



# *In vivo* 4D dual gated cardiac CT

## 4D cardiac-respiratory gated CT of the mouse heart

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### Abstract

*In vivo* cardiac imaging in mouse models has shown to facilitate the study of human cardiovascular diseases, as well as the development of potential treatment strategies<sup>1</sup>. However, due to the small size of the mouse heart as well as the animal's high cardiac and respiratory rates, murine cardiac imaging is rather challenging and requires recognition of both spatial and temporal scales. Despite these challenges, we herein report a feasible method using the U-CT<sup>UHR</sup>  $\mu$ CT system combined with the CT contrast agent ExiTron<sup>TM</sup> nano 12000 to effectively visualize the beating mouse heart *in vivo*.

### Introduction

The introduction of  $\mu$ CT has enabled substantial improvements in the anatomical imaging of small animals since its high spatial resolution enables non-invasive assessment of morphological changes in small structures. Besides its high spatial resolution, further

advantages of this imaging modality include its relatively low cost and short scan time. However, due to its relatively poor soft-tissue contrast, the use of contrast agents is required to improve visualization of these structures. Since clinical CT contrast agents are rapidly cleared from the blood pool of small animals, these agents are not optimal for small animal imaging<sup>2,3</sup>. As a result,  $\mu$ CT studies are generally combined with contrast agents, commonly nanoparticulate in nature, which avoid rapid clearance and persist in the blood pool for a prolonged period of time. ExiTron<sup>TM</sup> nano 12000 (Viscover<sup>TM</sup>, nanoPET Pharma GmbH, Berlin, Germany) is an innovative alkaline earth metal-based nanoparticulate contrast agent specifically formulated for preclinical CT. It has a prolonged blood half-life of approx. 4 h in mice and, due to its high metal content, provides exceptionally high contrast at a low injection volume. Owing to the high cardiac rate (~600 beats/min) and rapid respiratory rate (~300 breaths/min) of small animals, cardiac  $\mu$ CT requires not only the application of blood pool contrast agents but also of reconstruction methods that allow significant reduction of motion artifacts. The U-CT<sup>UHR</sup>  $\mu$ CT system (MILabs B.V., Utrecht, the Netherlands) provides simultaneous cardiac and respiratory motion compensation resulting in superior dual gated images. The device combines high resolution, high speed and low radiation dose making it ideal for routine CT imaging of small animals, especially for imaging of the heart and lungs. Herein, we provide a  $\mu$ CT method using the U-CT<sup>UHR</sup> system with intrinsic cardiac-respiratory gating combined with ExiTron nano 12000 to obtain real-time, high-resolution images of the beating mouse heart *in vivo*.

