

# Dynamic Perfusion Study of Mouse Pancreas with an Intravascular Contrast Agent

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## Introduction

Insulin secretions by beta-cells in the pancreatic islets are critical in maintaining blood glucose homeostasis. Beta-cell failure eventually leads to hyperglycemia, resulting in diabetes. The pancreatic islet is highly vascularized, receiving about 10-20% of the pancreatic blood flow. Thus detection of blood flow and volume to the islets are indicators of their viability and function. A popular method for the measurement of perfusion is dynamic contrast-enhanced MRI (DCE-MRI), in which a T1-agent, usually Gd-chelated, is infused into the blood stream causing signal increase in perfused tissues<sup>1</sup>. However, commonly used low-molecular-weight contrast agents diffuse out of the blood vessels into the tissue, giving false positive enhancement. This would render quantification difficult. The use of a high-molecular-weight intravascular contrast agent could eliminate this problem. Vasovist<sup>TM</sup> (Gadofosveset trisodium)<sup>2</sup> is negatively-charged and hydrophilic, thus it does not diffuse easily across lipid bilayer cell membranes, achieving a long vascular half-life of at least 1h. It has 6 to 10 times higher T1-relaxivity than Gd-DTPA<sup>3</sup>, offering larger signal enhancement. Furthermore, pancreatic islets in rodents are especially challenging to image because of their scattered distribution throughout the acinar tissue of the pancreas. This is exacerbated by the low contrast of the pancreas from fast gradient-echo imaging and respiratory motion artifacts. In this study we aim at precisely locating the rodent's pancreas and study the contrast kinetics of Vasovist<sup>TM</sup>.

## Materials and Methods

Three male wild-type mice were anaesthetised with 1.5% Isoflurane and ventilated with 1L of air/oxygen mixture, in accordance with local IACUC. MRI with respiratory monitoring was implemented at 9.4T. Localization of the pancreas was accomplished first by multi-slice gradient echo imaging to locate the spleen, and then followed by T2-weighted fast-spin-echo sequence to identify the pancreas.

**DCE-MRI:** Dynamic T1-weighted FSE scan was started with respiration trigger. Echo-train length was 8, giving a temporal resolution of 13secs per volume. MR parameters were: TR = 0.81sec, TE = 11.8ms, Matrix = 128x128, FOV = 23 x 16mm, slice thickness = 0.5mm. A 30ul (1ml/kg) bolus of Vasovist<sup>TM</sup> was injected intravenously via a catheter after 3mins of baseline scan.

**Results:** Figure 1 displays the localization steps to identify the pancreas. The pancreas appears below both kidneys (K) with a significant section attached to the spleen (depicted in transverse slices). Figure 2 tracks the signal intensity changes in the pancreas and kidney across a 32mins dynamic scan, with region-of-interest (ROI) analysis. Pancreas enhancement peaks at about 6mins after bolus injection (time-to-peak, TTP). Observe that there is no false positive enhancement in the pancreas (i.e. no gradual increasing enhancement), corroborating Vasovist's intravascularity. Its long lifetime is apparent in the prolonged high signal intensity. Kidney enhancement though is constantly high due to clearance by glomerular filtration.

**Conclusion:** We have shown that the pancreas of a rodent could be robustly identified with MRI in 2 quick scans, thus facilitating measurements of pancreatic blood flow and volume. DCE-MRI with an intravascular contrast agent is a potentially accurate tool to quantify blood flow and volume to the mouse pancreas, although more work is needed to provide complete quantification. Problems might arise with the potential ways of measuring a proper arterial input function. Time-to-peak measurements offer a quick qualitative indication of pancreatic blood flow. The long lifetime of the intravascular agent could be further capitalized to study the hemodynamic response to a physiological stimulus, like glucose infusion. This could further shed light on glucose metabolism.

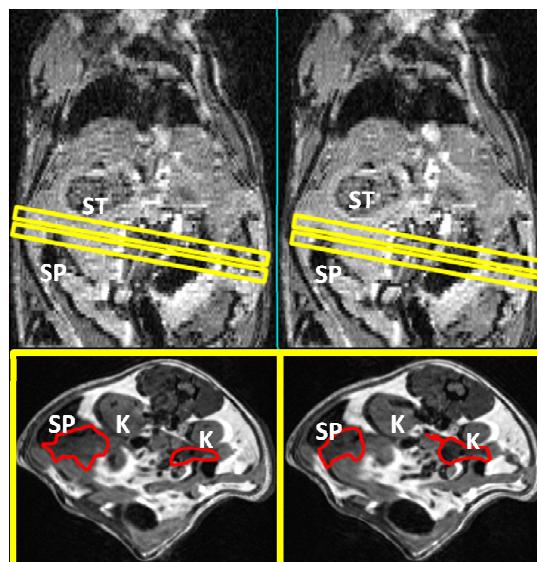


Figure 1: Mouse pancreas localization scheme.

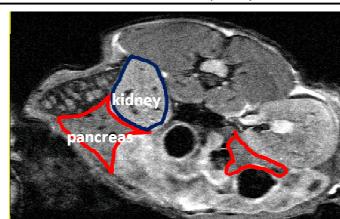
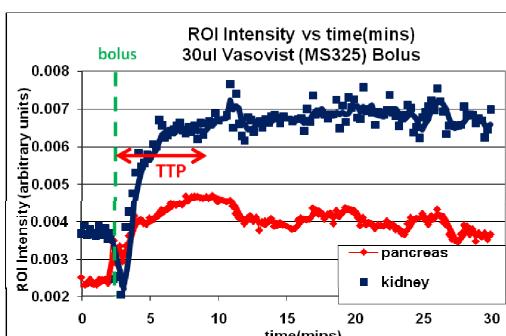


Figure 2: ROI analysis of DCE-MRI with 30ul bolus injection of MS-325.

## References

- 1) P.S. Tofts et al. JMRI 10:903-907 (1999)
- 2) Vasovist<sup>TM</sup>, EPIX Pharmaceuticals, Cambridge, MA and Schering AG, Berlin, Germany.
- 3) Lauffer et al. Radiology 207: 529 – 538 (1998).