Dear Editor,

Angiogenesis is an essential physiological process that involves formation of new blood vessels from the pre-existing ones and is one of the fundamental processes required for normal growth and development [1]. The ability to non-invasively evaluate angiogenesis might provide new insights into cancer biology pathway. This approach might lead to opportunities to more appropriately select patients likely to respond to anti-angiogenic drugs.

Polyamidoamine dendrimers are a member of a versatile, new class of dendritic polymers and are the most well characterized and widely used polymers [2]. In the present study we have utilized them for imaging of a crucial process of angiogenesis in a cancer model of mice. Amongst, several PET radionuclides, there has been a renewed interest in ⁶⁸Ga for many reasons. Gallium-68 is well suited for use as a radiolabel for PET because of its comparatively shorter half-life of 68min (3-4). The emission of two divergent photons per decay allows the construction of three-dimensional images. Furthermore, the advances in generator technology for ⁶⁸Ga production and its favorable chemistry for radiocomplexation have paved the way for emerging applications of ⁶⁸Ga radiopharmaceuticals.

A recent study reported the blood pharmacokinetics of different generations of PAMAM dendrimers (generations 3-6) derivatized with large chelating ligands to facilitate complexation of gadolinium ions for imaging applications [5]. It was observed that the resulted PAMAM gadolinium complexes cleared from the blood circulation in a biphasic manner (fast component-10min; slow component-1h). The rapid clearance of the dendrimers from blood observed in our study was in accordance with previous observations [6-7].

The biodistribution studies of ⁶⁸Ga-DOTA-G₄ PAMAM showed the major uptake at an early time interval of 15min in the kidneys. This confirmed that kidneys are the major excretory organs for DOTA conjugated G₄ PAMAM dendrimers. The radioactivity in kidneys, as compared with other organs was higher initially and declined with time. A study in the recent past also reported a high uptake of indium-111 (¹¹¹In)-DOTA analog-PAMAM dendrimer in rats’ kidneys, immediately after administration of radioactivity [8]. A considerable amount of radioactivity was also recovered from organs which were higher in case of ⁶⁸Ga-DOTA-G₄ PAMAM conjugate. Lung is an important component of the reticulo-endothelial system (RES) and thus is involved in the clearance of macromolecules [9]. Additionally, due to its rich vasculature, lungs are likely targets for the location of intravenously injected dendrimer nanoparticles.

The animal biodistribution data in tumor bearing mice demonstrated that the tumor uptake (at 1h) of ⁶⁸Ga-DOTA-G₄ PAMAM dendrimer was 0.33%. It has been reported that using higher generation PAMAM dendrimers, magnetic resonance imaging (MRI) agents affect the biodistribution patterns in animal tumor models [10]. Animal PET imaging data showed that maximum tumor to background ratio was obtained at 1h post injection of ⁶⁸Ga-DOTA-G₄ PAMAM dendrimer suggesting that the designed nanoprobes could efficiently target tumor tissues and be retained there due to their enhanced permeability and retention (EPR) effect. Dendrimers can achieve passive EPR mediated targeting to a tumor by controlling their size and physicochemical properties. Further, an earlier study reported that branched PAMAM dendrimer showed significantly higher accumulation in ovarian tumor bearing mice than the conventional linear N-(2-hydroxypropyl) methacrylamide (HPMA) copolymer of comparable molecular weight [11]. The use of radiolabeled dendrimers due to their topology, functionality and dimensions has been described as a promising approach for the molecular visualization of tumor angiogenesis. So, the successful radiolabeling of ⁶⁸Ga-DOTA-G₄ PAMAM dendrimers is encouraging as it showed good localization of both the radiolabeled by ⁶⁸Ga and ¹¹¹In products in the tumor.

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Bibliography

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