Bone Mass and Fracture Prevalence in Childhood Brain Cancer Survivors 2, 5 or 7 years after off therapy

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BACKGROUND and AIM

Multifaceted risk factors impair bone mass (BM) in childhood brain cancer survivors (CBCS), yet their impact on bone mineral density (BMD) and the potential for recover of BM over time are still unclear. Aims of the study were to evaluate bone mass and it's determinants and fracture prevalence in CBCS 2 (G+2), 5 (G+5) or 7 (G+7) years after off therapy (OT).

SUBJECTS and METHODS

CBCS subjects

- G+2: n=73, 36 F and 37 M, mean age 12.9±4.2 yrs;
- G+5: n=87, 38 F and 49 M, mean age 14.9±4.4 yrs;
- G+7: n=66, 29 F and 37 M, mean age 16.6±4.4 yrs;
- Diagnoses:
  - astrocytic tumors (G+2:n=25,G+5:n=24,G+7:n=20)
  - embryonal tumors (G+2:n=19,G+5:n=28,G+7:n=20)
  - germinomas (G+2:n=13,G+5:n=18,G+7:n=12)
  - sellar region tumors (G+2:n=13,G+5:n=10,G+7:n=9)
  - ependimomas (G+2:n=3,G+5:n=7,G+7:n=5)
- Radiotherapy:
  - CRT G+2: n=38/73, mean total dose 45.7±13.5 Gy
    G+5: n=44/87, mean total dose 44.7±14.0 Gy
    G+7: n=33/66, mean total dose 45.1±14.2 Gy
  - CSRT G+2: n=27/73, mean total dose 31.0 ±14.3 Gy
    G+5: n=37/87, mean total dose 31.9 ±12.4 Gy
    G+7: n=27/66, mean total dose 30.3±10.0 Gy
- Hormone defects:
  - Growth hormone deficiency (GHD) n=38 (G+2), n=67 (G+5), n=46 (G+7)
  - Hypogonadism (HH) n=15 (G+2), n=28 (G+5), n=22 (G+7)

Study design: monocentric cross-sectional observational study

Methods: All patients underwent:

- height (cm, SDS), BMI (SDS), pubertal (Tanner stage) evaluation
- DXA (Lunar Prodigy Advance, GE) measurements for:
  - BMD (g/cm^2, Z-score), BMC (g) at the lumbar spine (L1–L4=L) and at the total body less head (TB); lumbar BMAD (g/cm^3) was calculated;
  - fat (FM, Kg) and lean mass (LM, Kg)

RESULTS

Table 1. Age, clinical and body composition characteristics of CBCS 2, 5 or 7 yrs after OT in females and males

	G+2 Females M ± SD, n=36	G+2 Males M ± SD, n=37	G+5 Females M ± SD, n=38	G+5 Males M ± SD, n=49	G+7 Females M ± SD, n=29	G+7 Males M ± SD, n=37
Age at DGN *(yrs)*	8.2 ± 4.4	9.1 ± 4.2	7.7 ± 4.2	8.2 ± 4.5	7.3 ± 4.1	7.4 ± 4.3
Age at OT *(yrs)*	10.3 ± 4.2	11.5 ± 4.2	9.5 ± 4.7	10.2 ± 4.1	9.0 ± 4.3	9.9 ± 4.6
Age at DXA *(yrs)*	12.3 ± 4.2	13.5 ± 4.2	14.5 ± 4.8	15.2 ± 4.2	16.1 ± 4.3	17.0 ± 4.6
Ht *(SDS)*	-0.7 ± 1.4*	-0.4 ± 1.6	-0.9 ± 1.1**	-0.2 ± 1.3	-0.8 ± 1.4	-0.5 ± 1.5
BMI *(SDS)*	0.8 ± 1.2*	0.7 ± 1.1	0.7 ± 1.4*	0.6 ± 1.2	0.9 ± 1.3*	0.9 ± 1.2
Fat Mass *(kg)*	20.4 ± 12.2	19.8 ± 8.5	20.8 ± 10.6	19.0 ± 8.5	24.4 ± 11.5	25.9 ± 13.5
Fat Mass *(%)*	44.6 ± 7.2**	39.7 ± 8.7	44.5 ± 6.7**	35.2 ± 7.9	44.6 ± 5.5**	36.7 ± 8.0
Lean Mass *(kg)*	23.4 ± 10.3**	30.6 ± 13.5	24.6 ± 9.5**	34.1 ± 11.0	28.6 ± 10.3**	38.9 ± 13.1
Tanner PP; P *(n, %)*	8; 28 *(22.2; 77.7)*	11; 26 *(29.7; 70.3)*	8; 30 *(21.0; 78.9)*	9; 40 *(18.4; 81.6)*	3; 26 *(10.3; 89.7)*	4; 33 *(10.8; 89.2)*
Fractures *(n, %)*	4 *(11.1)*	1 *(2.7)*	2 *(5.3)*	0	1 *(3.4)*	0

*P-value: *<0.05 (F vs M); **<0.0001 (F vs M);* PP=prepubertal, P=pubertal

Figure 1. Height SDS, BMI SDS, L1-L4 and TBLH BMD Z-score in Groups +2, +5 and +7 CBCS

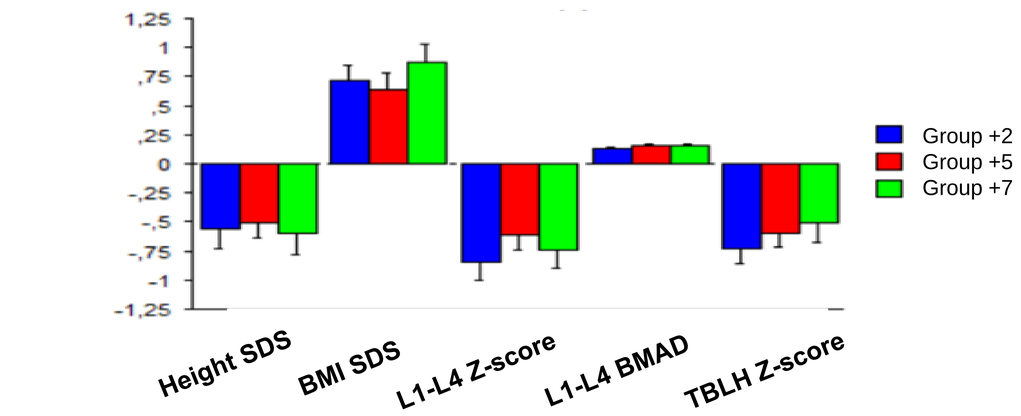

Figure 2. BMD Z-score distribution based on OT and gender

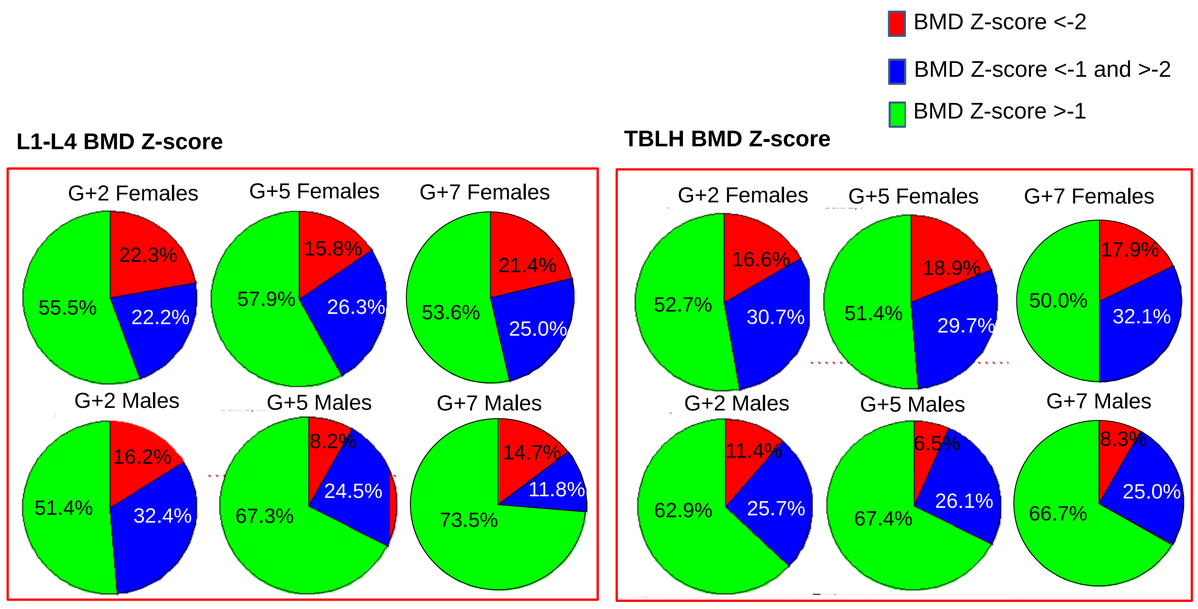

Figure 3. L1-L4 and TBLH BMD Z-score in GHD and no GHD CBCS in Groups +2, +5 and +7

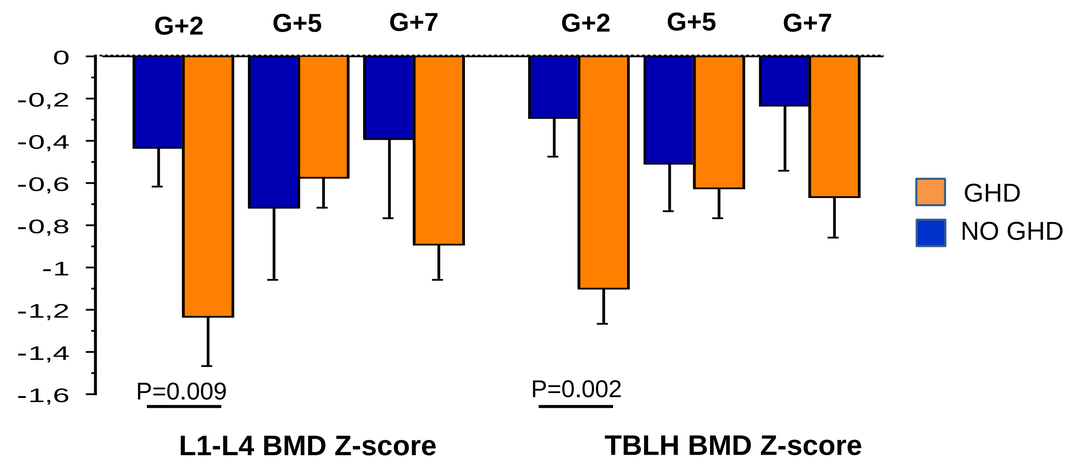

Figure 4. L1-L4 and TBLH BMD Z-score in HH and no HH CBCS in Groups +2, +5 and +7

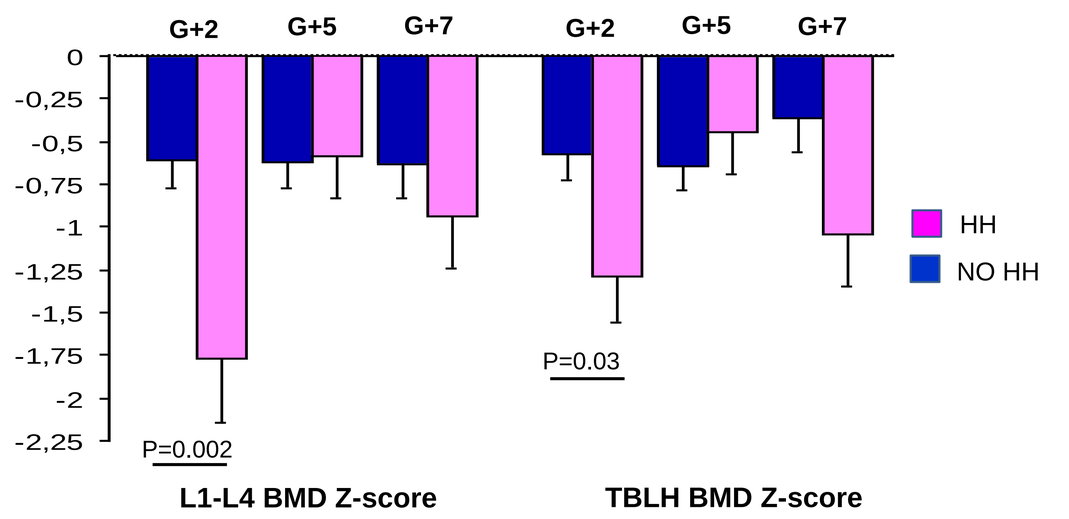

Table 2. Multivariable Regression Analyses for L1-L4 and TBLH BMD Z-score prediction in Groups +2, +5 and +7

L1-L4 BMD Z-score*	β stand.			P value			Adj.R^2		
	G+2	**G+5**	**G+7**	**G+2**	**G+5**	**G+7**	**G+2**	**G+5**	**G+7**
HH	0.09	0.10	0.11	<0.001	<0.001	0.004	0.351	0.159	0.113
Ht SDS	0.32	0.26	0.33	0.02	ns	ns			

TBLH BMD Z-score*	β stand.			P value			Adj.R^2		
	G+2	**G+5**	**G+7**	**G+2**	**G+5**	**G+7**	**G+2**	**G+5**	**G+7**
Ht SDS	0.07	0.08	0.11	<0.001	0.002	ns	0.835	0.428	0.229
Lean Mass	0.01	0.01	0.02	ns	<0.001	0.009			

* After correction for gender, GHD, HH, height SDS, %fat mass, lean mass

CONCLUSIONS

- Older, shorter, GHD and HH CBCS are at risk of decreased BM after 2 yrs OT
- A low BMD for age and sex (< -1 Z-score) persists at both L1-L4 and TBLH sites up to 7 years after OT, in particular in females
- However, the fracture prevalence remains low
- Strategies to optimize height should be undertaken:
  - early diagnosis and treatment of GHD and HH
  - optimization of lean mass.

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Bone, growth plate and mineral metabolism

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