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Sensitization of chondrosarcoma cells with PARP inhibitor and impact on cancer stem cells

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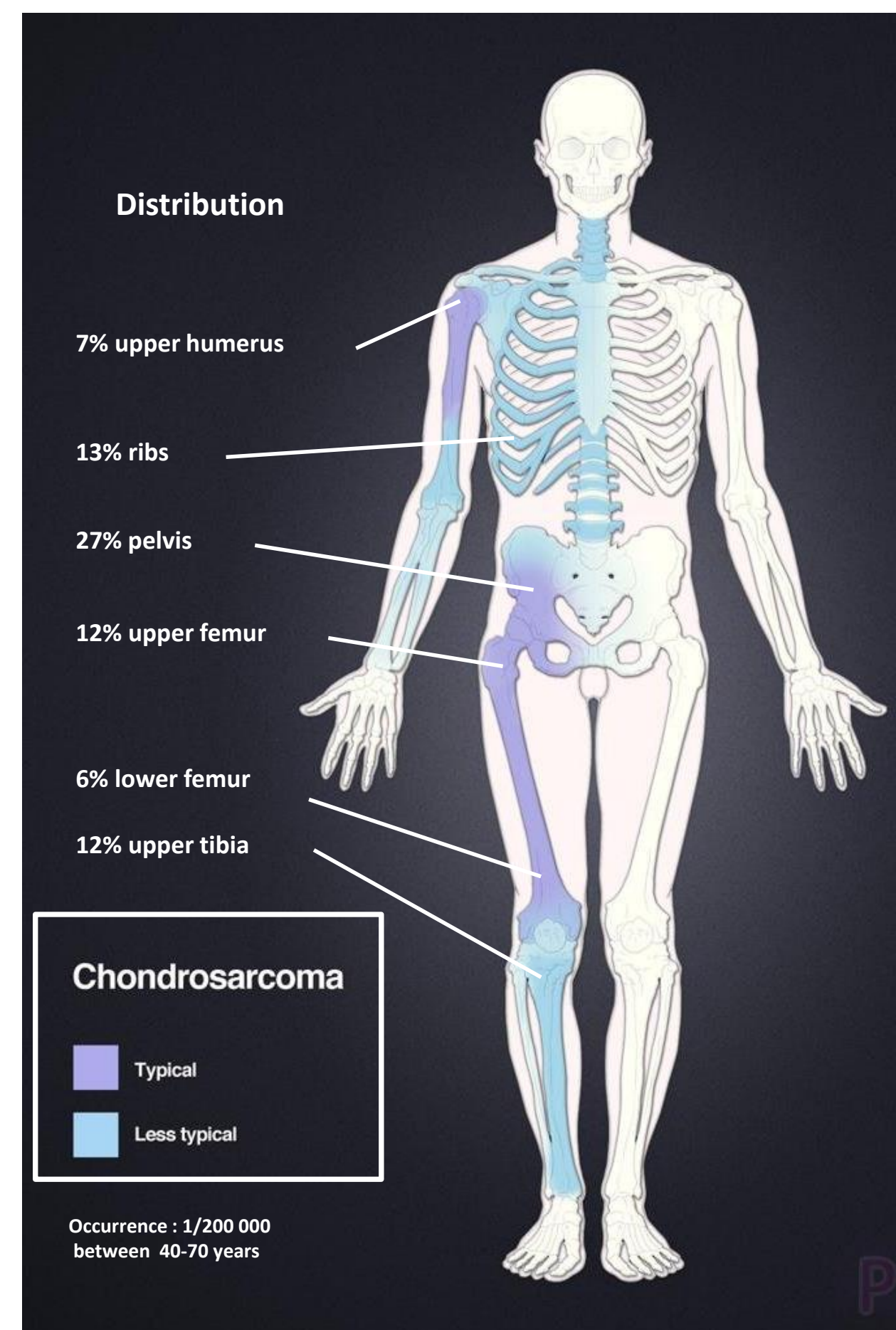
RÉGION NORMANDIE

Chondrosarcoma is a primary tumour of bone and cartilage. One of the gold standard treatments is conventional X-ray therapy but chondrosarcomas of high malignancy are resistant. One of the mechanisms of radioresistance concerns the compartment of cancer stem cells (CSC) via their self-renewal and tumorigenesis capabilities. Radiosensitizing molecules, such as PARP inhibitors (PARPi) and carbon ions irradiation (C-ions), could overcome radioresistance and act on the CSC [1–3]. We investigated the cell survival and the impact on CSC of a chondrosarcoma line L835 in 2D and 3D culture models after X-ray (225 kV) compared to C-ions (Ganil, 73 keV/μm) in combination or not with PARPi. For the study of cell survival, we carried out clonogenic tests. For the study of the CSC, we determined the ability of cells to form tumorspheres in wells containing a depleted culture medium. We also performed a kinetic analysis on 3D models of spheroids, using DNA damage tests (γ-H2AX foci) and immunohistochemistry of ALDH, an enzyme more expressed in CSC.

- Vares, G. et al. *Radiother Oncol* 2020, 150, 253–261.
- Chevalier, F. et al. *Technol Cancer Res Treat* 2019, 18, 1533033819871309.
- Césaire, M. et al. *J Bone Oncol* 2019, 17, 100246.

Aim of this study

- explore the differential cellular responses of chondrosarcomas to conventional radiotherapy and hadrontherapy
- estimate the capacity of PARP inhibitors in radio-sensitizing chondrosarcoma cells
- estimate the impact of hadrontherapy and PARP inhibitors on chondrosarcoma cancer stem cells



Experimental plan

