In vivo renal imaging in mice via contrast-enhanced CT using a novel polymeric contrast agent

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Introduction & Objective

Computed tomography (CT) is a valuable diagnostic imaging modality because it provides rapid, high-resolution images in a non-invasive and cost-effective manner. Due to the technique's intrinsic poor soft tissue contrast, the delineation of organs generally requires the use of CT contrast agents. In clinical application, the most widely used contrast agents are water-soluble iodinated compounds such as iodixanol. In mice, these contrast agents are cleared via the kidneys at such a rapid rate that kidney CT imaging requires the administration of larger volumes of the contrast agent via infusion, which in turn results in hemodynamic effects. In this study, we develop a CT method using a novel contrast agent that highlights the kidney for a prolonged period of time, enabling efficient kidney imaging after a single injection.

Materials & Methods

CT imaging was performed on healthy CD-1 mice using a nanoSPECT/CT plus (Bioscan/Mediso) before and after administration of the contrast agent, ExiTron™ P (Viscover™, nanoPET Pharma) *via* intravenous injection in the lateral tail vein (100 µL per 25 g mouse). During imaging, the mice were kept anesthetized using 1.5% isoflurane and were maintained at a body temperature of 37˚C.

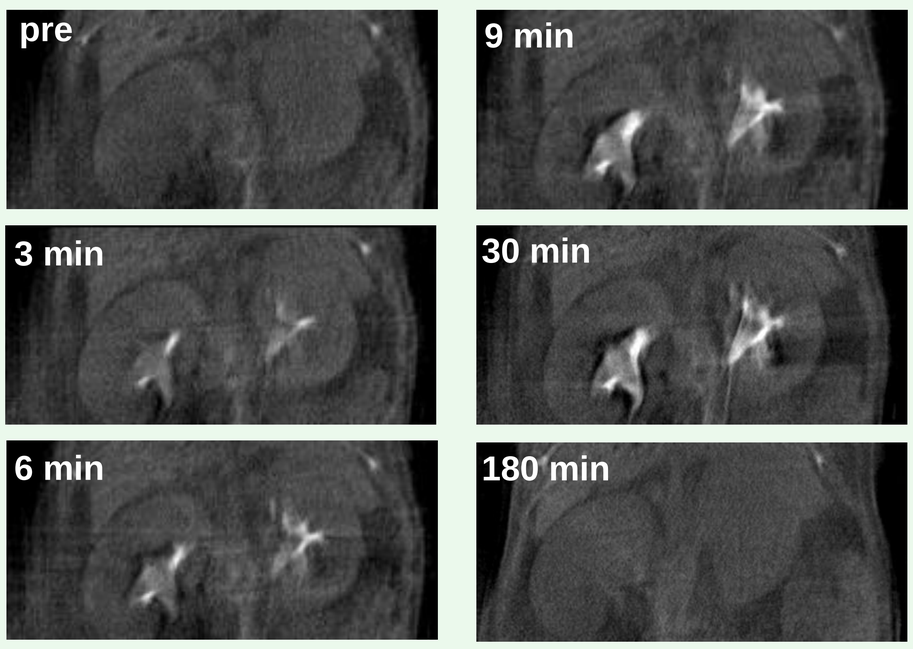
Initially, rapid scans were performed using 55 kVp X-rays, an exposure time of 1000 ms per projection, 240 projections over a 360˚ rotation and a binning factor of 4. Images were obtained at a small field-of-view (FOV) before and every 3 min within the first 9 min after contrast agent injection, so as to observe flow of the agent within the kidney. Thereafter, images were obtained at 30 min, 60 min and 180 min post injection. In a second experiment, higher resolution scans were performed by increasing the X-ray tube voltage to 65 kVp and using 360 projections over a 360˚ rotation. Using these scan parameters, larger FOV images were obtained before and at 20 min and 40 min after contrast agent injection. Data analysis was performed by placing regions of interest (ROIs) in various tissues including the renal pelvis, medulla, cortex, liver, spleen as well as in muscle tissue as control, and plotting the signal intensities *vs.* time.

Results & Discussion

After injection of ExiTron P, significant contrast can be clearly observed in the renal pelvis as well as in the renal calyx (Fig. A). The time-dependent plot of signal intensity in the renal pelvis (Fig. B) illustrates that this signal increases rapidly during the first 9 min after injection and then continues to increase with the maximum enhancement being obtained at ca. 30 min post injection. Signal enhancement in the pelvis persists for approximately 100 min post injection, after which it reaches a baseline value. The image obtained at 180 min post injection is similar to the pre-injection image (Fig. A), denoting that by this timepoint the contrast agent has been practically cleared from the kidney.

Using the higher resolution images (Fig. C), the signal intensities in various tissues within 40 min after contrast agent injection were evaluated (Fig. D). After injection, signal intensity in the pelvis increases steadily until ca. 30 min post injection, after which it starts to decline, as observed in the rapid scans. Significant signal enhancement can also be observed in the medulla and cortex, and these signals both increase steadily during the 40 min time course. In comparison, within the 40 min post injection, the liver and spleen do not show any significant uptake of the contrast agent. Since the rapid scans over 180 min also do not show increased contrast in the liver and spleen, the results imply that the contrast agent is mainly cleared from the body via renal excretion and not via the hepatic route. As expected, the muscle tissue acting as control does not show uptake of the contrast agent.

A



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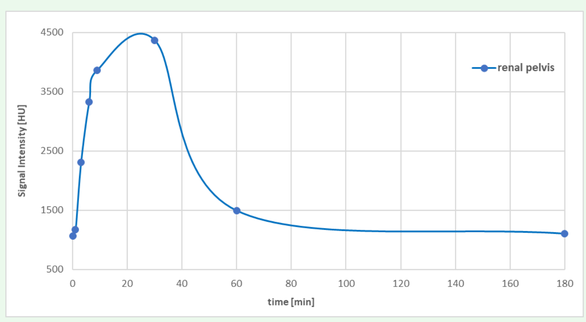

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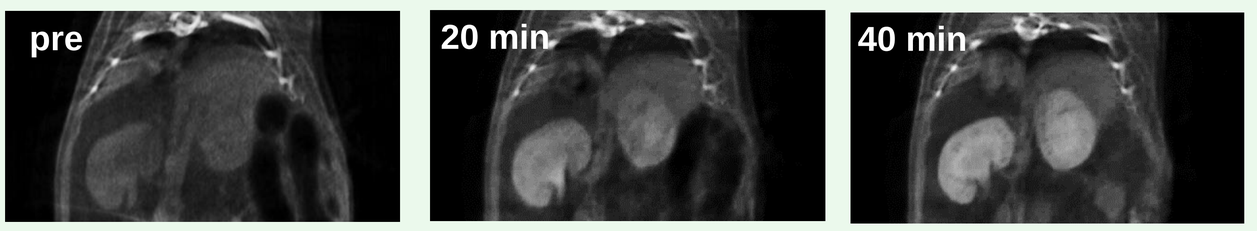

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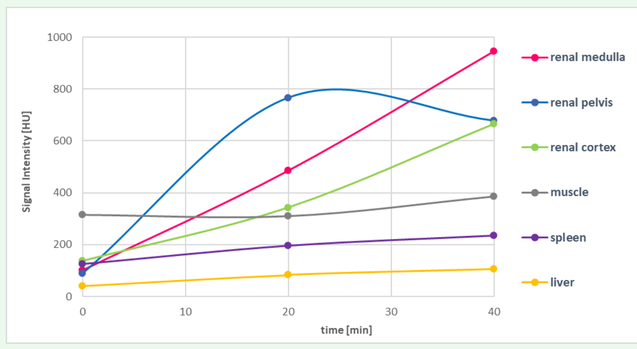

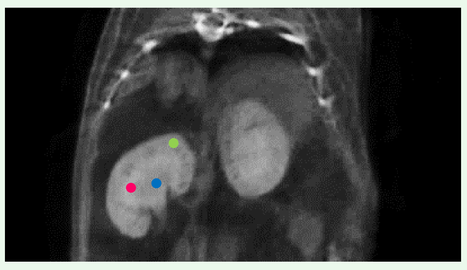

A: *Coronal CT images of the mouse thorax obtained before and at different time points after intravenous injection of ExiTron P.*
B: *Plot of signal intensity (SI, in Hounsfield Units) of the renal pelvis over a period of 180 min post injection.*
C: *Higher resolution coronal CT images of the mouse thorax obtained before and at 20 min and 40 min after administration of ExiTron P. The contrast agent clearly highlights the kidney structure enabling distinction between the pelvis, medulla and cortex.*
D: *Plot of signal intensity (SI, in Hounsfield Units) at different ROI locations over a period of 40 min post injection.*

Conclusion

In this study we report on a CT method involving the use of the novel iodine-containing polymeric agent, ExiTron P, that enables *in vivo* visualization of the kidneys in small animals with a high contrast efficiency as well as optimal biocompatibility. By providing contrast in the kidneys that persists for a relatively long period, the contrast agent facilitates studies of kidney structure and function. Since the agent is completely eliminated from the body via renal excretion within 3 hours, it can be utilized in longitudinal imaging studies where multiple injections are required.