



High metabolic risk is associated with small hypothalamic volume in Acute Lymphoblastic Leukemia survivors 34 years after cranial radiotherapy

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Conclusion

ALL women treated with CRT are at high risk of metabolic abnormalities in association with a smaller HT volume 34 years after ALL diagnosis. These findings suggest an hypothalamic effect of the metabolic complications.

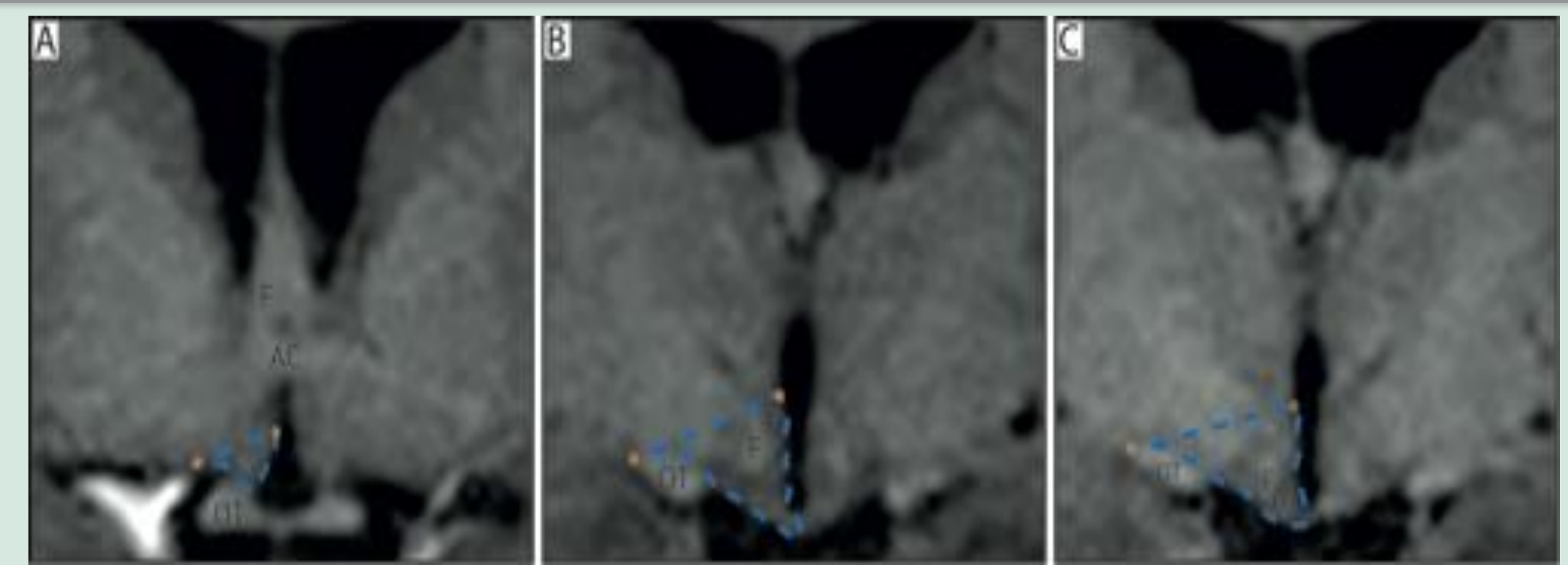
Background: There is an increased risk for metabolic complications in ALL survivors treated with cranial radiotherapy (CRT). These complications include obesity, lipid abnormalities, insulin resistance and the etiology is not well understood. The hypothalamus (HT) is a small complex area of the brain involved in endocrine function and metabolic control. In ALL survivors, assessment of the volume of the HT in relation to metabolic parameters including ghrelin, an orexigenic peptide stimulating food intake, has not been performed previously.

Aim: To assess the volume of the HT in relation to metabolic parameters including, insulin, leptin and ghrelin in ALL survivors.

Method

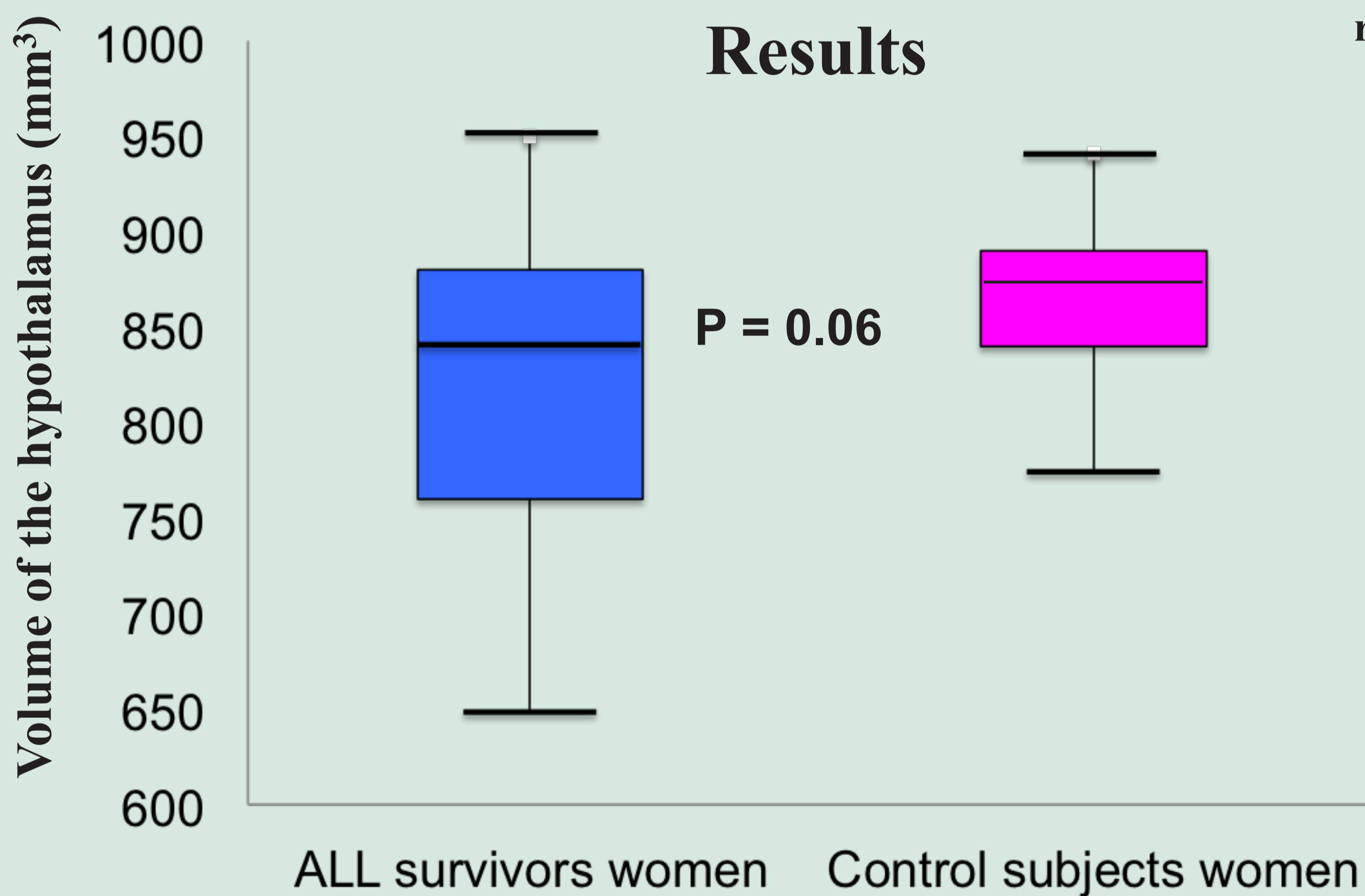
- Thirty-four (21 women) ALL survivors, on complete hormone supplementation
- 34 years after ALL diagnosis.
- Median-age: 38 (27-46) years
- CRT dose of 24 Gy.
- Comparison was made with 31 matched controls.

- BMI (kg/m²)
- Waist (cm)
- Fat mass (kg)
- Fat free mass (kg)
- P-glucose (mmol/L)
- P-Insulin (mIE/L),
- Homa-Index,
- S-leptin (µg/L) and
- S-Ghrelin (ng/L)
- MRI (3 tesla)



Overview of the boundaries used to delineate the hypothalamus in T1-weighted MRI acquired at 3T according to the procedure established by Gabery et al., 2014 (20). A-C represent the hypothalamic region in a coronal plane from rostral to caudal direction. The blue dashed lines illustrate how the hypothalamic region was delineated. Landmarks such as the hypothalamic sulcus and the lateral or medial edge of the optical tract represented by orange stars were identified for the delineation. A straight line between these two points was drawn to set the superior/lateral border of the area. The optical tract was excluded in all slides.

Results



ALL women (N=21)

	ALL women	Controls women	P
• BMI	27.9 (18.1-39.1)	22.6 (20-33)	0.002
• Waist	89 (73-110)	79 (69-105)	0.002
• Fat mass	29.9 (12.9-55.2)	22.4 (15.6-48.5)	0.001
• Fatfree mas	35.4 (26-48.9)	41.6 (35.5-46.7)	0.002
• P-Glucos	5.2 (4.1-6.5)	4.9 (4.1-6.0)	0.07
• Insulin	10 (2-31)	6 (4-16)	0.003
• Homaindex	0.15 (0.02-0.5)	0.07 (0.04-0.19)	0.04
• S-Leptin	33 (13-90)	13 (7.3-40.0)	<0.001
• Leptin/kg FM	1.09 (0.7-1.9)	0.6 (0.4-1.0)	<0.001
• fs-Ghrelin	1560 (556-3670)	993 (585-1710)	0.01

S-leptin levels were negatively correlated with the HT volume among the 34 ALL survivors, but not among the matched controls (P > 0.3)

The volume of the HT was negatively correlated with fat mass among the 34 ALL survivors, but not among the controls

