-mail preferred due to high volume of robo-calls**)
TELEPHONE: 877-217-4166 or 301-515-2900
Volunteers welcome!

Grant Summary, Thank You, CFC

2022 New Grant funded, two-year study

Institution: Dana-Farber Cancer Institute (DFCI)

Grant Title: *A pilot feasibility study of high intensity interval exercise in young adult survivors of pediatric brain tumors*

PI: Tabitha M. Cooney, M.D., Pediatric Neuro-Oncology

Brain and spinal cord tumors are the second most common pediatric cancer, and pediatric central nervous system (CNS) tumor survivors are at extreme risk for late mortality and new chronic medical conditions. Effective non-pharmacologic interventions to improve neurocognitive, physical and social/emotional functioning in pediatric CNS tumor survivors are fervently needed. We are launching a pilot study of a 4-month virtual home-based high-intensity interval exercise for young adult survivors of pediatric CNS tumors. Survivors will receive an exercise bike and 3 weekly supervised exercise training sessions for 4 months via Zoom.

Our primary aim is to determine feasibility of our virtual HIIT exercise program, and our secondary aims are to measure preliminary effects of our program on cognitive, physical, and emotional health. Our exploratory aims are to measure sustainability of indoor cycling use, as well as disparities in participation and/or outcomes. We will examine executive abilities, physical fitness, and health related quality of life. The overall design will allow us to inform a multi-institutional, randomized control trial adequate powered to test whether our program will mitigate cognitive, physical and emotional deficits for pediatric CNS tumor survivors. Our protocol is currently being reviewed by the IRB, and we intend to launch this Fall.

Thank you to our friends who donated through workplace charitable **giving campaigns this year, inclusive of the CFC.**

The Childhood Brain Tumor Foundation, friends and families are very appreciative of your support. (National) CFC **12035**

Charity Campaign and other independent

Campaign donations may be made for the United Way (**UW**) through the "donor option" or "donor choice." Please check with your employer in reference to **UW** campaigns. You may write us in.

A huge Thank You donors!

AMERICA'S BEST CHARITIES

Maryland Charity Campaign

Thank you so much!

Special thanks from CBTF to our supporters, advisors and the medical, community for their dedication!

BY CHECK: Make out to CBTF or Childhood Brain Tumor FDN.

Send to: CBTF
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THANK YOU FOR YOUR SUPPORT!

Your contributions make it possible for CBTF to fulfill its mission.

Please note if you are supporting: ☐ General ☐ Research ☐ Education

If in memory or in honor of please include the name of the person and the contact information for the person/family to receive acknowledgment.

impacted by deficits due to treatment. Children are most likely to have compulsory education, are less likely to marry, and are not so likely to be employed.

They are looking at reducing radiation therapy for tumor control while lessening side effects. A study of low-grade glioma patients showed an improvement in cognitive outcomes: learning, memory, academic skills, and intellectual functioning.

In medulloblastoma and posterior fossa syndrome (PFS) post treatment IQ is lower, and processing speed and attention, and working memory are a bit slower by year 1, 3, or 5. Comparative studies indicated the most sensitive symptoms with PFS were dysmetria, ataxia, with speech/language being the most sensitive. Efforts have improved neuroimaging correlates and improved diagnostics.

Deaf children and those with sensorineural hearing loss have academic disparities due to ototoxicity. They tend to have worse cognitive outcomes. Brain tumor treatment increases the need for neurosensory modifications, requiring visually based phonics, hearing adherence, and cochlear implants. Cochlear-sparing radiation and protectants, along with hearing aids and implants can improve QoL.

Intervention is used with CogMed to assess working memory and using training techniques to help improve and sustain working memory. Cognitive intervention starts around age 4 and older. Socioeconomic status can impact patients, demonstrated with decline in math, reading and IQ.

Future: imaging neurofeedback, fMRI, prophylactic intervention, combination interventions, neuroprotection, virtual reality as goals to improve QoL for survivors.

Treatment versus tumor is not always easy to determine since most patients do not have a pre-diagnostic baseline assessment. All aspects are considered, including tumor, location, and treatments. Genetic variants and susceptibility are assessed regarding cognitive decline following treatment. Another approach is connectivity mapping to show alterations in working memory neural systems.

Recent advances in improving neuropsychological outcomes for pediatric brain tumor patients. Are we entering a new era? Session Speaker: Donald J. Mabbott, University of Toronto, CANADA

Dr. Mabbott declared we are already in a new era. Treatment and late effects have some new understandings like the progress made in the understanding of the biology of tumors. There are new therapeutic approaches based on pre-clinical and clinical studies of injury mechanisms. Cognitive, exercise, and light therapy are proving to be good for the neural precursor stem cell niche in promoting cell renewal in brain plasticity.

Injury is associated with the brain tumor type and treatment. Types of injury include neurotoxic astrocytic reactivity, impaired myelination, impaired neurogenesis, neurometabolic disruption, neuroinflammation due to reactive microglia, alterations from angiogenesis, and changes in synaptic functioning.

In pre-clinical mouse studies of cranial radiation and a very small pilot trial in survivors' metformin can activate brain stem cells, promote neurogenesis (growth/development of nerve tissue), and may enhance spatial memory. More studies will be required to assure efficacy going forward. The study was published in Neuro-Oncology and a phase III study is being conducted. More sites are opening.

Tuesday, June 14, 2022; Cerebellar Mutism, Chairs: Karen Walsh, Children's National and Astrid Sehested, Copenhagen, Denmark

Cerebellar mutism syndrome (CMS): Incidence, symptoms, risk factors, and prognosis, *Results and Future Perspectives*, from the Nordic European Study of the Cerebellar Mutism; Astrid Sehested, MD, Copenhagen, Denmark

Post-surgery from childhood posterior fossa tumors, cerebellar mutism can manifest from complications of surgery. Mutism, ataxia, irritability, dysphagia, and cranial nerve impairment occurs in 10-20%, delayed and transient. Assessment related to mutism include imaging correlates, genetic disposition, and use of corticosteroids.

Testing includes speech tests: word race with picture cards, a fish story which includes narrative pictures, and ataxia forms. Patients that have a speech impediment after day one are assessed. Of the 376 evaluable patients in

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the study 14% had mutism, 16% had reduced speech, and 70% habitual speech. Fifty percent tend to speak within 16 days of surgery. Tumor locations includes brain stem, vermis, 4th ventricle, and cerebellar hemisphere. Some tumor types with risk are medulloblastoma, pilocytic astrocytoma, ependymoma, and ATRT. The risk of cerebellar mutism is greater in younger children with medulloblastoma and ATRT patients. Patients undergoing re-operative surgery are at lesser risk.

They will study communication with peers, assess re/post MRI, look for signs of gliosis, hypertrophy, and atrophy. Continued studies are ahead, and more are to be done. *Patient centered monitoring and care of cognitive late effects in pediatric brain tumor survivors without cerebellar mutism syndrome (CMS)*, Karen Walsh stated that, Twenty-five percent of medulloblastoma patients have CMS 103 days post-surgery. Research summary: Data suggests CMS infers increased risk of cognitive and emotional late effects.

Novel therapeutic approaches are discovered through preclinical and clinical studies of injury mechanisms.

- Combination approaches
- Cell renewal, endogenous repair

Light therapy, cognitive therapy, exercise, plasticity, lifestyle, interventions, and novel therapies.
Running increases hippocampal neurogenesis. The study duration was for 12 weeks, three days a week. Training repairs white matter damage and volume of the hippocampus. They found that cognitive functioning, attention, and reaction time increased for completion of activities with exercise. Aerobic activity will increase white matter, hippocampus growth, and faster reactions.

Roundtable – Personalized Medicine Phase III trials, Chaired by Ira Dunkel, New York and Darren Hargrave, London, United Kingdom, Several topics were covered prior to the Roundtable discussion.

Personalized Medicine and Phase III Trials: How to Reconcile the Two Seemingly Contradictory Concepts, Roger J. Packer, Children's National, Washington, DC

During the first era of phase III brain tumor clinical trials, development was easier. The trials were simple, and the national and international playing field was more even. However, there was some competition between groups, POG, COG, and SIOP for example. There was minimal data about the standard of care and no interest from industry. The competition of ideas was less than today. The WHO classification system has been broadened. Medulloblastoma has been classified in 3-4 subgroups and now there are 13+. The low-grade neuroglial tumors have many subgroups that overlap. There is more complexity and many discoveries ahead with changes in biology. In some cases, molecular stratification may not be the key.

Personalized medicine and phase III trials "how to reconcile the two seemingly contradictory concepts? Françoise Doz, Université Paris Cité Paris, France

The Innovative Therapies for Children with Cancer (ITCC) European Consortium in 2021, most clinical trials for brain tumor patients were devoted to targeted treatments and a few new immunotherapy approaches. They strive to avoid competing trials and use similar strategies to those tested in other consortia.

Phase 0 design and consideration for tissue collection within later stage phase clinical trials, Sabine Müeller, University of San Francisco, USA
Phase 0 trials are needed because of the limited models for assessing the blood brain barrier. Other studies include new trends -chip technology/Orgnoids, imaging assessment of CNS penetration that is not easily available, and CNS biopsies. Challenges involve understanding the impact of study intervention on tumor cells. Alternative tissue, collecting

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In Honor of

Our dedicated scientific medical advisors who have tirelessly dedicated their time to care for the patients and families and their commitment of voluntary service to review grants and assist CBTF as needed.

Fae Daniels
Roger Packer
Michael Schoenfeld

Much appreciation to Drs. Roger Packer, Kristina Hardy, Tobey MacDonald, and Gilbert Vezina for working with our videographer, Neil Rubino, to tape presentations on various topics. No charge to view, register for log-in to access the videos: cbtf@childhoodbraintumor.org

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through the CSF; autopsy specimens when available are the sufficient, ethics regarding patients and families, and the costs associated with tissue collection are some ongoing challenges.

Roundtable Discussion Participants: Eric Bouffet, Toronto, Françoise Doz, Damar Gajjar, Sabine Müeller, Roger Packer, Olaf Witt, and audience question and comments (in-person and by telephone).

Françoise Doz commented that perhaps patients can be grouped together biologically, instead of via frontline trials with small subgroups with specific and randomized trials. Roger Packer commented it will be a tremendous challenge to look at different outcome measures, possible early relapse, and problems, and still be adaptable with trial design. He further commented that Phase III trials should not be ongoing for more than 2-3 years or they can be outmoded. Eric Bouffet expressed concern for low-income countries like India, and the need for institutions to work together. Ira Dunkel, Phase III said that trials need to be fine-tuned to smaller randomized trials. Amar Gajjar reiterated that groups need to come together but it has not been so successful. Sabine Müeller felt greater interaction with industry is important. Packer commented there are too many people to see the benefits of study drugs and mentioned that trust issues between groups/ subgroups and institutions cause repeating studies for data checking and that delays progress. Dr. Ken Cohen: Even with perfect data, drug companies and the medical community would benefit in partnering by supporting and building constructs.

Comment was made by Dr. Jonathan Finlay, stating that NCI had tried to encourage continuance of randomized trials for DIPG. Now, there are changes with molecular profiling. It is important to diagnose diffuse middle glioma sooner before late stage. Dr. Sabine noted changes that have developed or increased since COVID-19 caused a more regular use of tele-medicine. It was believed by the panel that clinical trials may need to be approached in a different way. Dr. Katherine Warren mentioned the use of artificial intelligence (AI) and others agreed it will become more prevalent in the future. Dr. Eric Bouffet commented that lack of communication can be an issue. A data safety monitoring board (DSMB) is needed to determine the best studies for moving forward. The goal is to do trials that provide answers.

KEYNOTE: WHO Classification of CNS Tumors

Chair: Torsten Pietsch, Bonn, Germany

WHO 2021 Classification of CNS Tumors, Pieter Wessling Utrecht, The Netherlands, Amsterdam Universities Medical Center

The 2016 WHO Blue Book of the Classification of Central Nervous System Tumors was updated in 2021 regarding tumor types and molecular features.

Changes: Methylation fingerprinting has improved brain tumor diagnosis. There are many new brain tumor classifications. Tumors are increasingly grouped by genetic alterations. Classification is moving from the microscope to DNA. Grading of brain tumor neoplasms are within the tumor. PNET (primitive neuroectodermal tumor) is a neuroepithelial tumor. Ependymoma is in the posterior fossa group. They are assessing low-income countries and the way to bridge the gap and there was mention of some countries sharing with institutions that have less technological options.

Microscopy, immunohistochemistry can be effective with molecular and can be less expensive as a diagnostic tool. A multidisciplinary approach is very important. Pietsch anticipates that artificial intelligence guided analysis of histological slides will be more precise. The WHO tumor classification strongly focuses on diagnostics and prognostic markers.

Visit WHO Website for details:
https://radiopaedia.org/articles/who-classification-of-cns-tumours-1?lang=gb or
https://pubmed.ncbi.nlm.nih.gov/34185076/

ISPNO, Remembrances

Wednesday, June 14 Immunotherapy and Immune Microenvironment; Chairs Karin Straathof, London, UK and Nicholas Vitanza, Seattle, USA

Liquid Biopsy/innovative diagnoses, Chairs: Franck Bourdeaut, Paris France and Paul Northcott, Memphis

LLG-61 *Cerebrospinal fluid (CSF) as a source for liquid biopsy*

Liquid biopsies detect tumor DNA in CSF and biopsies are accessed via blood, urine, cerebrospinal fluid and saliva/ stool. Cerebral spinal fluid is used as a source for liquid biopsy via lumbar puncture or Omaya reservoir. CSF will be used for diagnostics, prognosis, personalized medicine, monitoring tumor response, tumor evolution, and minimal residual disease. The whole genome will be assessed, not just specific mutations, with a focused sequencing of 21 genes. CSF biopsies provide results. Challenges include blood brain barrier, volume of sample in children, low shedding tumors, and tumor location. The investigators' studies will assess structural variants, CNV, and point mutations of ctDNA panel sequencing in LPWG. The goal is to include ctDNA studies in clinical trials.

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Thanks to all of the organizers and speakers for sharing your knowledge and updates! We look forward to 2024 for the 21st ISPNO.

ISPNO Hamburg, Germany

Bequests, Planned Giving, and Trusts

Through a trust, bequest, or planned giving you can contribute to furthering the future research and programs of the Childhood Brain Tumor Foundation, Inc. By including the CBTF in your estate planning you can minimize your taxes.

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together, reaching for a cure!

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***SAVE THE DATE**: Casino Party, Saturday December 3*

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