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High LET Radiation Overcomes in vitro Resistance to X-rays of Chondrosarcoma Cell Lines

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Chondrosarcoma is a malignant tumor arising from cartilaginous tissues, described as radiation- and chemo-resistant to conventional treatments. The primary treatment consists in wide surgical resection, which may lead to severe disabilities; in addition, this procedure is not feasible for some inoperable locations such as skull base chondrosarcoma. Carbon-ion irradiation (hadron-therapy) has been successfully used in the treatment of chondrosarcoma, due notably to a higher biological effectiveness and a better ballistic as compared with conventional radiotherapy with X-Rays.

The aim of this study was to examine the differential cellular responses of chondrosarcomas to conventional radiotherapy and hadrontherapy in order to better understand the biological effects of carbon beams in cancer treatment. Four human chondrosarcoma cell lines of different grades and displaying differential radio-sensitivities, were irradiated with photons (250 kV, 2Gy/min) or carbon ions (95 MeV/A, LET 33 keV/μm).

REF : from Chevalier et al., TCRT, 2019, in press

Irradiations / treatments

Four human chondrosarcoma cell lines of different grades were used : SW1353 GII, L835 G II, CH2879 GIII and OUMS27 GIII

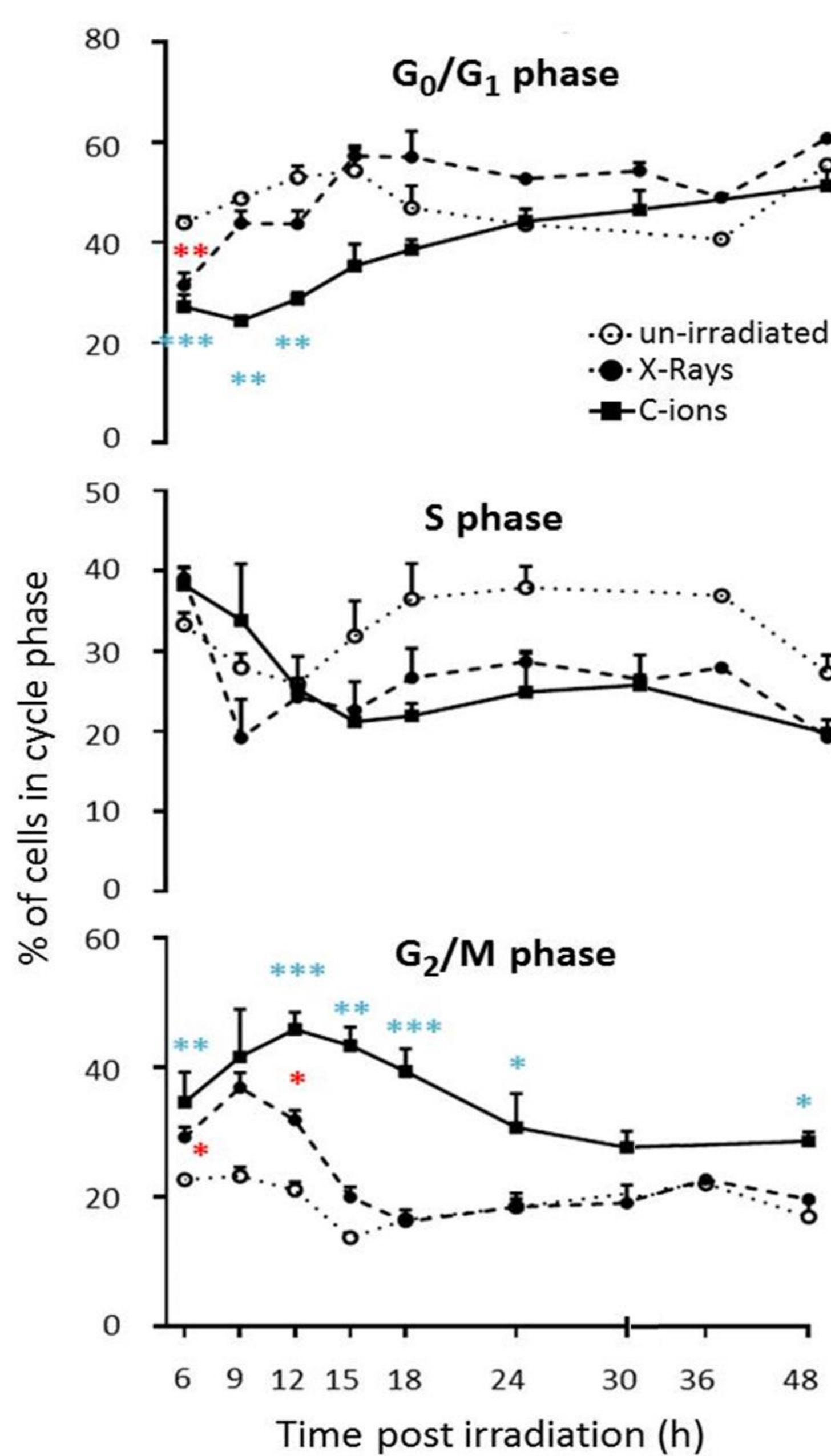
Cells were irradiated with X-Rays (X-Rad 225 Cx), or with Carbon ions of two LET and analyzed by :

- clonogenic assays
- Micro-nuclei assays
- Cell cycle analyses
- Western blotting (P21 / g-H2AX)

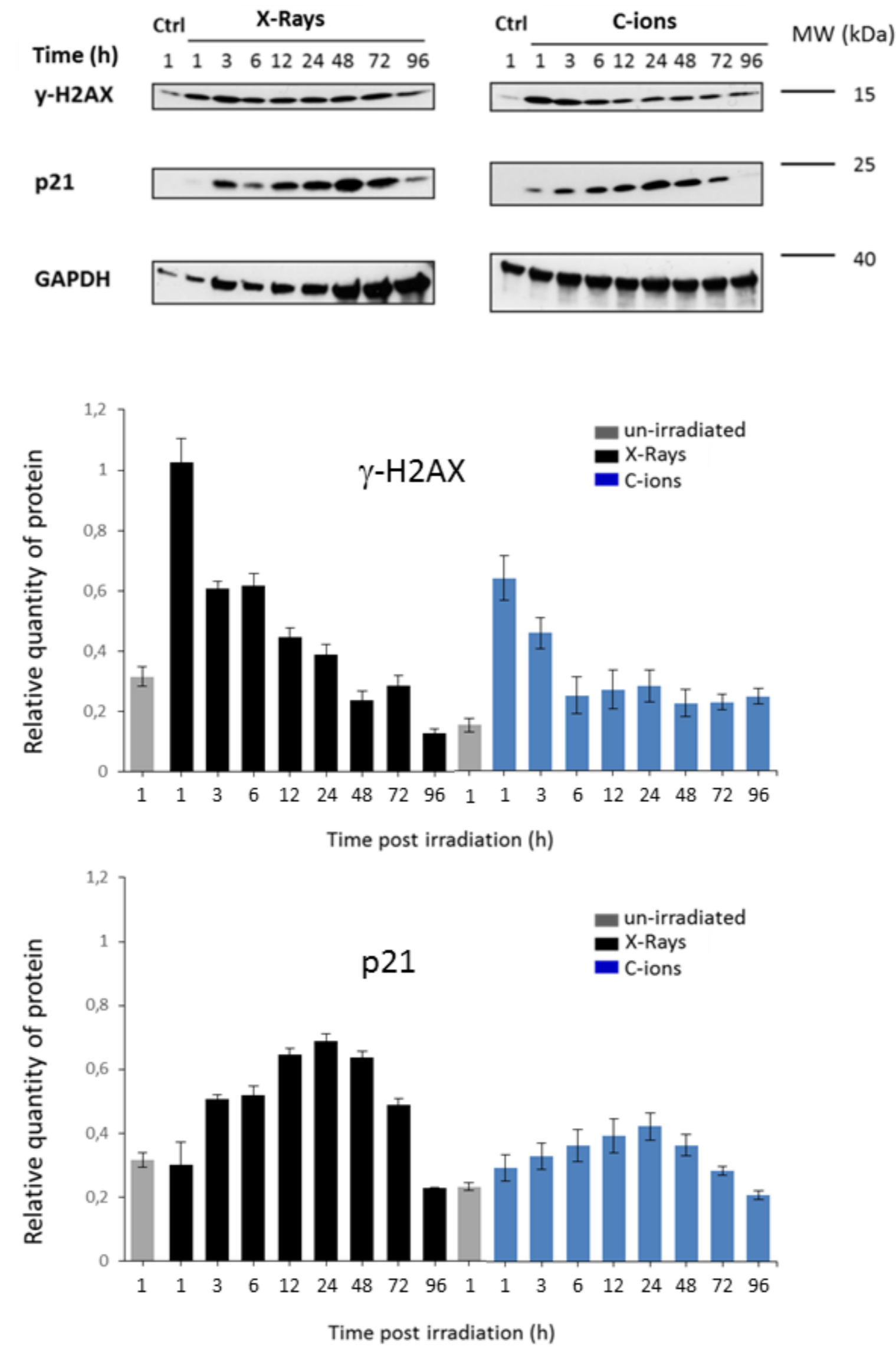
Aim of this study

- explore the differential cellular responses of chondrosarcomas to conventional radiotherapy and hadrontherapy
- understand the biological effects of carbon beams in cancer treatment

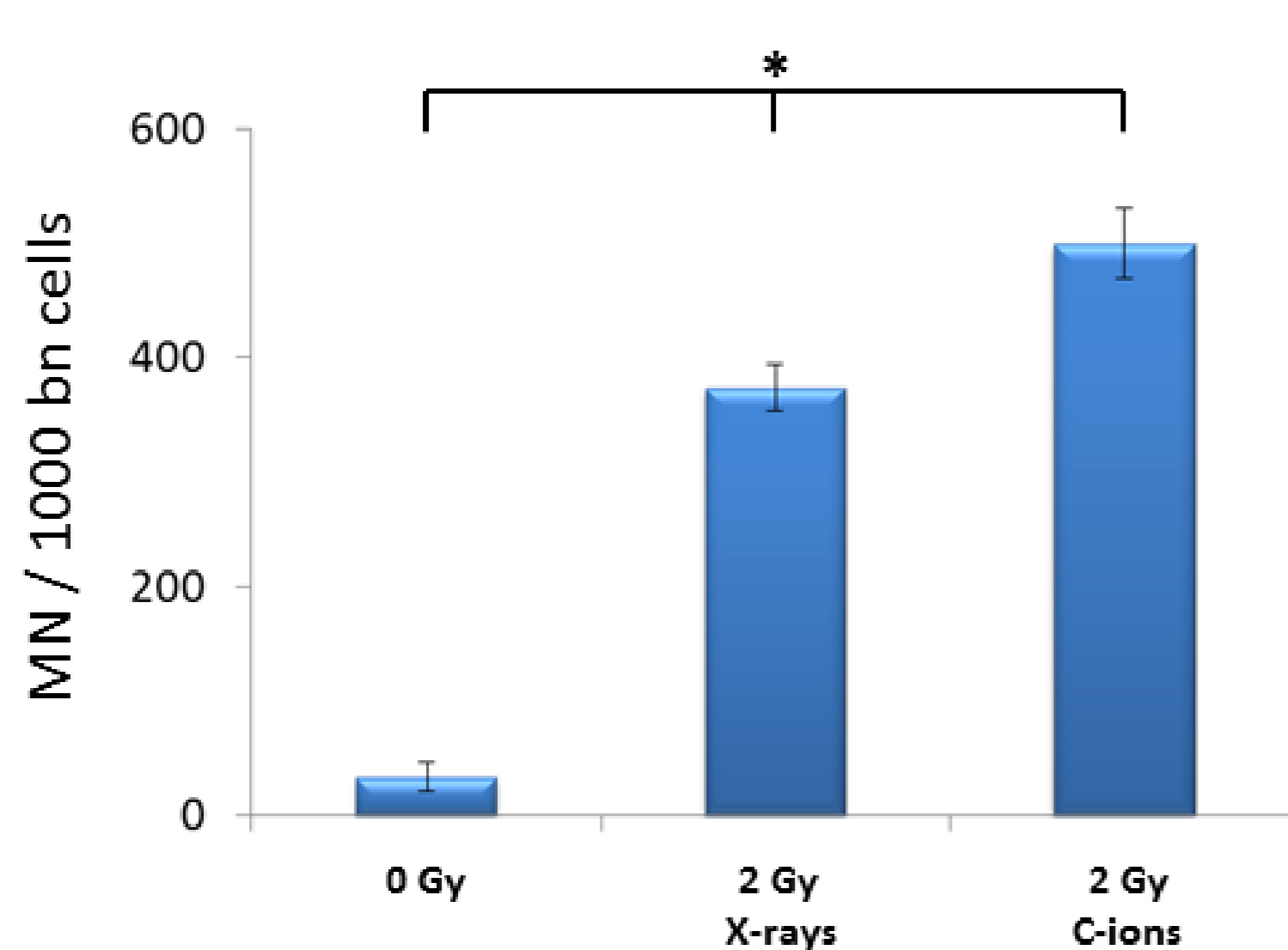
Cell cycle analysis : SW1353



Western Blotting : SW1353



Micro-nuclei assays : SW1353



Conclusions

Chondrosarcoma cells showed a heterogeneous sensitivity towards irradiation s:

- Chondrosarcoma cell lines were more sensitive to C-ions exposure compared to X-rays. Using D10 values, the relative biological effectiveness of C-ions was higher (RBE = 5.5) with cells resistant to X-rays (CH2879) and lower (RBE = 3.7) with sensitive cells (L835).
- C-ions induced more G₂ phase blockage and micronuclei in SW1353 cells as compared to X-rays with the same doses.
- Persistent un-repaired DNA damage was also higher following C-ions irradiation.

These results indicate that chondrosarcoma cell lines displayed a heterogeneous response to conventional radiation treatment; however treatment with C-ions irradiation was more efficient in killing chondrosarcoma cells, compared with X-rays.

