# MRI changes in time after cranial irradiation, and their relation with pituitary function in survivors of childhood medulloblastoma

Wilhelmina Children's Hospital

C. van Ommen[1], L. van Iersel[1], M. Lequin[2], S. Clement[3], G. Janssens[4], A.M. Boot[5], H.N. Caron[3], H.L. Claahsen-van der Grinten[6], B. Granzen[7], K.S. Han[8], E.M. Michiels[9], A.S.P. van Trotsenburg[3], W.P. Vandertop[3], D.G. van Vuurden[3], A.Y.N. Schouten-van Meeteren[3], L. Kremer[3], H.M. van Santen[1]

[1]Pediatric Endocrinology, Wilhelmina Children's Hospital, University Medical Center Utrecht (UMCU); [2]Radiology, UMCU; [3]Amsterdam University Medical Centres; [4]Radiotherapy, Princess Maxima Center & UMCU; [5]Pediatric Endocrinology, University Medical Center Groningen; [6]Pediatric Endocrinology, Radboud University Medical Center, Nijmegen; [7]Pediatric Oncology, Maastricht University Medical Center; [8]Neurosurgery, UMCU, [9]Pediatric Oncology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam.

## Background

Hypothalamic-pituitary (HP) deficiencies are frequent in childhood brain tumor survivors (CBTS) after cranial radiation. It is not known whether MRI changes in time in the HP-region or in brain volume are predictive of HP dysfunction.

We performed this study to quantify changes in the HP-region on MRI in CBTS after exposure to craniospinal radiotherapy (CRT) and analyzed its relationship with changes in HP-function.

## Methods

Ninety childhood medulloblastoma survivors selected from a previous reported nationwide cohort[a] and treated with CRT between January 2002 and December 2012, were included.

All MRI scans were retrospectively systematically evaluated regarding the anatomy of the HP-region, at time of diagnosis, post-neurosurgical intervention, post-radiation and during follow up at 2 time points until 5 years of FU.

The observers were blinded for outcome of HP function. Additional data on endocrine function and growth were collected.

## Measurements

The pituitary gland (PG) was measured on mid-sagittal and coronal images. The pituitary stalk (PS) was assessed by measuring the ratio of the PS to basilar artery (BA) on axial images on the same plane in the middle of the PS.

Volume measurements of the PG were performed. Absolute and Z scores were calculated for pituitary volume and measurements of PG and PS in childhood and adolescence[b,c].

Statistical analyses were performed by SPPS (General Linear Model repeated measure with Bonferroni correction).

**Table 1.** Patient Demographics and Clinical Characteristics (N = 90)

| Characteristic | No. (%) |
|---|---|
| Sex | |
| Male | 35 (38.9) |
| Female | 55 (61.1) |
| Age at diagnosis (y) (categoral) | |
| 0-5 | 26 (28.9) |
| >5-10 | 35 (38.9) |
| >10-15 | 24 (26.7) |
| >15 | 5 (5.6) |
| Hydrocephalus at diagnosis | |
| Yes | 75 (83,3) |
| No | 13 (14.4) |
| Relapse since primary cancer diagnosis | |
| Yes | 5 (5.6) |
| No | 85 (94.4) |
| Availability of MRI images: | |
| Pre-surgery | 70 (77.8) |
| Post-surgery | 71 (78.9) |
| 6 weeks after radiotherapy | 75 (80.0) |
| 1 year after radiotherapy | 72 (80.0) |
| 5 years after radiotherapy | 78 (86.7) |
| Pituitary disorder before treatment * | |
| Yes | 1 (1.1) |
| No | 89 (98.9) |
| Pituitary disorder after treatment * | |
| Yes | 57 (63.3) |
| No | 33 (36.7) |

* Pituitary disorder was defined as presence of growth hormone deficiency, central hypothyroidism, central hypocortisolism, central diabetes insipidus, or central pubertas praecox.

**Figure 1** (right):

(A) height and coronal width of the PG on coronal plane. (B) Width of the PG on sagittal plane. (C) PS and BA on axial plane.

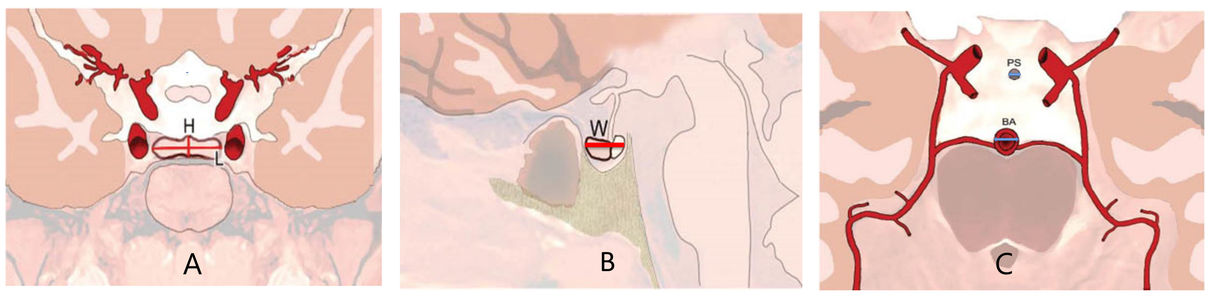
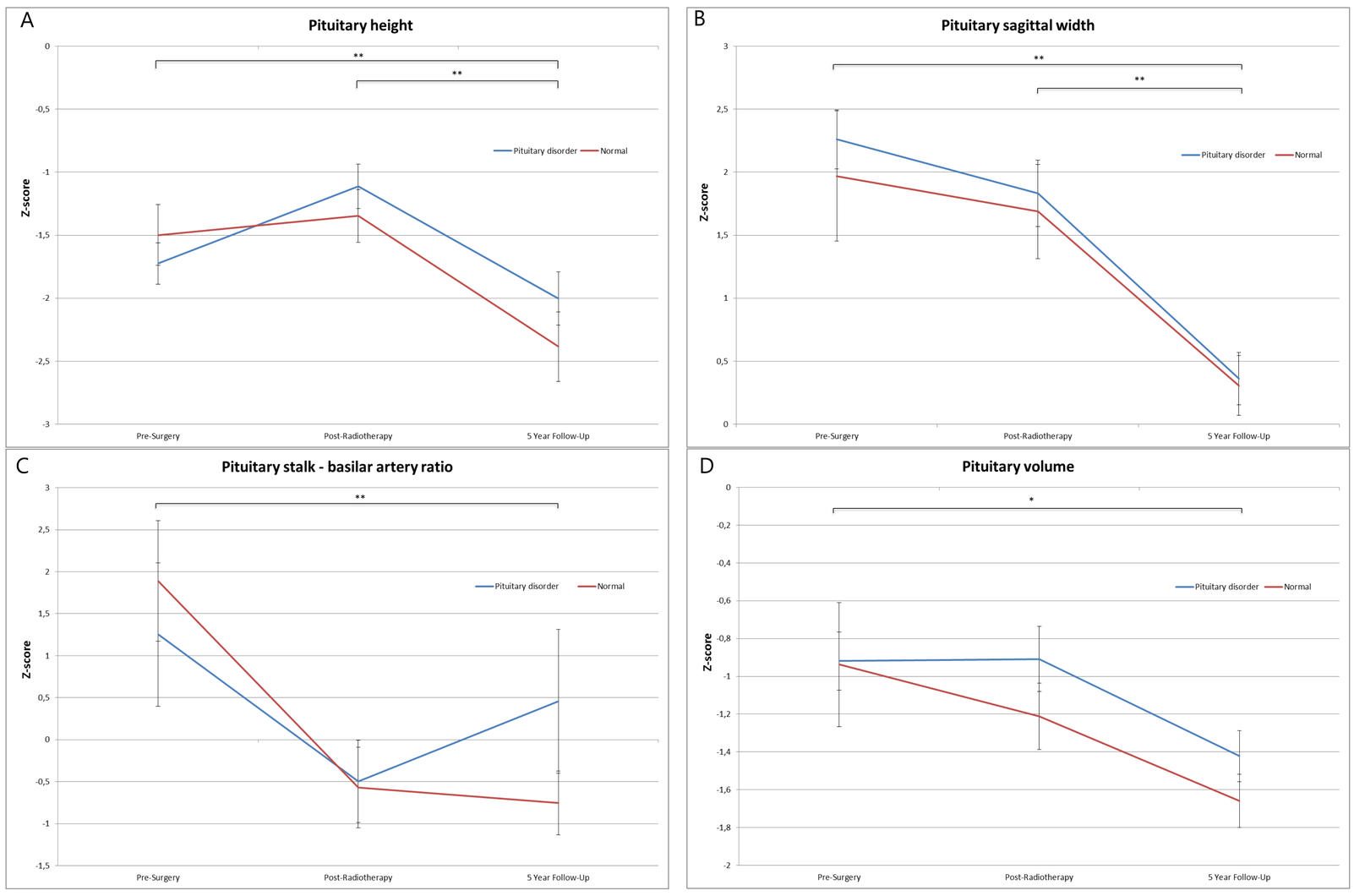



**Figure 2** (below):

Development of (A) pituitary height, (B) pituitary sagittal width, (C) PS/BA ratio, (D) pituitary volume in time (Z-score) for CBTS with and without pituitary disorder after CRT.
* = p < .05 ** = p < .01




## Results

In CBTS exposed to CRT, Z-scores for pituitary height, sagittal width, PS/BA ratio and pituitary volume decline in time, potentially indicating an effect of radiation damage with significant differences between start of treatment and last moment of follow-up. The presence of pituitary disease did not have an overall effect or interaction with time. Pituitary disease only showed an interaction effect with time and group on a marginal trend level towards significance for PS/BA ratio.

## Conclusions

Preliminary results show that cranial radiation in childhood has a negative effect on size of pituitary height, sagittal width, PS/BA ratio and pituitary volume. These effects could not be related to development of endocrine dysfunction as no significant difference was found between children with and without pituitary disease. This may possibly be explained by under diagnosis of pituitary dysfunction in the patients now classified as having adequate pituitary function. Further subgroup analyses will be performed.

[a]Prevalence and Risk Factors of Early Endocrine Disorders in Childhood Brain Tumor Survivors: A Nationwide, Multicenter Study. JCO 34:4362-4370. 2016
[b]Measures of pituitary gland and stalk: from neonate to adolescence. JPEM 2014; 27 (11-12): 1071-1076 [c]Normative human brain volume growth. J. Neurosurg Pediatr 21: 478-485, 2018