In Vivo Two-Photon Microscopy of Cerebral Vascular Damage after Synchrotron Irradiation Protocols

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The in vivo evaluation of cerebral vascular damage after synchrotron irradiation protocols: microbeam radiation therapy (MRT) and photon activation therapy (PAT), is important to avoid changes in blood brain barrier (BBB) permeability, blood perfusion, volume and consequently tissue necrosis at long term. Two-photon microscopy (2PM) offers the possibility to analyze in vivo and at a microscopic scale these vascular parameters.

2PM has been used to analyze the cerebral blood volume and BBB permeability after MRT and PAT within three months after irradiation in the brain cortex of normal mice at a maximum observation depth of 600 µm. In these studies, a cocktail of FITC-dextran (70 kDa) and sulfo-rhodamine B (SRB, 0,58 kDa) was injected i.v. to measure simultaneously changes in the blood volume (1) and in the BBB permeability with the diffusible SRB.

In MRT of the normal mouse brain cortex with 18 microplanar-beams, 25 µm width, center to center spacing 211 µm, entrance doses: 312 and 1000 Gray, no significant changes in the cerebral blood volume and perfusion were observed for both doses. At 1000 Gy, but not at 312 Gy, diffusion of sulforhodamine B in microbeam regions was observed from 12 h until 12 days (2).

In PAT studies, the same protocol for the irradiation of F98 glioma bearing rats was applied that contained the high Z-compound cis-platinum (see 3). The irradiation energy was just above the Pt K-edge of the platinum (79keV) and the dose was 15 Gy. In this configuration, no BBB leakage or changes in cerebral blood volume and perfusion were observed for both fluorescent molecules from day 1 to day 30 after irradiation.

In conclusion, both synchrotron irradiation protocols conserve the cerebral blood volume, blood perfusion and the BBB integrity within 3 months after irradiation. The BBB permeability was only temporally increased for the MRT protocol with peak doses of 1000 Gy.

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