Translational imaging findings in a pediatric patient-derived orthotopic xenograft brain tumor model

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1 OVERVIEW

Malignant brain tumors are the most common cause of solid cancer death in children. Innovative therapies are vital to improve treatment outcomes, but must be developed to enable trafficking across the blood brain barrier (BBB). For this advent, animal models provide important information prior to clinical studies. Among the different in vivo models orthotopic patient-derived xenografts (PDX) models represent a valuable tool to study diversity in patient tumors and hence replicate response rates in the clinical trials better as compared to other more simplistic models. Especially in the brain tumor field, imaging has a central role in clinical diagnosis and as a prognostic factor to monitor therapy response. It enables longitudinal patient monitoring in a fully translational manner. Magnetic resonance imaging (MRI) and positron emission tomography (PET) are widely used for clinical diagnosis and disease follow-up. Choosing the most suitable imaging application depends on the target of interest or mechanism of action. MRI offers unencumbered soft tissue contrast, high spatial resolution and non-invasive nature renders MRI in rodent a perfect tool for preclinical work in oncological applications. In case of orthotopic brain tumor models, MRI offers the state-of-the-art anatomical tumor monitoring over disease progression. PET can be applied to study tumor proliferation, metabolism, metastasis, and BBB integrity. Functional ultrasound has a major advantage compared to study cerebral blood flow was applied using functional ultrasound. 3D reconstruction of the brain can be utilized to study vascularization

The purpose of this work was to characterize orthotopic PDX brain tumor model using MRI, functional ultrasound and PET imaging. By direct comparison of the imaging data derived from the preclinical model with similar data-sets from the donor patient the translational value of the model as well as the read-out system will be achieved.

As a conclusion, translational in vivo imaging techniques were applied to study orthotopic tumor model. This results provide a powerful and translational research tool together with oncological disease animal models allowing comprehensive evaluation of disease progression and treatment interventions for in vivo studies.

2 MRI, FUS AND PET IMAGING

Total of 8 NSG mice were used to model an orthotopic paediatric PDX glioma. During the course of the experiment the weight of the animals was monitored daily. The experiment was conducted in AAALAC animal models allowing comprehensive evaluation of disease progression and treatment interventions for in vivo studies.

3 NEUROLOGICAL INDEX

In this study individual pathological findings in PDX glioma model were studied using MRI, functional ultrasound and PET imaging. MRI clearly showed the pathological changes in brain as well variability within model, which resembles well the clinical situation. Perfusion maps obtained with fUS demonstrated vascular abnormalities along the enlarged ventricles but no dramatic changes in localized metabolic activity. The following behaviors were identified during the process jumping, freezing, and rapid eye blinks. For the righting reflex, each mouse was then removed from its home cage and placed on its back allowing the mouse to recover itself. As a conclusion, translational in vivo imaging techniques were applied to study orthotopic tumor model. This results provide a powerful and translational research tool together with oncological disease animal models allowing comprehensive evaluation of disease progression and treatment interventions for in vivo studies.

4 CONCLUSIONS

In this study individual pathological findings in PDX glioma model were studied using translational imaging modalities. MRI clearly showed the pathological changes in brain as well variability within model, which resembles well the clinical situation. Perfusion maps obtained with fUS demonstrated vascular abnormalities along the enlarged ventricles but no dramatic changes in localized metabolic activity. The following behaviors were identified during the process jumping, freezing, and rapid eye blinks. For the righting reflex, each mouse was then removed from its home cage and placed on its back allowing the mouse to recover itself.