

SUPPLEMENTARY DATA

Individual description of the four patients:

Patient 1 - A 16-year-old man diagnosed with a pineal lesion in 2010 whose stereotaxic biopsy revealed a dysgerminoma. Chemotherapy and radiotherapy were performed with good response and no medication was in use recently. His BMI was 19.3 kg/m² and the highest salivary melatonin level was 1 pmol/L at 22:00.

Patient 2 – A 19-year-old man diagnosed with a pineal tumor in 2013 was submitted to two surgical procedures and two cycles of chemotherapy and radiotherapy and to four autologous bone marrow transplantations. The pathological examination revealed a pineoblastoma grade IV. He did not use any medication and his BMI was 22.03 kg/m². The salivary melatonin levels were below the limit of detection.

Patient 3 – A 20-year-old man diagnosed with a pineal lesion after a ventriculoperitoneal shunt procedure due to hydrocephalus had 25 radiotherapy and nine chemotherapy sessions performed resulting in panhypopituitarism, diabetes insipidus and depression, taking hydrocortisone, phenytoin and desmopressin, testosterone cypionate injections, levothyroxine and amitriptylin. His BMI was 28.6 kg/m² and salivary melatonin levels were below the limit of detection.

Patient 4 – A 32-year-old man with a pineal tumor diagnosed in 2007 was submitted to a surgical procedure with pathological examination showing a germinoma and to one radiosurgery and 20 sessions of radiotherapy. The only medication used was levothyroxine due to primary hypothyroidism. The BMI was 30.4 kg/m² and the highest salivary melatonin level was 1.36

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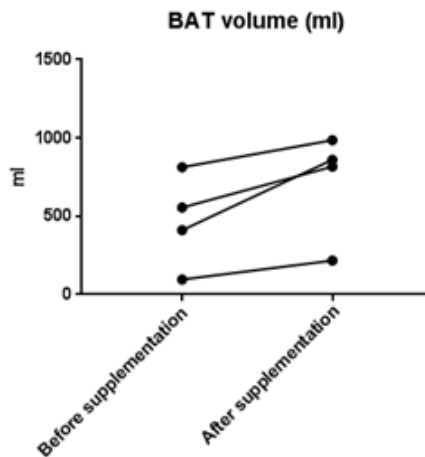
Supplementary Table SA1. Peak melatonin levels and time of each individual patient during an overnight stay in Hospital before and after melatonin replacement (BLD – below level of detection)

	Before intervention	After intervention
Patient 1	1 pg/mL (22:00)	22.83 pg/mL (22:00)
Patient 2	BLD	16.28 pg/mL (04:00)
Patient 3	BLD	7.48 pg/mL (01:00)
Patient 4	1.36 pmol/l (13:00)	Not performed

Supplementary Table SA2. Mean outdoor temperature in the day of each exam (source: timeanddate.com)

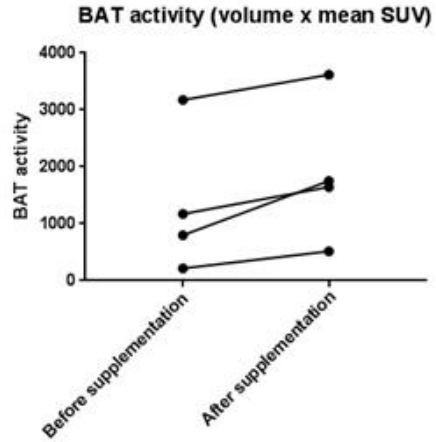
	Before melatonin supplementation	After melatonin supplementation
Patient 1	19.5 °C	12 °C
Patient 2	17 °C	18 °C
Patient 3	17.5 °C	26 °C
Patient 4	16.5 °C	24.5 °C

Supplementary Figure SA1. BAT volume (ml) before and after melatonin supplementation, considering a SUV threshold of 1.5 ($p= 0.0159$)



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Supplementary Figure SA2. BAT activity (ml x mean SUV) before and after melatonin supplementation, considering a SUV threshold of 1.5 (p=0.0199)



Supplementary Figure SA3. BAT volume by outdoor temperature – p=0.26

