[^18F]-FET and [^18F]-FAZA PET guided irradiation of glioblastoma in rats

J. Verhoeven[^1], J. Bolcaen[^2], B. Descamps[^3], T. Baguet[^1], G. Hallaert[^4], K. Kersemans[^2], T. Boterberg[^5], K. Deblaere[^6], C. Vanhove[^3], F. De Vos[^1], I. Goethals[^2]

1 Ghent University, Lab for Radiopharmacy, Ghent, Belgium
2 Ghent University Hospital, Department of Nuclear Medicine, Ghent, Belgium
3 iMinds-IbITech-MEDISIP Ghent University, Department of Electronics and Information Systems, Ghent, Belgium
4 Ghent University Hospital, Department of Neurosurgery, Ghent, Belgium
5 Ghent University Hospital, Department of Radiation Oncology, Ghent, Belgium
6 Ghent University Hospital, Department of Radiology and Medical Imaging, Ghent, Belgium

Introduction

Glioblastoma (GB) is the most common primary malignant brain tumor of the central nervous system[^1]. The standard therapy consists of maximal possible surgical resection with concomitant radiation (RT) and chemotherapy. An accurate definition of the tumor volume is of utmost importance for guiding radiation therapy. Currently the target volume delineation is based on CT and MRI[^2,3]. In this project we investigated the feasibility of incorporating [^18F]-FET and [^18F]-FAZA for guiding RT and the impact on treatment outcome by applying subvolume boosting to a PET-defined tumor part.

Methods

F98 GB cells inoculated in the rat brain were imaged using T2- and contrast-enhanced T1-weighted (CE-T1w) MRI. After tumor growth, a 30 min [^18F]-FET (30min p.i.) or [^18F]-FAZA (2h p.i.) PET was acquired. Subsequently, a treatment planning CT was obtained on the small animal radiation research platform (SARRP). A dose of 20 Gy (3x3 mm) was delivered to the target volume delineated based on CE-T1w-MRI (group 1-3). In group 2 and 3 an additional radiation boost of 5 Gy (1x1 mm) was delivered to the region with maximal PET tracer uptake. Temozolomide (TMZ, 5 mg i.p.) was administered in groups 1-3 on five consecutive days. The 4th group received sham injections with saline. Tumor volumes on follow-up MRI were determined by drawing volumes of interest around the tumor on CE-T1w-MRI (PMOD).

Results

CE-T1w-MRI showed a heterogeneous tumor, enabling to select the MRI target volume. Both [^18F]-FET and [^18F]-FAZA showed an increased tumor uptake. After co-registration of the planning CT with the CE-T1w-MRI and PET images, PET-guided RT was performed. Using three non-coplanar arcs, the dose delivered to the normal surrounding brain tissue was minimized. The average, minimum and maximum dose, as well as the D[^90-], D[^50-] and D[^2-] values were calculated for nine rats with both RT plans. The dose volume histograms (DVH) are represented in figure 1. A slight shift to the right for the graph could be noted of the DVH based on the RT with PET based subvolume boosting. The evolution of the normalized tumor volumes is shown in figure 2. Significant differences were found between the therapy and control groups. No significant differences were observed between the different therapy groups.
Conclusions

MRI guided irradiation with PET subvolume boosting is feasible, but very labor-intensive. Tools for faster and more accurate image co-registration would be helpful. Based on tumor growth, a significant difference was found between therapy and no therapy, but no significant difference could be observed between the three treatment groups. Additional information from molecular imaging techniques enables the visualization of metabolically highly active regions. As GB are highly heterogeneous solid tumors, the concept of biological target volume and multidimensional conformal RT seems promising.

Figure 1: Indication of the overlapping volume of the three rotating bundles (green, A). Dose volume histogram with isocenter based on the center of the gadolinium containing contrast uptake on the T1-weighted MRI (B). Dose volume histogram with the second isocenter based on the hot spot showed by the PET scan (C).
Figure 2: Graphical representation of the median change of the tumor volume by day.

References

