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Impact of Radiotherapy on Oxidative Stress and Inflammatory Biomarkers in Brain Tumor Patients – preliminary studies

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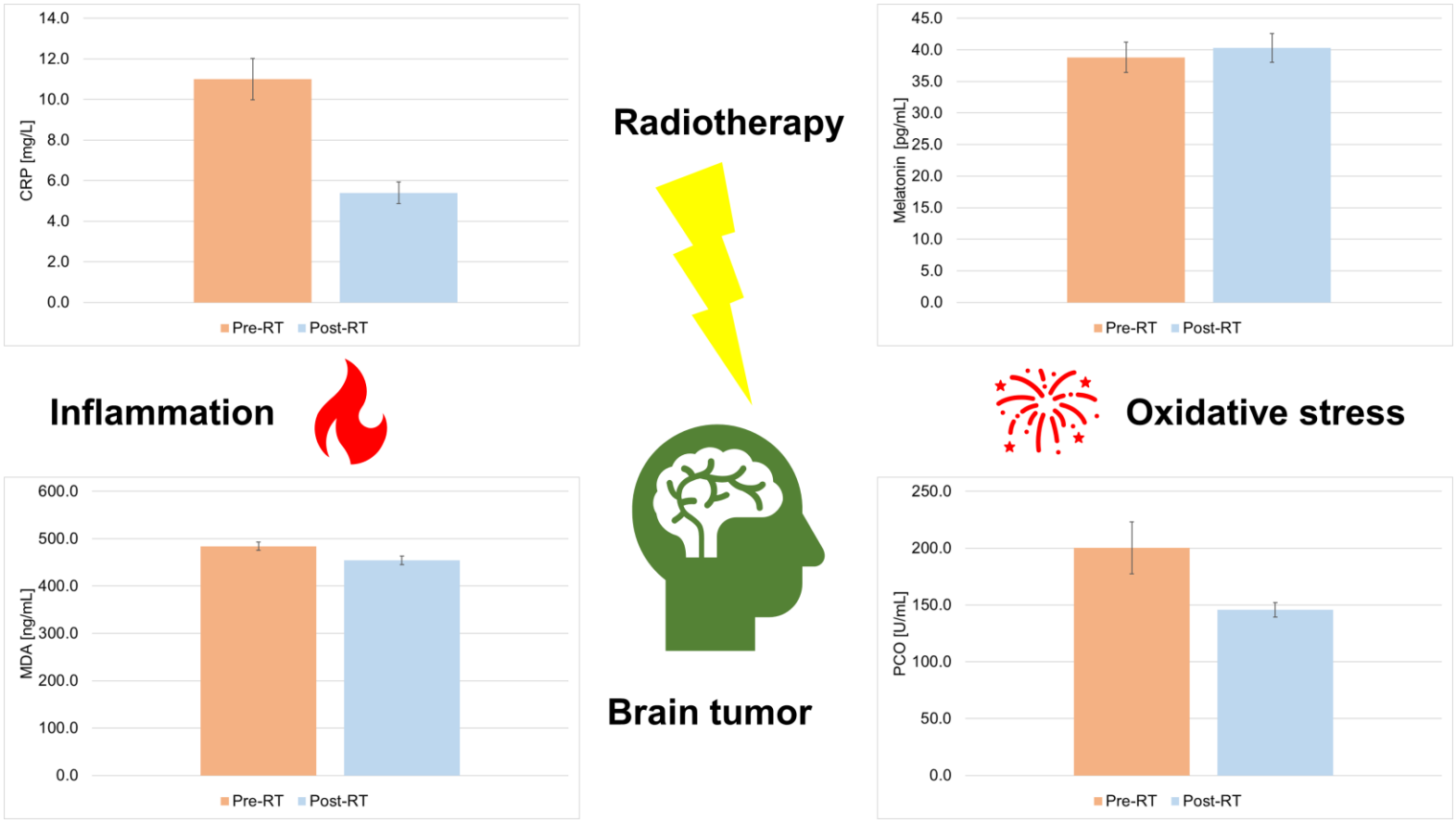
Graphical Abstract



Abstract:
Brain tumors (BTs) represent a varied group of intracranial neoplasms. Among the treatment methods, radiotherapy is common. However, both the tumor and radiotherapy may induce oxidative stress, potentially impacting tumor progression and eliciting inflammation. This preliminary study aimed to assess the levels of C-reactive protein (CRP), melatonin, malondialdehyde (MDA), and protein carbonyl groups (PCO) in BT patients, both immediately before radiotherapy and 6-8 months after treatment. The study encompassed 16 patients (9 males and 7 females; average age of 51.75 ± 3.07 years) diagnosed with primary BT. Blood samples were procured at two timepoints: initially during the radiotherapy planning phase and, subsequently, after an average of 219.11 ± 14.40 days from the first collection. Blood serum samples underwent biochemical testing. A *p*-value of less than 0.05 was considered statistically significant. Results, expressed as mean value ± standard error of the mean (SEM), demonstrated a decrease in CRP levels from 11.01 ± 1.02 mg/L to 5.40 ± 0.54 mg/L. Melatonin levels remained comparable at 38.81 ± 2.40 pg/mL and 40.31 ± 2.29 pg/mL, respectively. MDA concentrations reduced from 483.86 ± 8.61 ng/mL to 454.25 ± 9.42 ng/mL, and PCO levels decreased from 200.33 ± 22.76 U/mL to 145.75 ± 6.20 U/mL. Statistically significant variations were noted in the levels of CRP, MDA, and PCO pre- and post-radiotherapy. Among long-term effects of BTs radiotherapy, a decrease of oxidative stress and inflammatory markers could be noticed. Those changes might be important for the patient's health improvement.

Keywords: biomarkers; brain tumors; inflammation; oxidative stress; radiotherapy

Introduction

- Brain tumors (BTs) are a diverse group of intracranial neoplasms with varied pathology and clinical manifestations.
- Radiotherapy, employing high-energy radiation to target cancer cells, is a common treatment modality for BTs.
- An adverse outcome of radiotherapy is the induction of systemic oxidative stress due to an imbalance between reactive oxygen species (ROS) production and biological detoxification.
- Oxidative stress may either promote tumor progression or induce cancer cell death, portraying a double-edged sword in BT management.
- Both the tumor itself and radiotherapy-induced oxidative stress can trigger an inflammatory response.
- This inflammatory response may further exacerbate tumor progression and impact the patient's prognosis and quality of life.

Introduction

C-reactive Protein (CRP):

- An acute-phase protein, indicative of inflammation.
- Elevated levels may signal infection, inflammation or malignant neoplasms including BTs.
- Its levels may provide insight into the inflammatory response associated with BTs and the impact of radiotherapy on systemic inflammation.

Melatonin:

- A hormone known for regulating circadian cycles, also presents antioxidant properties.
- Can modulate oxidative stress and may have potential neuroprotective effects in BTs.
- Its role in mitigating radiotherapy-induced oxidative stress and improving radio-sensitivity of tumor cells is of research interest.

Introduction

Malondialdehyde (MDA):

- A marker for oxidative stress, indicative of lipid peroxidation.
- Elevated levels may reflect increased oxidative stress in BT patients, potentially exacerbating tumor progression.
- Monitoring MDA levels pre and post-radiotherapy may provide insights into the oxidative stress dynamics in BT management.

Protein Carbonyl Groups (PCO):

- Markers of protein oxidation and oxidative stress.
- Elevated levels suggest protein damage which could be due to the pathological processes of BTs or the oxidative effects of radiotherapy.
- Understanding PCO levels in BT patients could shed light on the oxidative damage and its relation to tumor progression and radiotherapy outcomes.

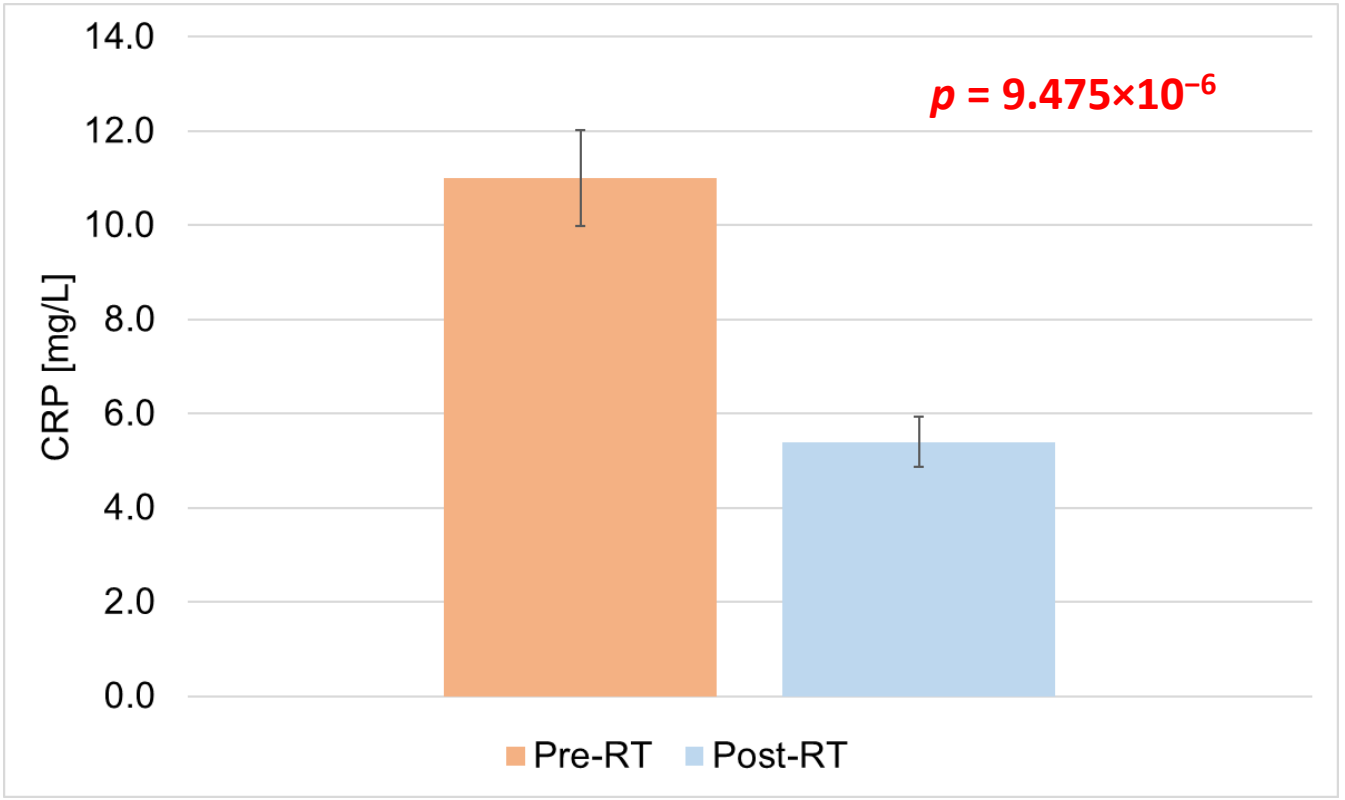
Introduction – aim of the study

- The objective of this preliminary investigation was to evaluate the concentrations of CRP, melatonin, MDA, and PCO in the blood serum of individuals diagnosed with BTs, both prior to undergoing radiotherapy and at a follow-up period of 6-8 months post-treatment.
- Blood samples were collected at two distinct timepoints: initially during the phase of radiotherapy planning, and later, after an average duration of 219.11 ± 14.40 days from the initial collection. The serum from these blood samples was subjected to biochemical analysis - enzyme-linked immunosorbent assay (ELISA). A *p*-value of less than 0.05 was deemed statistically significant. The findings are presented as the mean value ± standard error of the mean (SEM).

Results and discussion – characteristics of the study participants

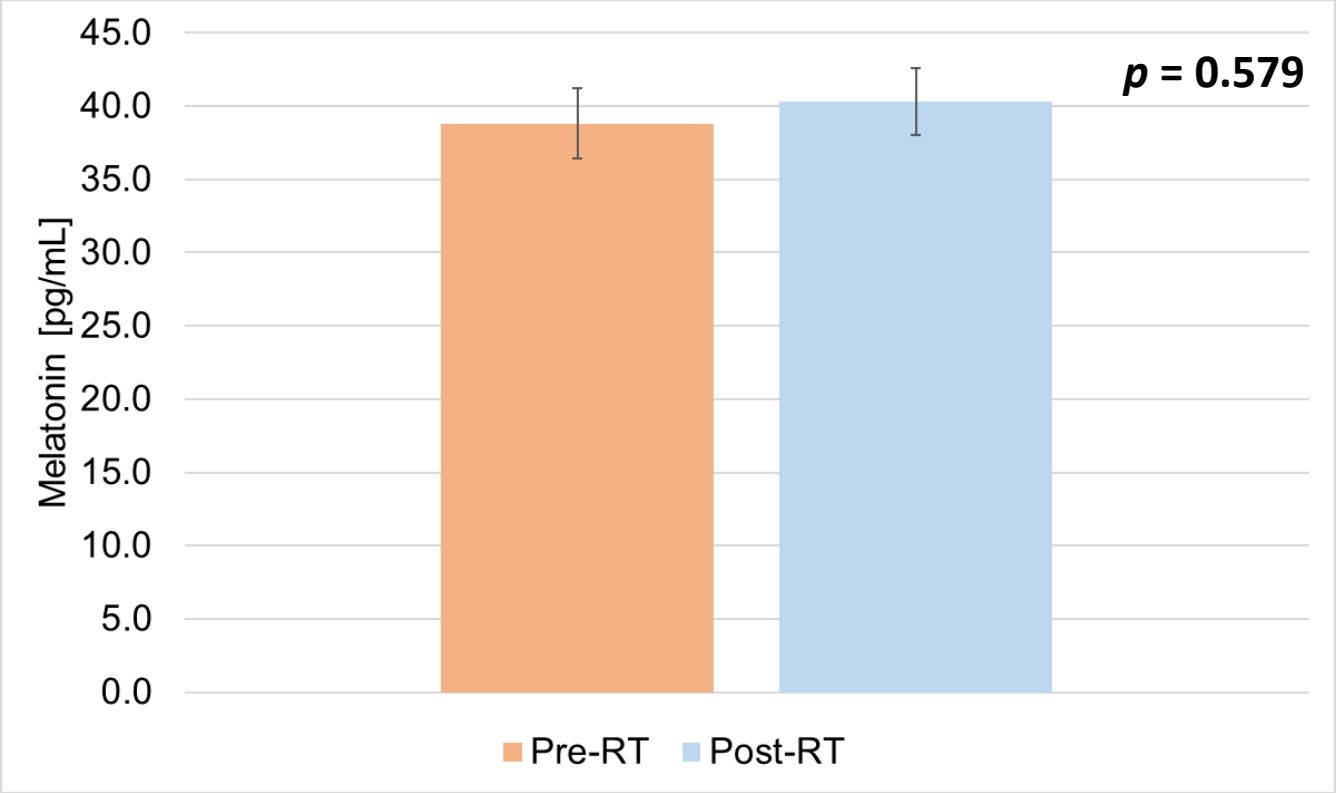
	Pre-radiotherapy (Pre-RT)	Post-radiotherapy (Post-RT)	*p*-value
n	16		-
Sex (f/m)	7/9		-
Age [yrs]	51.75 ± 3.07		-
Body mass [kg]	75.94 ± 3.61	73.55 ± 4.21	0.233
Height [cm]	170.88 ± 2.94		-
BMI [kg/m^2]	25.88 ± 0.79	24.95 ± 0.93	0.220

Results and discussion – CRP



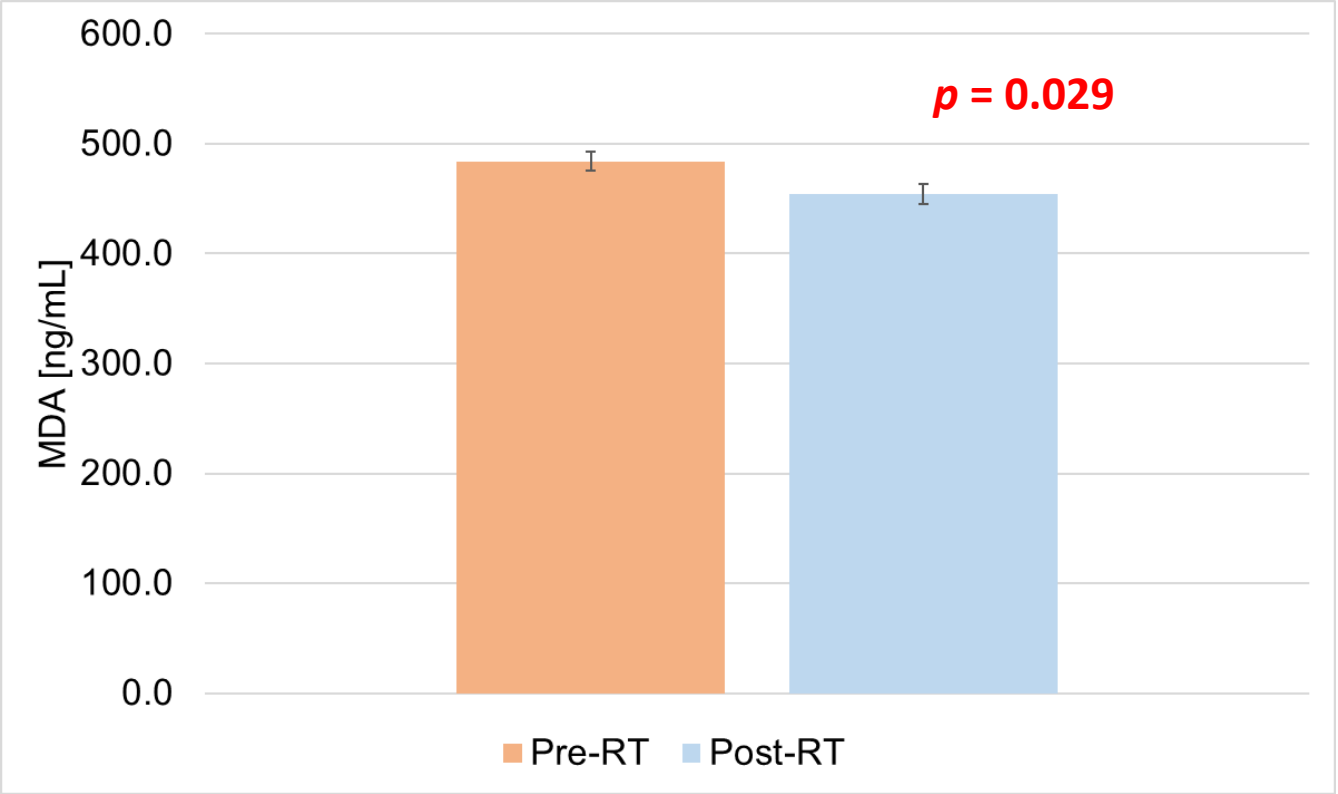
CRP [mg/L]	Pre-radiotherapy (Pre-RT)	Post-radiotherapy (Post-RT)	*p*-value
Mean ± SEM	11.01 ± 1.02	5.40 ± 0.54	9.475×10^{-6}

Results and discussion – melatonin



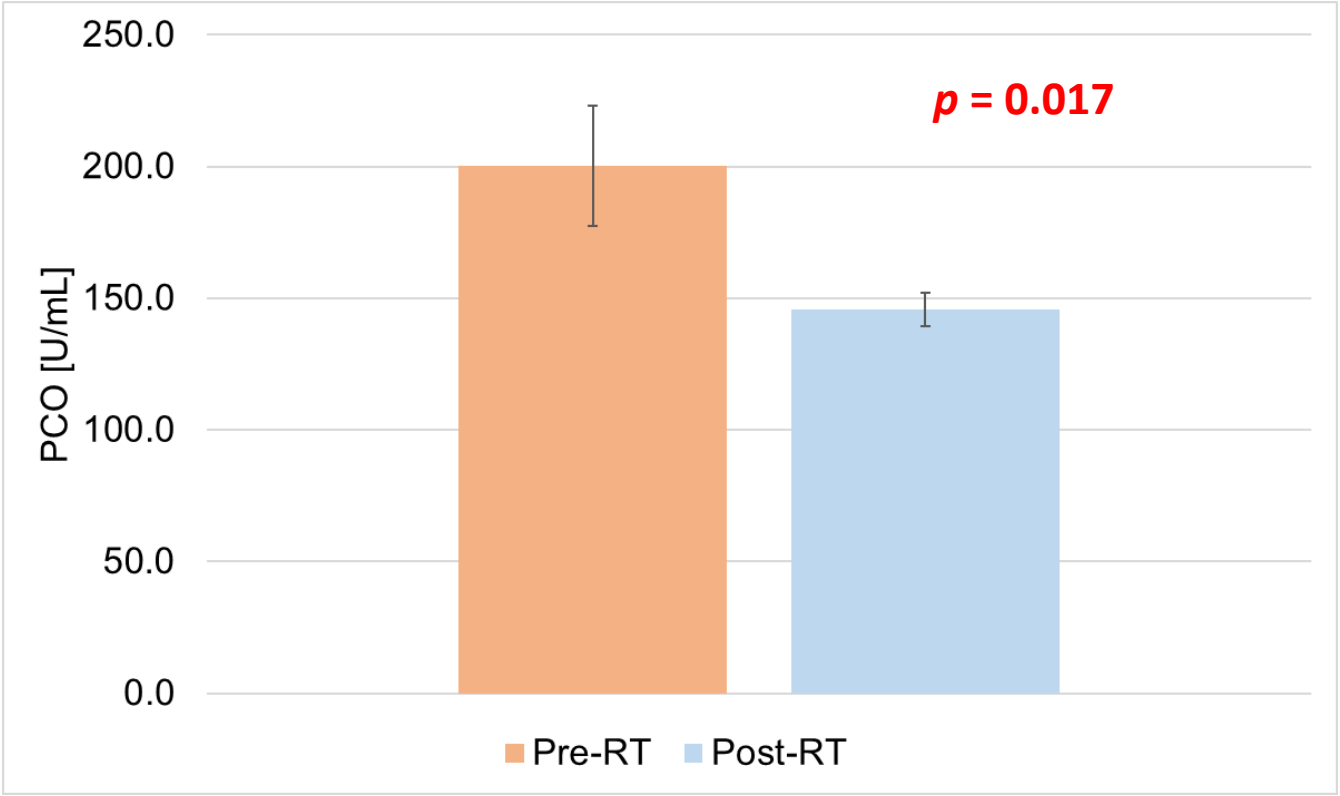
Melatonin [pg/mL]	Pre-radiotherapy (Pre-RT)	Post-radiotherapy (Post-RT)	*p*-value
Mean ± SEM	38.81 ± 2.40	40.31 ± 2.29	0.579

Results and discussion – MDA



MDA [ng/mL]	Pre-radiotherapy (Pre-RT)	Post-radiotherapy (Post-RT)	*p*-value
Mean ± SEM	483.86 ± 8.61	454.25 ± 9.42	0.029

Results and discussion – PCO



PCO [U/mL]	Pre-radiotherapy (Pre-RT)	Post-radiotherapy (Post-RT)	*p*-value
Mean ± SEM	200.33 ± 22.76	145.75 ± 6.20	0.017

Conclusions

- The study observed a significant reduction in the levels of CRP, indicative of a decreased inflammatory response, in BT patients post-radiotherapy.
- A notable decrease was also observed in the levels of MDA and PCO, suggesting a reduction in oxidative stress post-radiotherapy.
- Melatonin levels remained relatively stable before and after radiotherapy, indicating that the treatment did not significantly affect melatonin concentrations in the blood serum of BT patients.
- The observed decrease in oxidative stress and inflammatory markers post-radiotherapy could be indicative of positive therapeutic outcomes, thus potentially contributing to an improved health status of BT patients.
- These results underscore the necessity for further comprehensive studies to explore the long-term impacts of radiotherapy on oxidative stress, inflammatory markers, and overall health in BT patients.

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