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Infrared microspectroscopy to uncover the in vivo biochemical effects of proton minibeam radiation therapy

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Background: the biology underlying proton minibeam radiation therapy (pMBRT) is not fully known yet. Therefore, this study reports on the in vivo biochemical mechanisms following pMBRT irradiations using Fourier Transform Infrared Microspectroscopy (FTIRM). This technique can reveal details of the biochemical structure of the main biomolecules and their possible modifications by measuring infrared absorbance spectra.

Materials and methods: radiotherapy (RT) was performed at Institut Curie Proton Therapy Center using 100 MeV proton beams. Both healthy and tumour-bearing (F98 cell line) Fischer rats were subjected to conventional (BB) proton RT and pMBRT, delivering 30 Gy to whole brains (excluding the olfactory bulb and cerebellum). Brain sections were fixed at 2 and 24 hours post-RT. FTIRM measurements were then conducted at ALBA Synchrotron, where infrared raster scanning maps of the sections were collected for each sample and irradiation condition. Data analysis included hyperspectral imaging and assessment of spectral markers of biochemical modifications.

Results: in healthy animals, a large absorbance increase of protein-related spectral bands was observed in the brain cortex at 2 hours post-RT, indicating modifications in the secondary structure of proteins. Conversely, a reduced absorbance of nucleic acid bands was indicative of the radiation-induced damage to the DNA and carbohydrates, especially for BB-RT. Most of pMBRT damage was reduced 24 hours after treatment. Phosphate bands were altered in the tumours of glioma-bearing rats one day post pMBRT, indicating enhanced DNA damage. In the lipid spectral region, both RT modalities produced similar hydrocarbon chain modifications.

Conclusions: this is the first study to report in vivo biochemical modifications resulting from pMBRT. Spectral differences were dependent on the brain region, irradiation configuration and fixation time. In healthy rats, almost all early damage induced by pMBRT decreased after one day, while greater DNA damage due to pMBRT was observed in the tumours of glioma-bearing rats.

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