Introduction:
Human gliomas are diffusely growing in the brain showing various grades and aggressiveness. Tumorogenesis and its effect on cerebral metabolism can be studied in vivo following the implantation of human glioma cells into rodents brain. In vivo 1H MRS allows to non-invasively characterize brain metabolism in a wide range of disease models. Glioma initiation cells (GIC), a subpopulation of stem-cell-like cancer cells, can be cultured as spheroids in serum-free condition, maintaining their undifferentiated state. It was shown that stereotactic injection of GIC into mice brain leads to the development of brain tumor1-2. So far very few studies have been carried out to evaluate brain metabolism in tumors developed from GIC2-3. In this context, we show that stereotactic injection of human GIC into immunodeficient rat results in the development of glioma tumors. The biochemical profile of these human GIC was studied in vivo by 1H MRS.

Methods:
GIC were obtained from human glioma biopsy as described in ref(1). Cells were then cultured (passage 14) and injected (10⁶ cells) stereotactically into the striatum in the right hemisphere of immunodeficient 7 weeks old nude female rats (200 gr). MR measurements were carried out on a 9.4 T/31 cm actively shielded animal scanner (Varian/Magnex) using a home-built 1H quadrature probe. Field inhomogeneity was corrected using the FASTMAP protocol. The animals were anesthetized using 1.5% isoﬂurane and their physiology was monitored during the entire length of the experiments. Fast spin echo multi slice (fsems) T₂ weighted images were acquired (TR = 4000 ms, effective TE = 52 ms, 6 scans). Fsems T₁-weighted images were recorded following the infusion of Gd contrast agent (TR = 350 ms, TE = 10 ms,10 scan). Localized single voxel 1H MRS measurements were acquired using the SPECIAL sequence (TR = 4000 ms, TE = 2.8 ms, 200 ms acquisition in 10 blocks of 16 scans)3. The metabolites concentrations were deduced using a LCModel-based fitting routine3.

Results and discussion:
Typical T₂-weighted (T₂W) images showed the appearance of diffusible tumor resulting from the stereotactic injection of GIC (Fig 1). Lack of contrast enhancement in the T₁-weighted (T₁W) images indicates the very little neovascularization in this type of tumors2-3 (Fig. 1). 1H spectra measured in the tumorous site and the contra lateral hemisphere exhibited excellent signal-to-noise ratio and notable differences in metabolites signals were discernible (Fig. 2). The neurochemical profile (mean ± SD) measured on 3 different rats is presented in Fig. 3 in absolute and tNAA concentrations were lower in tumors whereas a significant increase in Ins, Lac, Asp, Tau, tCho, Gly and Gln was observ. The metabolites concentrations were reduced using a LCModel-based fitting routine3.

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