

⁶⁸Ga-labeled WVP peptide for biological diagnosis of unstable thoracic aortic aneurysm and early dissection by molecular PET imaging

Description

Unstable aortic aneurysm and early dissection attracts much attention of surgeons and physicians as progressing to aortic dissection would threaten patient life [1,2]. Therefore, the early and biological molecular diagnosis becoming more important for forming reasonable therapy strategies and getting good prognosis for patients. It is well known that nuclear medicine hybrid Positron Emission Tomography (PET) with Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) techniques have been proven valuable in molecular functional imaging of many different diseases based on a variety of specific radionuclide probe [3]. Detailed information on the associated findings of the structural and functional biological characteristics is helpful in selecting the best management plan and repeatedly assessing the treatment response [4]. Consequently, adopting a multidisciplinary approach and achieving an earlier and more precise molecular biological diagnosis for unstable aneurysms becomes essential. This approach is essential in identifying high-risk patients who can potentially benefit from timely surgical interventions and the right treatment strategy. By implementing these measures in clinical scenarios, we can enhance the outcomes and optimize the overall care of these patients [5].

It has been demonstrated that progressive endothelial injury occurs before intimal tearing in unstable aortic aneurysm and early stage of dissection, including Endothelial Cell (EC) loss, increased permeability, and subsequent exposure of the sub-endothelial basement membrane [6,7]. In which type IV Collagen (Col-IV), a major component of the sub-endothelial basement membrane, is initially exposed at the sites of EC loss and vessel early and small injuries. Individuals suffering from Thoracic Aortic Aneurysm and Dissection (TAAD) demonstrate a considerable rise in the exposure of aortic collagen within the arterial lumen. This elevation could potentially represent a novel target for molecular imaging and therapeutic approaches [8]. In previous studies, a multimodal Col-IV-DOTA-Gd-rhodamineB targeted Col-IV by peptide (CGGGKPLVWLK) probe was designed to identify the exposed Col-IV in the degenerated aorta for early detection of TAAD *via in vitro* fluorescence assays and *in vivo* Magnetic Resonance Imaging (MRI) and monitor disease progression in TAAD [9]. Researchers reported the development of a multifunctional Nano system, TP-Gd/miRNA-Col-IV, designed for nucleic acid delivery to target exposed Col-IV using the peptide WVP. This innovative therapy aims to treat Thoracic Aortic Aneurysm and Dissection (TAAD) by stabilizing vascular structures and preventing the deterioration of the condition [10]. However, there is a lack of research on radionuclide-based probes for Col-IV imaging, which could offer higher sensitivity in monitoring TAAD progression compared to MRI due to its focus on molecular functional detection and whole-body imaging.

Lingzhou Zhao¹, Feiran Qi^{2*}

¹Department of Nuclear Medicine, Northern Jiangsu People's Hospital, Yangzhou, Jiangsu, China

²Department of Nuclear Medicine, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China;

*Author for correspondence:

Feiran Qi, Department of Nuclear Medicine, Northern Jiangsu Peoples Hospital, Yangzhou, Jiangsu, China, E-mail: lxgf2222@163.com

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Short Communication

As a result, the potential for utilizing this method for a biological diagnosis of TAAD remains to be evaluated. Herein, the Col-IV-targeted WVP (KLWVLPK) peptide was radiolabeled with ^{68}Ga (^{68}Ga -DOTA-WVP) as a novel PET probe for TAAD imaging. This study aims to evaluate the feasibility of ^{68}Ga -DOTA-WVP as a Col-IV-targeted probe for PET/CT imaging of unstable thoracic aneurysms and early TAAD biological diagnosis. As far as our knowledge extends, this represents the first example of developing a WVP-based PET probe for TAAD imaging.

In our present study, the novel probe ^{68}Ga -DOAT-WVP which could combine to Col-IV exposed at the position of early and small injuries of unstable aortic aneurysm and early stage of dissection for PET imaging in animal study. Our study revealed that ^{68}Ga -DOAT-WVP PET/CT imaging is highly effective in extensively detecting unstable aneurysms and facilitating early diagnosis of TAAD in mice (after 2 weeks of BAPN administration). The probe targets Col-IV, which becomes exposed at a small tear site of the intimal aorta. As TAAD progresses, Col-IV exposure gradually increases due to the compensatory repair of the degenerated aorta with BAPN administration, leading to processive TAAD. This increase in Col-IV exposure is consistent with the gradual rise in ^{68}Ga -DOTA-WVP uptake and the intense signal observed on thoracic aortic wall lesions *in vivo* PET/CT imaging. An essential finding is that *in vivo* biodistribution results demonstrated high ^{68}Ga -DOTA-WVP uptake in the heart, while lower uptake was observed in the liver, brain, lung, bone, muscle, and intestine. This biodistribution pattern contributes to achieving excellent imaging quality and reinforces the probe's potential clinical applications in screening high-risk TAAD patients.

Conclusion

In conclusion, we effectively synthesized ^{68}Ga -DOTA-WVP using a straightforward method, achieving high Radiochemical Purity (RCP) and stability. The results demonstrated its capability to

detect the biological characteristics of unstable aneurysms and early TAAD. Since the biological diagnosis of dissection holds significant importance in clinical management, our study proposes a promising approach for screening dissection in high-risk patient populations, monitoring disease progression, and evaluating therapeutic response. Consequently, PET-based whole-body risk assessments can offer valuable guidance to clinicians, particularly surgeons, in patient management and surgical decision-making, ultimately benefiting patient outcomes.

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