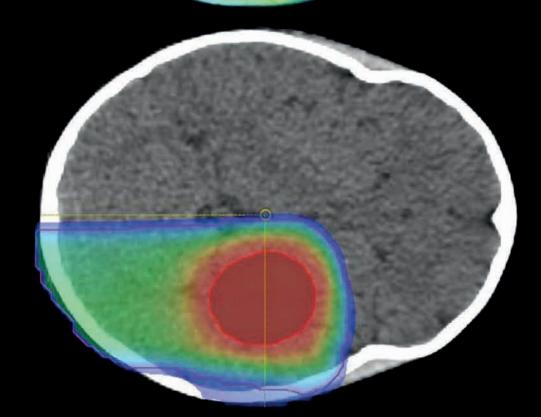


BRINGING THE LATEST IN PAEDIATRIC ENDOCRINOLOGY TO YOU

Late effects of cancer therapy

Special issue **P5-8** >



European Society for Paediatric Endocrinology

Improving care of children with endocrine diseases by promoting knowledge and research

ISSUE 47 / SPRING 2020 ISSN 2045-5003 (ONLINE)

Haematopoietic stem cell transplantation

Wassim Chemaitilly considers endocrine complications **P5** >

Fertility preservation

Issues for young cancer patients are examined by Rodrigo Romao **P6** >

Particle therapy for CNS tumours

Eva Bezak and colleagues compare X-ray and proton beam therapy **P7** >

ALSO INSIDE:

News

ESPE Grants and Awards **P2** >

Council and committee vacancies, Patient leaflets, e-Learning and more **P3** >

Hot topics

The latest research **P4** >

Events and diary

2nd ESPE Science Symposium plus ESPE Connect 2021 **P8** >

ESPE 2020 in Liverpool, plus ESPE Schools 2020 **P9** >

Future meetings, dates and deadlines **P10** >

ESPE 2020 – Submit your abstracts by 6 April at www.espe2020.org

EDITORIAL

Welcome

In this issue, we look at endocrine and other late effects associated with radiotherapy and chemotherapy in young patients. When and how should we screen for problems? How can we mitigate the risks? What are the best ways to increase understanding among health professionals and improve patient care?

All these questions and more are addressed by our authors, who have a global distribution and address a broad range of topics in the field.

On **page 5**, Wassim Chemaitilly looks at haematopoietic stem cell transplantation, which can be used to address haematological malignancies as well as other blood disorders and inborn errors of metabolism. The treatment involves myeloablative chemotherapy and possibly also total body irradiation. Endocrine late effects are common and complex, and screening offers the possibility of early intervention.

Options for fertility preservation during cancer treatment are advancing, but discussion between the parties at the time of diagnosis is of paramount importance. Rodrigo Romao considers the strategies that are available on **page 6**: these depend on age and sex, and some approaches remain experimental in humans. Cost, and a desire to begin cancer treatment without delay, create barriers to fertility preservation.

Tumours of the central nervous system account for 20% of all cancers in patients under the age of 15. Protons and heavy ions offer superior dose distribution when compared with X-rays, with a greatly reduced radiation dose to surrounding healthy tissue (as illustrated on the cover of this issue). On **page 7**, Eva Bezak and colleagues compare the two approaches and look forward to the acquisition of higher quality evidence regarding the use of proton therapy.

Elsewhere inside, you can learn of the many grants, awards, opportunities and resources on offer to ESPE members. There's also a tantalising glimpse of ESPE's events for 2020: particularly the Science Symposium (**page 8**) and the forthcoming ESPE Meeting in Liverpool, UK (**page 9**). Finally, don't forgot the imminent deadlines for applications to several ESPE Schools that are taking place this autumn.

Sarah Ehtisham

Editor, ESPE News Sarah.Ehtisham@mediclinic.ae

Cover image:

Dose distributions comparing X-ray (above) and proton (below) plans in a 5-year-old with a 3-cm diameter supratentorial ependymoma. Read more in the article by Bezak et al. on **page 7** of this issue (CT image courtesy of St Jude Children's Research Hospital, Memphis, TN, USA)

Editorial Board:

Meghna Chawla Antje Garten Abel López-Bermejo María Salomón Estébanez

GRANTS AND AWARDS

NEW!

NEWS

Undergraduate Achievement Award

This award aims to attract undergraduates towards a career in paediatric endocrinology. **Please encourage and sponsor applications from students with a research interest in the field.**

- €750 grant plus free registration for ESPE 2020
- 6 grants available each year
- requires submission of an abstract to ESPE 2020 and a supporting statement from an ESPE member

www.eurospe.org/grants-awards/grants/ undergraduate-achievement-award

Research Fellowship

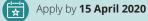
Apply by 15 April 2020

Open to ESPE members based in Europe who can demonstrate an interest in, and potential for, performing high quality research in paediatric endocrinology. One successful applicant will be awarded a grant of up to $\leq 140,000$ to conduct research at a leading institution.



Valentina Chiavaroli (Italy), ESPE Research Fellow 2015

Watch videos of two previous winners describing the impact of the Fellowship on their careers at the web address below.



www.eurospe.org/grants-awards/grants/ research-fellowship

44

I believe that I saw more than 300 patients with endocrine problems during my fellowship. Some cases I would not be able to see in my home centre" Elzbieta Niechcial (Poland)

Clinical Fellowship

Open to those wishing to pursue a career in paediatric endocrinology who have limited training opportunities in their home country.

Successful applicants will be supported to undertake practical, clinical training at a European centre of excellence.

Apply by **31 May 2020**

www.eurospe.org/ grants-awards/grants/ clinical-fellowship



Follow ESPE online...

Keep an eye on the latest ESPE news and activities at **www.eurospe.org**

You can also follow ESPE on Facebook and Twitter

f /EuroSPE



OPPORTUNIT

Council vacancies

Be at the heart of ESPE's strategic decisionmaking and help shape the field of paediatric endocrinology through its activities. Apply now if you are interested in joining ESPE's Council in September, as:

- Science Committee Chair
- Communication Committee Chair or
- Strategic & Finance Committee Chair.

Apply by **2 April 2020**

www.eurospe.org/about/vacancies/ council-vacancies-2020

Committee vacancies

NEWSLETTER EDITORIAL BOARD

Could you be part of the friendly, collaborative and productive team that creates and collates content for this popular newsletter? We would love to hear from you if you are interested in sourcing features on fascinating, cutting-edge research. Board members also help to write short hot topics (around three per year), so we're looking for someone comfortable with medical writing. The team receives lots of support from the ESPE Team and the Newsletter Project Manager.

Apply by **30 April 2020**



www.eurospe.org/about/vacancies

OTHER VACANCIES

We are also currently welcoming applications for members of our Communication, Clinical Practice and Andrea Prader Committees. All ESPE vacancies are advertised at the web address above.

EVENTS

We thank **Malcolm Donaldson** (UK), co-founder of the ESPE Maghreb School, who is stepping down as Steering Committee Co-ordinator. Malcolm is pictured with Asmahane Ladjouze (Algeria), the new Co-ordinator for 2020.



Asmahane Ladjouze and Malcolm Donaldson

RESOURCES

Patient leaflets

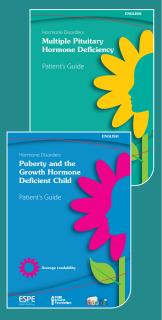
Recently reviewed and updated **patient information lea<u>flets</u>** are

now available on our website, covering diabetes, congenital adrenal hyperplasia, multiple pituitary hormone deficiency, craniopharyngioma, growth hormone deficiency, hypothyroidism and hyperthyroidism.

Produced as part of an ESPE initiative led by Gary Butler (UK), they are also endorsed by the British Society for Paediatric Endocrinology and Diabetes and by the Child Growth Foundation.

There are two readability levels: 'Easy' for patients and 'Average' for parents and guardians. Please use and share this resource (translations will be available in due course).







ESPE e-Learning

Supporting this issue's theme:

- Late Endocrine Effects of Treatment for Childhood Cancer – a chapter within Multiple Endocrine Deficits
- **Yu-Ting, a boy with leukemia** (in Growth and Growth Regulation) a case of small stature after oncological treatment.

In addition: the **Diabetes ISPAD Guidelines** have been updated and many cases have been added.

www.espe-elearning.org (registration is free)



John Gregory

We also thank **John Gregory** (UK), who has been Winter School Co-ordinator since 2014 and is stepping down this year. Justin Davies (UK) will be the new Co-ordinator for 2021.

SEE **PAGES 8–10** FOR MORE EVENTS NEWS:

- ESPE 2020
 Liverpool, UK
 10–12 September 2020
- ESPE Science Symposium Nijmegen, The Netherlands 30–31 October 2020
- > ESPE Connect 2021 Copenhagen Denmark 6–8 May 2021
- > ESPE Schools 2020
- > Dates and deadlines



Bringing you recent highlights from the world of research

Adiponectin receptor agonist counteracts adverse corticosterone effects

Systemic glucocorticoid (GC) treatment is the standard-of-care therapy for several autoimmune and inflammatory disorders. Because of its pleiotropic action, long term GC treatment can, however, lead to obesity, insulin resistance and osteoporosis, and induces growth retardation in children.

Nicolas et al. used the adiponectin receptor agonist AdipoRon in young mice treated with corticosterone for 7 weeks, to test whether the negative effects of GC treatment could be ameliorated. Application of AdipoRon during the last 20 days of treatment reversed weight gain by acting mainly on intra-abdominal fat and on corticosterone-induced adipocyte hypertrophy. Increased leptin and insulin were normalised by AdipoRon, as well as corticosterone-induced hypoglycaemia. There was, however, no effect on lean mass, bone mass and, consequently, body length, which was decreased by corticosterone treatment.

Since AdipoRon effectively reversed weight gain and partly normalised disturbances in glucose metabolism, it could be considered a potential therapeutic tool to counteract GC-induced side effects.

Read the full article at Nicolas et al. 2019 Metabolism 103 154027

Teplizumab: a step towards prevention of type 1 diabetes mellitus

A phase 2, randomised, placebo-controlled, double-blind trial of teplizumab (an Fc receptor non-binding anti-CD3 monoclonal antibody) was conducted in relatives of patients with type 1 diabetes who were at high risk for development of clinical disease. The study included 76 participants (55 (72%) were <18 years of age), who were randomly assigned to receive a single 14-day course of either teplizumab (n=44) or placebo (n=32).

Progression was assessed on the basis of oral glucose tolerance test at 6-monthly intervals. The disease was diagnosed in 19 (43%) of those who received teplizumab and in 23 (72%) of those who received placebo. The median time to the diagnosis was 48.4 months in the teplizumab group and 24.4 months in the placebo group. Thus, teplizumab delayed the progression of clinical disease in high risk participants.

Further studies with a larger number of at risk subjects and frequent dosing are required to see if teplizumab will prevent type 1 diabetes mellitus completely.

 \square

Read the full article at Herold et al. 2019 New England Journal of Medicine 381 603–613

Obesity-associated pancreatic islet inflammation

Chronic, low grade inflammation is a characteristic of obesity and type 2 diabetes mellitus (T2DM). Ying et al. have reviewed the immune cell-mediated inflammation in pancreatic islets in these insulin-resistant states and the consequences thereof for β -cell function.

In contrast to type 1 diabetes mellitus, the dominant immune cell type causing inflammation in obese and T2DM islets is the macrophage. The increased macrophage accumulation in T2DM islets primarily arises through local proliferation of resident macrophages, which then provide signals (such as platelet-derived growth factor) that drive β-cell hyperplasia (a classic feature of obesity). In addition, islet macrophages also impair the insulin secretory capacity of β-cells.

Through these mechanisms, islet-resident macrophages underlie the inflammatory response in obesity and mechanistically participate in the β -cell hyperplasia and dysfunction that characterise this insulin-resistant state. These findings point to the possibility of therapeutics that target islet inflammation, to elicit beneficial effects on β -cell function and glycaemia.

Read the full article at Ying et al. 2020 Nature Reviews in Endocrinology 16 81-90

Reduced mortality in carriers of CYP21A2 mutations

deficiency has an incidence of 1:10 000 to 1:20 000 in most

CAH patients identified from the Swedish National CAH Registry). matched for age and sex. The mortality and cause of death were

changes in the hypothalamic pituitary adrenal axis, with a more efficient cortisol response to stress in carriers of CYP21A2

Read the full article in Nordenström et al. 2019 Journal of Clinical Endocrinology & Metabolism 104 6148-6154

Late effects of haematopoietic stem cell transplantation

Wassim Chemaitilly examines the endocrine complications of paediatric haematopoietic stem cell transplantation, and the value of systematic screening.



Wassim Chemaitilly

Endocrine late effects are common in survivors of paediatric HSCT. Systematic screening creates opportunities for early diagnosis and treatment"

Indications for paediatric haematopoietic stem cell transplantation (HSCT) include haematologic malignancies, non-malignant haematologic disorders and inborn errors of metabolism. Conditioning for HSCT requires high dose myeloablative chemotherapy with or without total body irradiation (TBI). Prolonged treatment with glucocorticoids may be necessary to treat graft versus host disease. Long term survivors may experience late-onset complications after a variable latency period. Endocrine late effects have been reported in 60% of survivors treated before the age of 10 years.¹

Prevalence and risk factors

Impaired linear growth has been reported in 20-80% of survivors. Individuals treated with TBI are at risk for growth hormone deficiency (GHD), especially if TBI was delivered at higher doses and/or in a single fraction. Younger age at HSCT and previous treatment with cranial radiotherapy are additional risk factors for GHD.² Radiation-induced growth plate injury may further contribute to the risk of short stature.3

Among female survivors, 65-85% experience premature ovarian insufficiency, while 48-85% of males have azoospermia. This is due to the gonadotoxic nature of TBI and chemotherapy agents such as cyclophosphamide and busulfan. Males experience Leydig cell failure less frequently, unless they were previously treated with testicular irradiation.²

Up to 50% of survivors are diagnosed with primary hypothyroidism; TBI is the main risk factor. Transfer of autoimmune disease from the graft donor may further contribute to the risk.⁴ Survivors were reported to experience secondary thyroid cancer after a median latency time of 8.5 years post-TBI.⁵ Up to 21% of 5-year survivors have severe bone mineral density (BMD) deficit.6 Changes induced by leukaemia, exposure to TBI and/or glucocorticoids, endocrinopathies and lifestyle variables may contribute to the risk. Higher than expected rates of insulin resistance, impaired glucose tolerance and diabetes mellitus have been reported in survivors, especially following TBI. These complications frequently occur in the absence of obesity, and seem related to body composition alterations (decreased lean mass, increased body fat).7

Screening and management

It is reasonable to initiate screening 1 year after HSCT in the absence of symptoms, using recommendations such as those provided by the Children's Oncology Group.8 The management of endocrine disorders may follow guidelines used in non-cancer populations, with some adjustment to account for specific situations.

Attention to body proportions and careful pubertal staging are of utmost importance. Skeletal irradiation

disproportionately impacts spinal growth; this is best assessed by measuring and tracking sitting heights. Evaluation for GHD should include dynamic testing, as serum insulin-like growth factor-1 and insulin-like growth factor-binding protein-3 levels are not always reliable. GH replacement in survivors with GHD does not increase the risk of cancer recurrence or death from cancer; reported associations with secondary neoplasia are an area of active research.9 Treatment with GH may not allow full recovery of growth potential, given the frequency of other causes of poor growth.3

Treatment toxicity may impact testicular size without impairing testosterone secretion. Testicular volume is not a reliable indicator of puberty in male survivors. When in doubt, medical providers should measure morning serum testosterone levels.9 Fertility preservation via mature oocyte cryopreservation or sperm banking should be offered whenever feasible. Strategies using gonadal tissue cryopreservation are considered experimental, and may carry the risk of cancer cell re-seeding in individuals treated for haematologic malignancies.10

The use of ultrasound to screen for secondary thyroid cancer remains an area of controversy, given the lack of evidence supporting long term benefit when compared with periodic neck palpation by an experienced provider.¹¹ There is a paucity of data to guide the frequency of BMD screening studies and the long term benefits of bisphosphonates.¹² Similarly, it is unknown whether the use of glucose-lowering medications could delay the onset of diabetes mellitus in survivors with insulin resistance.7

In conclusion

Endocrine late effects are common in survivors of paediatric HSCT. Systematic screening creates opportunities for early diagnosis and treatment. Interventional studies aiming at improving metabolic health are lacking in this population.

Wassim Chemaitilly

Department of Pediatric Medicine, Division of Endocrinology, St Jude Children's Research Hospital, Memphis, TN, USA

References

- Hows et al. 2006 Bone Marrow Transplantation 38 799-805.

- Hows et al. 2006 Bone Marrow Transplantation **38** 799-805. Dvorak et al. 2011 Biology of Blood & Marrow Transplantation **17** 1725-1738. Chemaitilly et al. 2007 Bone Marrow Transplantation **40** 29-35. Boulad et al. 1995 Bone Marrow Transplantation **15** 71-76. Cohen et al. 2007 Journal of Clinical Oncology **25** 2449-2454. Kaste et al. 2004 Bone Marrow Transplantation **33** 435-441. Armenian et al. 2017 Biology of Blood & Marrow Transplantation **23** 201-210. Chow et al. 2016 Biology of Blood & Marrow Transplantation **22** 782-795. Sklar et al. 2018 Journal of Clinical Endocrinology **3** 556-567. Clement et al. 2018 Cancer Treatment Reviews **63** 28-39. Carpenter et al. 2007 Biology of Blood & Marrow Transplantation **13** 683-690.
- 10.

Fertility preservation in children and adolescents with cancer

Rodrigo Romao considers the issues surrounding fertility preservation for young people with cancer, and the importance of raising the subject with patients and their families.

A cancer diagnosis places an enormous burden upon paediatric patients and their families. Initial exchanges between families and the medical team will fittingly be devoted to treatment approaches, outcomes and the possibility of cure. Nonetheless, the overall positive survival outlook for paediatric oncologic patients compared with adults demands that long term treatment effects and survivorship issues be included in the discussion early on.

The impact of cancer treatment on fertility is real and multifactorial. Surgical removal of gonads, chemotherapy (particularly with alkylating agents like cyclophosphamide) and radiation exposure can impact reproductive function and lead to infertility.

Survivors of childhood cancer and their families *want* to know about these risks and what can be done to mitigate them. Some have argued that information about the potential for infertility and strategies for fertility preservation are part of the disclosure process of a new cancer diagnosis.¹

Strategies for fertility preservation

Fertility preservation strategies are variable, depending on age and sex. Sperm banking for post-pubertal males who are able to ejaculate is the most straightforward method, and should be considered in every male teenager diagnosed with cancer. In pre-pubertal boys, some centres have been offering a biopsy for testicular tissue cryopreservation, performed during the same anaesthetic as for other procedures, such as central line insertion, bone marrow biopsy and intra-thecal chemotherapy



using cryopreserved pre-pubertal testicular tissue in rodents and primates are promising, this option remains experimental in humans at this stage.² In post-pubertal females, embryo or oocyte cryopreservation are hindered by the need for ovarian hyperstimulation for at least 2–3 weeks, which can pose an often unacceptable delay in the start of cancer therapy Experimental ovarian tissue cryopreservation is also

an often unacceptable delay in the start of cancer therapy. Experimental ovarian tissue cryopreservation is also possible in pre-pubertal girls; the need for intra-abdominal surgery, albeit minimally invasive (laparoscopy), represents an important drawback. Laparoscopic ovarian transposition is also an option, to move the gonads out of the pelvic radiation field.³

administration. While recent reports of viable pregnancies

Barriers to fertility preservation

Despite the increase in understanding about this topic, many barriers still prevent fertility preservation in children and adolescents with cancer being offered routinely. Lack of knowledge among treating physicians, coupled with a desire to start treatment as quickly as possible, can be addressed by education and awareness campaigns.

Cost remains a major deterrent to fertility preservation, since upfront and maintenance fees for sperm and tissue banking are prohibitive to many families. Insurance coverage tends to be minimal to non-existent, from both private and public insurers.

At the IWK Health Centre in Halifax (Nova Scotia, Canada), a multidisciplinary oncofertility committee has been created. It meets regularly and has developed educational materials to be shared with patients and treating physicians at the time of diagnosis. We also assist newly diagnosed patients with information and in navigating the process for banking specimens and/or tissues, when so desired.

The field of fertility preservation for children and adolescents with cancer is still very much in its infancy, but it is unquestionable that significant advances have been made in the last few years, and great opportunities lie ahead.

Rodrigo Romao

Associate Professor of Surgery and Urology, IWK Health Centre, Dalhousie University, Halifax, Nova Scotia, Canada

References

- . Gupta et al. 2016 Journal of Urology doi:10.1016/j.juro.2016.02.2967. 2. Romao & Lorenzo 2017 Canadian Urological Association Journal **11** 97–102
- Romao & Lorenzo 2017 Canadian Urological Association Journal 11 97-102.
 Algarroba et al. 2018 Best Practice & Research: Clinical Obstetrics & Gynaecology 48 147-157.



Rodrigo Romao



Some have argued that information about the potential for infertility and strategies for fertility preservation are part of the disclosure process of a new cancer diagnosis"

Late effects of particle therapy for CNS tumours

Eva Bezak, Myxuan Huynh, Mikaela Dell'Oro and Thomas Merchant discuss the side effects of X-rays versus proton therapy.



Eva Bezak



Myxuan Huynh



Mikaela dell'Oro



Thomas Merchant

Paediatric tumours of the central nervous system (CNS) are the most common solid tumours, accounting for 20% of all cancers in children below the age of 15.¹ In the USA alone, more than 500 new cases of medulloblastoma, the most common malignant brain tumour in children, are diagnosed annually. CNS tumours, and brain tumours more specifically, are the leading cause of cancer-related burden in childhood cancer survivors, due to their high incidence of mortality and long term effects which impact somatic, neurologic, endocrine and cognitive outcomes.² Standard treatment strategies include a combination of surgery, chemotherapy and radiotherapy, all associated with complication risks.

X-rays (photons) are the most commonly used radiation therapy, but protons and heavy ions (e.g. carbon ions) are of increasing interest, due to the superior properties of their dose distribution, resulting in more conformal dose delivery to the tumour, and much lower dose to healthy tissues compared with traditional X-ray irradiation (see Figure, and this issue's cover). Questions remain regarding the long term effects of proton radiation therapy on paediatric patients.

X-ray radiotherapy

Paediatric brain tumour patients who undergo radiotherapy using photons experience a wide range of short and long term side effects. Short term side effects include nausea, vomiting, loss of appetite, headache, fatigue and hair loss.² Paediatric CNS cancer patients are also at increased risk of hormonal and growth problems, cognitive development deficits, and probability of developing second malignancies later in life.² Up to 62% of childhood cancer survivors report one or more radiationrelated late toxicities, with 33% being severe.³

Hearing loss impacts patient quality of life (QoL), communication skills, and social development,⁴ occuring with a latency of approximately 4 years. It is typically considered to be radiation-induced, though radiation is known to potentiate early ototoxicity effects of cisplatin.⁴

Neurocognitive effects of radiation therapy are associated with reductions in academic performance, employment rates and education opportunities in tumour survivors.² Survivors often report decreased QoL due to difficulties in attention and cognitive processing speed.² Cranial irradiation is associated with an IQ decline of 2–4 points per year.⁵ Risk factors for increased neurocognitive decline include younger age during treatment (<3 years old), large irradiated volumes and higher dose delivered.⁵ Deficits are known to correlate with the volume of cerebral white matter irradiated, particularly in the supratentorial brain, temporal lobe and hippocampal dentate gyrus.³

Up to 43% of survivors reported endocrine deficits, including osteoporosis, hypothyroidism and growth

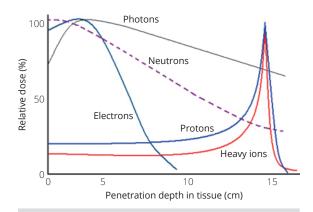
hormone deficiency (GHD).³ Total doses <30Gy to the pituitary have been associated with GHD in approximately 30% of patients, whilst mean doses <16.1Gy to the hypothalamus resulted in GHD in 50% of patients.³ Reductions in gonadotrophins and adrenocorticotrophic and thyroid-stimulating hormones have also been reported.³ These endocrine deficits correlate with high total doses to the hypothalamic-pituitary axis, and are increased when patients are treated at a younger age.³

All paediatric malignancies are associated with increased risks of second cancers following radiation therapy.⁶ X-ray therapy is associated with the development of solid malignancies, such as thyroid neoplasms and sarcomas, particularly in the treatment of CNS tumours such as gliomas and meningiomas.³

Proton therapy

Proton therapy has been found to provide survival and tumour control outcomes for paediatric CNS cancers comparable with photon therapy, with reduced incidence of severe acute and late toxicities. This includes reduced severity of endocrine and neurological deficits. Papers comparing proton and photon cohorts also reported reduced haematological and gastrointestinal toxicities,⁷ improved QoL scores,⁸ and reduced IQ changes with the use of proton therapy.⁵ Reduced incidence of second cancers with proton therapy has also been reported.⁶

While the technology is still fairly novel and data collection is still in progress, the literature reports no significant reduction in IQ scores from baseline to follow up with the use of proton therapy.^{9–13} However, increased risks of neurological decline have been associated with patients <7 years of age, high doses to the left temporal lobe or hippocampus, infratentorial tumour location,



Radiation dose deposition in water by X-rays, electrons and protons. Dose deposition by protons for cancer therapy is superior to that of X-rays and electrons, as most of the energy can be deposited within the tumour volume, sparing the adjacent healthy tissues.

ESPE NEWSLETTER / ISSUE 47 / SPRING 2020

EVENTS

FEATURE

medulloblastoma/pancreatic neuroendocrine tumour histology, larger tumour size, and longer time since radiation therapy.^{5,9} A significant decline in processing speed scores by a mean of 5.2 points (despite no significant change in overall full scale intelligence quotient (FSIQ) scores) was also reported.¹² Another study reported an overall decrease in FSIQ of 1.5 points per year, related to decreases in processing speed and verbal comprehension index with the use of proton therapy.14

Reported endocrine deficits as a result of proton therapy ranged from grade 0 to grade 2. The majority of reported endocrine deficits included GHD or hypothyroidism, 10,11,13-18 while others included adrenal/ cortisol deficiency and sex hormone deficiency.^{10,14} Doses >40Gy to the hypothalamus and pituitary correlated with the incidence of neuroendocrine deficits.^{9,14} 73% of patients receiving ≥40Gy to the hypothalamus reported neuroendocrine deficits, compared with 44% in patients receiving doses <40Gy.14

While evidence exists in support of proton therapy for paediatric CNS patients, it is still scarce. Data are often difficult to analyse, as some studies used mixed patient cohorts (adults and children). Frequently, no distinction is made between higher risk patients (<3 years of age) and the main cohort. There are large variations in patients' overall treatments (e.g. surgery extent, details of chemotherapy regimens), which all have compounding or even synergistic effects on toxicities. Results are also affected by insufficient durations of follow up, thus limiting the validity and reliability of reported literature. However, the reports are positive and promising, and the medical specialists involved in the treatment of childhood brain tumour patients are eager to learn of high quality evidence for the use of proton therapy across all tumour types.

Eva Bezak, Myxuan Huynh and Mikaela Dell'Oro

Cancer Research Institute and School of Health Sciences, University of South Australia and Royal Adelaide Hospital, Adelaide, SA, Australia

Thomas Merchant

St Jude Children's Research Hospital, Memphis, TN, USA

References

- Parkin et al. (Eds) 1998 International Incidence of Childhood Cancer, Vol II. IARC Scientific Publication **144** https://publications.iarc.fr/Book-And-Report-Series/ Iarc-Scientific-Publications/International-Incidence-Of-Childhood-Cancer-Volume-II-1998
- Australian Institute of Health and Welfare 2017 Brain and Other Central Nervous System Cancers www.aihw.gov.au/reports/cancer/brain-other-central-nervous-2

- System-cancers. Gondi et al. 2016 Nature Reviews Neurology **12** 334–345. Moeller et al. 2011 Radiation Oncology **6** 58. Kahalley et al. 2013 International Journal of Radiation Oncology, **34** 1043–1049. Chung et al. 2013 International Journal of Radiation Oncology, Biology, Physics **87** 46–52. 5. 6.
- 8
- Song et al. 2014 Acta Oncologica **53** 1158–1164. Yock et al. 2014 Acta Oncology & Oncology **113** 89–94. Greenberger et al. 2014 International Journal of Radiation Oncology, Biology, 9. Physics 89 1060-1068.
- 10 Jimenez et al. 2013 International Journal of Radiation Oncology, Biology, Physics 87 120–126.
- MacDonald et al. 2011 International Journal of Radiation Oncology, Biology, Physics 11. 79 121-120
- Pulsifer et al. 2015 International Journal of Radiation Oncology, Biology, Physics 93 12 400-407. 13

- 400-407. MacDonald et al. 2013 Neuro-Oncology **15** 1552–1559. Yock et al. 2016 Lancet Oncology **17** 287–298. Ares et al. 2016 Journal of Neuroancology **128** 137–145. De Amorim Bernstein et al. 2013 International Journal of Radiation Oncology, Biology, Physics **86** 114–120. Indelicato et al. 2017 Pediatric Blood & Cancer doi: 10.1002/pbc.26654. Eigencember et al. 2007 Serableshbergie & Ocilectical **129** 2668. 16.
- 17. 18. Timmermann et al. 2007 Strahlentherapie & Onkologie 183 685-688



X-rays are the most commonly used radiation therapy, but protons and heavy ions are of increasing interest ... Questions remain regarding the long term effects of proton radiation therapy on paediatric patients"

ESPE SCIENCE SYMPOSIUM

CAH: from molecular medical research to clinical application

30-31 October 2020 Nijmegen, The Netherlands

Register now for ESPE's second Science Symposium, featuring interactive lectures by renowned scientists from around the world, along with discussion and networking time. Clinicians and researchers will discover the very latest developments in congenital adrenal hyperplasia (CAH), and make new connections.

- €80 including dinner on the first night
- 25 free registrations available to young cliniciansand scientists-in-training
- Hosted by Hedi L Claahsen and her team at the Radboud DSD Centre
- Supported by the Endo-ERN and the ESPE DSD Working Group



Apply by 1 June 2020

Programme and registration: www.espe-science-symposium-2020.com



CALL FOR PROGRAMME SUGGESTIONS

ESPE Connect 2021 6-8 May 2021

Copenhagen, Denmark

- ESPE's 60th Annual Meeting has moved to May • to make way for the International Meeting of Pediatric Endocrinology in September 2021
- It will focus on career development, forming • collaborations and a practical approach, with fewer symposia and more 'How do I...?' and 'Meet the Expert' sessions
- The Meeting's theme will be 'Sustainable excellence in endocrinology'



Please submit your programme suggestions by 23 April 2020

Send them to espe2021@bioscientifica.com or via www.surveymonkey.co.uk/r/ZBJ3CH8

EVENTS



020

6 April 2020 (23.59 BST)

(23.59 BST)



Lifelong endocrine care through collaboration, discovery and innovation

Mehul Dattani (President, ESPE 2020) Poonam Dharmaraj (Vice-President, ESPE 2020)

www.espe2020.org

Prizes and grants



www.eurospe.org/grantsawards/espe-meetinggrants

Fraudulent registration websites

The ESPE website (at www.eurospe. org or www.espe2020.org) is the

Apply for ESPE schools this spring

Application deadlines for a number of ESPE schools are fast approaching. Don't miss your opportunity to request a place.

www.eurospe.org/education





Obesity & Metabolism School 13-15 September 2020 Lake Windermere, UK



ESPE Caucasus & Central Asia School Nur-Sultan, Kazakhstan, October 2019



ESPE Maghreb School, Sousse, Tunisia, November 2019

Future meetings

See **www.eurospe.org/meetings** for details of all future meetings



59th Annual ESPE Meeting 10–12 September 2020 Liverpool, UK





60th Annual ESPE Meeting 6–8 May 2021 Copenhagen, Denmark





11th InternationalMeeting of PediatricEndocrinology25-28 September 2021

Buenos Aires, Argentina





OTHER EVENTS

SEPTEMBER

ESPE Summer School 7–9 September 2020 Lake Windermere, UK

ESPE Diabetes, Obesity & Metabolism School 13–15 September 2020 Lake Windermere, UK

OCTOBER

ESPE Caucasus & Central Asia School 7–10 October 2020

Tbilisi, Georgia **ESPE Science Symposium** 30–31 October 2020 Nijmegen, The Netherlands

NOVEMBER

ESPE Maghreb School 16–20 November 2020 Morocco

nber 2020 30–3 nere, UK Nijme

DEADLINES

APRIL

ESPE Council vacancy applications 2020 – 2 April 2020 ESPE Undergraduate Achievement Award applications – 15 April 2020 ESPE Research Fellowship applications – 15 April 2020 ESPE Research Unit final applications – 15 April 2020 ESPE Caucasus & Central Asia School 2020 applications – 15 April 2020 ESPE 2021 Programme submission of suggestions – 23 April 2020 ESPE News Editorial Board vacancy applications – 30 April 2020 ESPE Communication Committee vacancy applications – 30 April 2020

MAY

ESPE Clinical Practice Committee vacancy applications – 1 May 2020 ESPE Maghreb School applications – 15 May 2020 ESPE Clinical Fellowship applications – 31 May 2020

JUNE

ESPE Science Symposium 2020 registration – 1 June 2020 ESPE Diabetes, Obesity & Metabolism School 2020 applications – 3 June 2020



Paediatric Endocrinology

endocrine diseases by promoting knowledge and research

Secretary General:

Professor Anita Hokken-Koelega p.a. Stichting Kind en Groei PO Box 23068 3001 KB Rotterdam The Netherlands

ESPE Newsletter

© 2020 The European Society for Paediatric Endocrinology The views expressed by the contributors are not necessarily those of ESPE

Editor:

Dr Sarah Ehtisham Department of Paediatric Endocrinology Mediclinic City Hospital Dubai, UAE E: Sarah.Ehtisham@mediclinic.ae

Editorial Board:

Dr Meghna Chawla (Pune, India) Dr Antje Garten (Leipzig, Germany) Dr Abel López-Bermejo (Girona, Spain) Dr María Salomón Estébanez (Manchester, UK)

Sub-Editor: Caroline Brewser

Designed by: www.corbiculadesign.co.uk

Published by:

Bioscientifica Ltd Starling House 1600 Bristol Parkway North Bristol BS34 8YU, UK W: www.bioscientifica.com *Bioscientifica is a subsidiary of the Society for Endocrinology*

ESPE Office

Bioscientifica Ltd (address above) manages the ESPE Office. It is also the Professional Congress Organiser (PCO) for ESPE's Annual Meetings.

ESPE Senior Operating Officers: Joanne Fox-Evans and Hannah Bonnell

For ESPE enquiries, including membership: T: +44 (0)1454 642246 F: +44 (0)1454 642222 E: espe@eurospe.org W: www.eurospe.org

f www.twitter.com/EuroSPE

y www.facebook.com/EuroSPE

ESPE News archive

You will find previous newsletters in the archive at www.eurospe.org/ news/newsletters