

POSTER PRESENTATION

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# Osteosarcoma contains a subpopulation of cancer stem-like cells that are highly resistant to radiotherapy

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## Aim

The cancer stem cell (CSC) theory states that tumors contain a subset of cells responsible for tumor initiation and growth and recurrence after treatments. We aimed to identify the presence of putative CSCs in a human MNNG/HOS osteosarcoma cell line and investigate their role in response to radiotherapy.

## Methods

The isolation of CSCs was performed using the sphere formation assay in serum-free medium in non-adherent conditions. The cells were characterized for the expression of mesenchymal stem cell markers (CD90<sup>+</sup>/CD105<sup>+</sup>/CD73<sup>+</sup>) by flow cytometry. MNNG/HOS and CSCs were irradiated with X-rays at different doses (0–20Gy). The sensitivity to ionizing radiation was evaluated using the MTT assay after 7 days. Cell-cycle responses were studied at 24h post-irradiation using propidium iodide staining.

## Results

A subset of CSCs was identified in the MNNG/HOS cell line. The isolated cells formed sphere-clusters and were positive for MSC markers. The mean lethal dose (LD50) obtained for CSCs was of  $8.0 \pm 3.0$ Gy, significantly higher than for MNNG/HOS cells (LD50 =  $3.4 \pm 0.6$ Gy,  $p < 0.05$ ). It was observed a dose dependent cell-cycle arrest in G<sub>2</sub>/M phase at 24h, in the MNNG/HOS cells. CSCs cell-cycle progression remained unaltered.

## Conclusions

Osteosarcoma contains a subset of cells with stem-like properties that are relatively resistant to radiation. The absence of alterations in cell-cycle progression of CSCs suggests that these cells may have higher capacity to repair the irradiation-induced DNA lesions and increased DNA damage checkpoints signaling. These results suggest that radiotherapy may not address the CSCs subpopulation allowing them to survive and regenerate the tumor.

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