

Preliminary results on 5-ALA PDT fractionation on a preclinical rodent model



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Glioblastoma Multiform (GBM) is a high-grade brain tumour with local recurrence and poor outcome. Photodynamic therapy to treat glioblastoma has been recently reported to improve overall survival. However, controlled study to evidence treatment efficacy is still expected and treatment delivery has to be optimized. Several parameters might be optimized such as fluence rate, dose escalation or fractionation of light delivery. Specially, fractionation of light delivery is expected to enhance treatment efficiency by restoring tissue oxygenation. Thus, we have evaluated light fractionation on a preclinical rodent model harbouring grafted GBM.

Thirty-nine “Nude” rats were grafted with human U87 cells. Cells were stereotactically grafted in rat brain. After the presence and the size of the tumour were assessed by microMRI, PDT was delivered interstitially. Light was delivered through an optical fibre introduced into the tumour after PS precursor intake (5-ALA). The rats were randomized in three groups: (1) without illumination, (2) with 2-steps light fractionation and (3) with 5-steps light fractionation. Brain immunohistology and microMRI images were achieved to evaluate the treatment effects.

On diffusion MRI, elevated diffusion values in tumour centre among treated animals were observed, especially for the 5-steps fractionation group. Perfusion decreased around the treatment site, especially in the 5-steps fractionation group. Histology confirmed our MRI findings, with a more extensive necrosis and apoptosis associated with a rarefied angiogenic network in the treatment area, after 5-steps fractionation PDT. However, more surrounding oedema and neovascularization in the peripheral ring after 5-steps fractionation PDT were also noticed.

Finally we observed that interstitial PDT induced more tumour necrosis and apoptosis when applying 5-steps fractionation. However, this scheme also led to significant peripheral oedema and neovascularization. Diffusion and perfusion were able to predict the histological lesions. Nevertheless, apoptosis cells death remains the preferred effect in order to decrease potential side effects. We hypothesize a lower fluence rate with the same light fractionation scheme might increase apoptosis while decreasing necrosis and oedema. Preclinical study is still on going to verify this hypothesis.

<http://dx.doi.org/10.1016/j.pdpdt.2017.01.169>

PDT in pneumology