Primary cilia and its importance in cell response to ionizing radiation exposure and chemotherapy drugs.

Ionizing radiation, metabolic and genotoxic stress affect the cytoskeletal stability and morphology of cells by causing DNA damage in the form of single or double stranded breaks, the latter being the most critical. When DNA damage occurs the cell cycle becomes arrested and the repair machinery is engaged; however, if this damage is not repaired the cell enters programmed cell death by apoptosis. Primary cilia have been shown to act as physical-chemical sensors and their biological functions include the perception of the extracellular milieu, the regulation of organogenesis and cell polarity, as such, they are dynamically regulated during cell cycle progression. Further, the impairment or loss of primary cilia leads to the development of ciliopathies and other diseases including cardiovascular disorders, arthritis and, ultimately, cancer. Moreover, the presence and temporary formation of primary cilia is essential for the repair process of certain cell types.

This work is focused on the evaluation of primary cilia changes caused by ionizing radiation, metabolic stress or cytostatic drugs (taxol and doxorubicin) in vitro. Our results showed a significantly higher number of ciliated C2C12 cells observed 24 hours after irradiation (2–20 Gy) when compared with non-irradiated cells. At 72 hours post-irradiation, the incidence rate of primary cilia increased even further in cells irradiated with 20 Gy. Multi-ciliated cells were also detected in cells irradiated with 10 and 20 Gy. Irradiation also caused a dose-dependent decrease in cell viability and proliferation. The presence and frequency of primary cilia was also evaluated in a triple negative breast cancer cell line and in breast fibroblasts after treatment with cytostatics. The highest incidence of primary cilia in fibroblasts was detected 72 hours after treatment with 120 nM doxorubicin. Furthermore, cells with multiple cilia were also detected after treatment with doxorubicin and the highest number of multi-ciliated cells was found 72 hours after treatment with 80 nM doxorubicin in breast fibroblasts. Treatment with taxol caused cell cycle arrest in G1 phase and increased the number of ciliated cells after treatment with lower concentrations although multiple cilia were not observed under any concentration of taxol. Primary cilia were not found in triple negative breast cancer cells under any concentration of doxorubicin or taxol 72 hours after treatment.