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## Investigation of folate receptor targeted imaging of ovarian cancer with newly <sup>68</sup>Ga-labelled folate dimer: <sup>68</sup>Ga-DOTA-FA<sub>2</sub>

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**Background and Aim:** Ovarian cancer is the leading cause of death among women with gynecologic malignancies. The survival rate has remained low largely because of difficulties of an early diagnosis. The high-affinity folate receptor (FR) has proven a valuable target for nuclear imaging using folic acid radioconjugates because of its frequent over expression in ovarian cancer but limited expression in normal human tissues and organs. Folate monomer, commonly used for folate receptor targeted imaging, demonstrate relatively low tumor uptake and high kidney accumulation. We prepared <sup>68</sup>Ga-DOTA-FA<sub>2</sub> with the aim to optimize its biodistribution and increase tumor uptake.

**Methods:** <sup>68</sup>Ga-DOTA-FA<sub>2</sub> was synthesised straightforward and its stability experiments were conducted in plasma. Cell uptake studies were performed on FR-positive SKOV3 Ovarian cancer cells. Biodistribution studies were performed in nude mice bearing SKOV3 ovarian tumors 1, 2, 4h after administration of <sup>68</sup>Ga-DOTA-FA<sub>2</sub> or <sup>68</sup>Ga-DOTA-FA monomer. MicroPET-CT imaging were carried out in nude mice bearing SKOV3 ovarian tumors or FR-negative A549 lung cancer 2h after tail vein injection of <sup>68</sup>Ga-DOTA-FA<sub>2</sub>. All animals accepted folate-free diet for 2 weeks.

**Results:** <sup>68</sup>Ga-DOTA-FA<sub>2</sub> was synthesised at a specific activity of 25MBq/nmol, a radiochemical yield of more than 95%. It was stable with radioactive purity of (96.3±1.5) over 4h in plasma. SKOV3 cells uptake and internalization of <sup>68</sup>Ga-DOTA-FA<sub>2</sub> was FR specific. This is confirmed by the biodistribution data. In biodistribution studies tumor uptake of <sup>68</sup>Ga-DOTA-FA<sub>2</sub> in SKOV3 group was (11.07±1.83)%ID/g at 2h and (12.19±1.72)%ID/g at 4h. They were higher than that of <sup>68</sup>Ga-DOTA-FA (7.36±1.28)%ID/g at 2h and (9.72±2.04)%ID/g at 4h. Retention of <sup>68</sup>Ga-DOTA-FA<sub>2</sub> in kidneys at 4h after injection (49.3±11.02)%ID/g was lower than that of <sup>68</sup>Ga-DOTA-FA (78.5±18.33)%ID/g. MicroPET-CT imaging demonstrated significantly higher tumor accumulation of <sup>68</sup>Ga-DOTA-FA<sub>2</sub> in SKOV3 ovarian tumors (10.18±1.52)%ID/g than that in A549 lung cancer (2.25±0.92)%ID/g.

**Conclusions:** <sup>68</sup>Ga-DOTA-FA<sub>2</sub>, with higher tumor uptake and less undesired accumulation in kidneys than FA monomer, was potential for targeted imaging of FR-positive ovarian tumors.

### Biography

Guoqiang Shao completed his PhD in Nanjing Medical University from 2009 to 2012. He further studied in Shuang Liu's Lab in Purdue University as visiting Scholar from May 2011 to March 2012. He took part in several research project in targeted brachytherapy with biodegradable seeds encapsulating 32P-Chromic phosphate. His interest focused on integrin αvβ3, folate and prostate specific membrane antigen receptor targeted tumor imaging and therapy. Two of his grants were funded by the Natural Science Foundation of China (NSFC) and of Jiangsu Province.

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