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Quantitative imaging of cell viability after graft in stroke rodent model with [¹⁸F]-FHBG

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Abstract:

Aim :

Cell transplantation therapy is an innovative therapeutic approach particularly in neurology to compensate the neural loss after stroke. We propose a molecular imaging approach to study cell viability with a gene encoding a thymidine kinase (HSV1-tk) and ([¹⁸F]-FHBG) as a reporter probe to image the expression of this enzyme. HSV1-tk phosphorylates radiotracer in its monophosphate form leading to intracellular accumulation.

Materials and methods:

We performed an incubation of 5 million of Neuro2a cells with 5, 55 MBq of [¹⁸F]-FHBG during 3 hours. After incubation, we realised 2 calibration ranges of 10 000 to 3 000 000 cells. One was counted in a gamma counter and the other was analysed by PET camera. We used a model of acute brain lesion in rat to test graft procedure. Brain lesion was induced by stereotaxic injection of malonate 3M (5µL). 15 days after the surgery, we performed a stereotaxic graft with different quantity of cells into brain lesion. Image acquisition of whole rat was performed during 15 min in PET-CT. Data analysis was performed with homemade software (Sisyphé) on co-registered image. We tested the correlation between quantitative analysis of brain signal and amount of cells. We performed an analysis of the graft injection quality comparing localisation of ROIs and localisation of signal with scan anatomical data.

Results

[¹⁸F]-FHBG uptake rate was 2.61%±0.8. (n = 9). We observed no significant difference (p=0, 75, n= 6) between signal on gamma counter and PET (Bq). We noted on lesion model a typical alteration of motor function on forelimbs 2 days after malonate injection. We observed a linear correlation between PET signal in rat brain and number of grafted cells (r = 0.996, p <0.00001, n =18). Scalp attenuation was insignificant. These acquisitions allowed the observation of quality of stereotaxic injection. We noticed three types of injection variability: reflux in CSF cisterna, cell reflux on the scalp and

parenchymal diffusion if the lesion was too small.

Conclusion

We proved that we can quantify the number of grafted cells and check the quality of the injection of these cells in vivo in a rat model of stroke through the use of molecular imaging with [¹⁸F]-FHBG. We plan to use this tracer to achieve a longitudinal follow up of a graft to quantify cell viability several weeks after injection. The repeated, non-invasive tracking of grafted cells will accelerate the development of effective stem cell therapy in stroke.

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Author Disclosure Information:

A. Salabert: None.

Topic (Complete): 507 Data Analysis & Quantification

Disclosures (Complete):

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