Quantitative assessment of brain tumor radiation treatment reveals decrease in tumor-supporting vessels

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Aims

Angiogenesis—the formation of new blood vessels—is an important factor for tumor growth [6]. Reducing tumor-supporting vessels by radiation treatment is a powerful option for treating tumors; specialized treatments that deliver high radiation doses have shown to enable *excellent* survival rate [3]. Among rodent models for brain tumors, the 9L-gliosarcoma model is a widely used one, since it mimics important features of human brain tumor growth.

Method

Brain tumors were induced in 10-week-old Fisher 344 rats (n=59) by inoculation of gliosarcoma cells into the right caudate nucleus through the skull [1].
Ten days after inoculation, tumor volume was assessed by MRI performed with a 4.7 T Bruker Avance III console [4]. Based on tumor volume, animals were split into groups with comparable tumor size ready for either microbeam radiation therapy (MRT), conventional radiation therapy (so called broad beam, BB) or no therapy (CTRL).
Irradiation was performed at the ID17 biomedical beamline at the European Synchrotron Radiation Facility. Details on the facility and the radiation treatment are described by [2].
Briefly, rats were irradiated ten days after inoculation using two 8 x 10 mm irradiation fields focused onto the tumor location in the anterior part of the right hemisphere. For the MRT-animals, the irradiation field was split into 40 microbeams (width 50 µm, 200 µm on-center spacing) using a multislit collimator. The in-microbeam entrance dose was 250 Gy, the valley dose approximately 9 Gy. For the BB-animals, the irradiation was homogeneously applied to the same area with a dose equivalent to the MRT valley dose.
On days 6, 10 and 14 after radiation treatment, rats were again imaged by MRI. Subsequently, they were infused with a contrast agent (µAngiofil, [5]) and their brains extracted. Fifty-four of those brains were imaged with a Bruker SkyScan 1272. The brains were immersed in 4 % PFA in a custom-made sample holder and imaged at 5 µm voxel size.
After manually delineating the tumor regions of interest (ROIs) in CTAn we used a custom image processing pipeline in Python to assess the data sets and extract the aforementioned values. The automatic assessment pipeline analyzes the 54 data sets fully autonomous and in a reproducible way.
Due to the contrast agent, separating blood vessels from the tumor volume was as easy as using standard gray value thresholding. This makes it possible to easily extract values like tumor and vessel volume and thus the vessel volume ratio. With a distance transformation we can also extract the vessel diameter and the vessel surface.

Results

Tumor ROIs can easily be visualized. Figure 1 shows three example tumors from the whole set of scans.

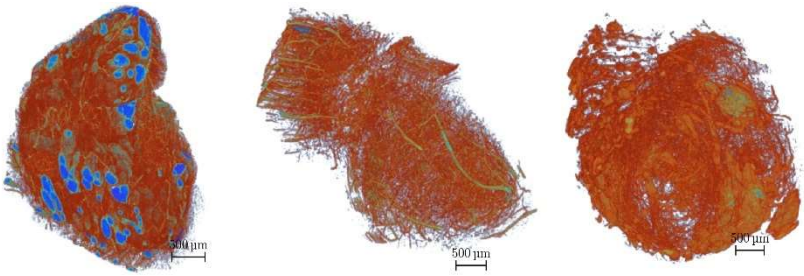

Figure 7: Visualization of three of the 54 scanned tumors. Left to right: Control, microbeam and broad beam radiation therapy.

Radiation treatment reduces the vasculature in the tumor, as can be seen in Figure 2 to the left.

Conclusion

Using the described approach, we show that radiation treatment decreases the vasculature in the tumor, i.e. less vessels are available to provide the tumor with nutrients. Our unbiased, automatic assessment shows that the performed radiation treatment is successful.

In parallel to performing the scans, we developed the analysis pipeline. The reproducible analysis made it possible to easily add more samples, i.e. preliminary results could be obtained early on in this study.

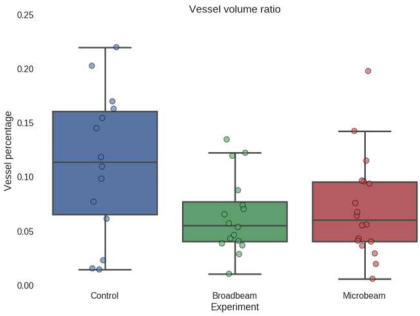

Figure 8: Box plots of the vessel volume per tumor volume.

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